aqueous acetone was sealed in a Carius combustion tube and heated to the specified temperature for the desired amount of time. The tube was then cooled, the acetone removed with a stream of N_2, and the resulting solution taken up in 25 mL of CH_2Cl_2. This was washed with 5% $NaHCO_3$ (2 × 30 mL) and water (30 mL), dried over Na_2SO_4, and evaporated to dryness. The resulting products were then subjected to HPLC analysis.

B. Benzene Solution. A mixture of ca. 100 mg of the compound and 10 mg of *p*-toluenesulfonic acid monohydrate in 25 mL of dry C_6H_6 was heated to reflux for 2 days. The reaction mixture was cooled and diluted with 20 mL of Et_2O, washed with 5% $NaHCO_3$ (2 × 20 mL) and water (20 mL), dried over Na_2SO_4, and evaporated to dryness. The resulting product was then subjected to HPLC analysis.

Acknowledgment. This work was supported by the National Cancer Institute (Grant CA25436). We thank Drs. Elie Abushanab and Steven Fesik for their help and cooperation concerning the ^{13}C NMR spectra and Jerome Munic for the HPLC assays.

Registry No. 7, 51020-64-5; 8, 51020-65-6; 9, 66510-94-9; 10, 41398-33-8; 11, 86954-81-6; 12, 87036-91-7; 13, 86954-82-7; 14, 87036-92-8.

Quinolizidine Alkaloid Synthesis via the Intramolecular Imino Diels–Alder Reaction. *epi*-Lupinine and Cryptopleurine

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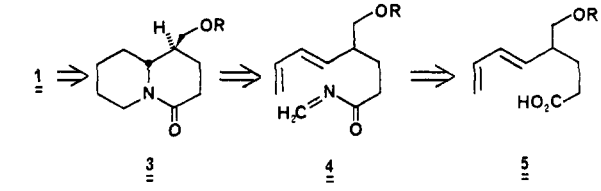
Received April 5, 1983

A totally stereoselective total synthesis of *epi*-lupinine (1) has been developed that starts with methyl sorbate (6). Alkylation of **6** with bromide **8** gave diene **10**, which was elaborated into the imino Diels–Alder precursor **17**. Thermolysis of **17** provided exclusively bicyclic lactam **18**. Acyl imine **4** (R = CH_2Ph) has been postulated as an intermediate in this cycloaddition. The stereoselectivity of the reaction is rationalized on the basis of a transition state, **22**, which has (1) a planar, *s*-cis acyl imine moiety, (2) a carbonyl group endo to the diene, and (3) a quasi-boat bridging-chain conformation. Reduction of **18** afforded racemic *epi*-lupinine. Cryptopleurine (**2**) was prepared by starting from the readily available phenanthrene aldehyde **33**. Cyclization of methylol acetate **37** gave lactam **38**. It was demonstrated that only the *E* form of **37** cyclizes via (*E*)-acyl imine **39**. The *Z* isomer **40** did not lead to a Diels–Alder product. Hydride reduction of lactam **38** gave racemic cryptopleurine.

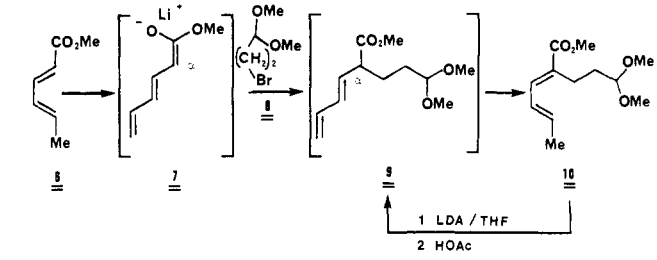
Recent papers from these laboratories have shown the utility of intramolecular Diels–Alder cycloadditions of *N*-acyl imino dienophiles in construction of annulated tetrahydropyridines.[1-3] Previous work has dealt primarily with applications of this methodology to synthesis of several types of indolizidine alkaloids. To date, we have reported total syntheses of δ-coniceine,[1a,d] tylophorine,[1a,d] elaeokanine A and B[1b,d] and slaframine.[1f] In addition, studies have been carried out to probe various stereochemical facets of the process, particularly regarding the relationship of imine substitution and geometry to product relative configuration. One other stereochemical feature investigated in a few cyclizations which formed 6/5 fused rings was the configurational outcome of substituents in the chain-bridging diene and dienophile.[1b,f] In general, Diels–Alder reactions which gave 6/5 systems showed excellent stereoselectivity when carboxyl-substituted *N*-acyl imines[1b,e,4] were used but little stereocontrol with respect to bridge substituents.

As an extension of this work, we wished to determine whether intramolecular imino Diels–Alder chemistry could also be used in synthesis of quinolizidines and to further explore stereochemical features of the reaction in such systems. Toward these ends, we set out to design total syntheses of the quinolizidine alkaloids *epi*-lupinine (**1**)[5] and cryptopleurine (**2**).[6]

Scheme I



Scheme II



In the case of **1**, it was our hope to use an intramolecular imino Diels–Alder strategy to simultaneously generate the quinolizidine ring system and establish the alkaloid relative

(1) (a) Weinreb, S. M.; Khatri, N. A.; Shringarpure, J. *J. Am. Chem. Soc.* **1979**, *101*, 5073. (b) Nader, B.; Franck, R. W.; Weinreb, S. M. *ibid.* **1980**, *102*, 1153. (c) Schmitthenner, H. F.; Weinreb, S. M. *J. Org. Chem.* **1980**, *45*, 3372. (d) Khatri, N. A.; Schmitthenner, H. F.; Shringarpure, J.; Weinreb, S. M. *J. Am. Chem. Soc.* **1981**, *103*, 6387. (e) Nader, B.; Bailey, T. R.; Franck, R. W.; Weinreb, S. M. *ibid.* **1981**, *103*, 7573. (f) Gobao, R. A.; Bremmer, M. L.; Weinreb, S.M. *ibid.* **1982**, *104*, 7065.

(2) A preliminary account of a portion of this work has appeared: Bremmer, M. L.; Weinreb, S. M. *Tetrahedron Lett.* **1983**, *24*, 261.

(3) Reviews of Diels–Alder reactions with imino dienophiles: (a) Lora-Tomayo, M. In "1,4-Cycloaddition Reactions"; Hamer, J., Ed.; Academic Press: New York, 1967; pp 127-142. (b) Weinreb, S. M.; Levin, J. I. *Heterocycles* **1979**, *12*, 949. (c) Weinreb, S. M.; Staib, R. R. *Tetrahedron* **1982**, *38*, 3087.

(4) Bailey, T. R. Ph.D. Thesis, The Pennsylvania State University, University Park, PA, 1983.

(5) For recent syntheses of lupinine and *epi*-lupinine see: (a) Iwashita, T.; Kusumi, T.; Kakisawa, H. *J. Org. Chem.* **1982**, *47*, 230. (b) Tufariello, J. J.; Tegeler, J. J. *Tetrahedron Lett.* **1976**, 4037. (c) Okita, M.; Wakamatsu, T.; Ban, Y. *Heterocycles* **1983**, *20*, 401.

(6) For a review see: Bick, I. R. C.; Sinchai, W. In "The Alkaloids"; Manske, R. H. F.; Rodrigo, R. G. A., Eds.; Academic Press: New York, 1981; Vol XIX, pp 193-218.

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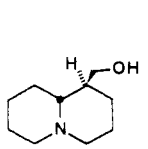
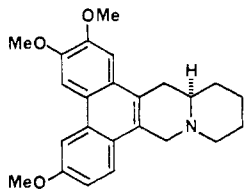


1

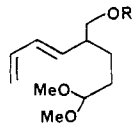


2

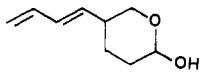
configuration as shown in Scheme I.

Thus, it was first necessary to find a method for synthesis of the requisite diene acid **5**. Stevens et al. reported that methyl sorbate (**6**) could be deprotonated with LDA to give ester enolate **7** (Scheme II), which upon reprotonation at the α-carbon gave the deconjugated diene ester.[7] We anticipated that if **7** could be alkylated at the α-position with a functionalized three-carbon fragment, we would have a very direct entry to diene **5**. To our knowledge, this interesting enolate had not previously been alkylated. In fact, **7** could be alkylated with bromo acetal **8**, but only if the reaction was run at high concentration at room temperature. Under these conditions the product was not the desired diene **9** but the fully conjugated compound **10** (44% yield). However, sorbate derivative **10** could be readily deconjugated by deprotonation with LDA, followed by kinetic α-protonation with acetic acid to give diene **9** (92%). The *E* geometry was assigned to the disubstituted double bond of **9** on the basis of the presence of an infrared absorption at 955 cm^{-1} and the absence of any peaks near 700 cm^{-1}.

Lithium aluminum hydride reduction of **9** gave the corresponding primary alcohol **11** (68%). Initially, the

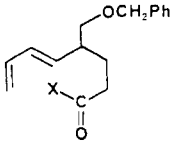


11 R = H
12 R = CH_2OMe
13 R = CH_2Ph

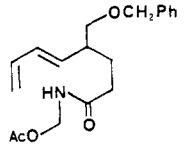


14

alcohol group of **11** was protected as the methoxymethyl derivative **12**. However, all attempts to selectively hydrolyze the dimethyl acetal function of **12** were unsuccessful, and only lactol **14** could be isolated from these reactions. Alcohol **11** was therefore protected instead as the benzyl ether **13** ($PhCH_2Br$, KH, THF; 86%). Acid hydrolysis of **13** afforded the corresponding aldehyde, which without isolation was oxidized with Jones reagent to produce the carboxylic acid **15** (85%). This compound

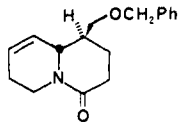


15 X = OH
16 X = NH_2



17

was converted to the primary amide **16** via the mixed anhydride with ethyl chloroformate (97%). Amide **16** was subsequently treated with paraformaldehyde and cesium carbonate in THF,[1f] and the crude product was acetylated with acetic anhydride/pyridine to yield the methylol acetate **17** (66%). We have routinely used this sort of functionality as an imino dienophile precursor.[1] When compound **17** was heated in refluxing *o*-dichlorobenzene for 2 h, a *single* bicyclic lactam was produced in 93% yield. This compound was assigned structure **18** on the basis of

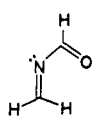


18

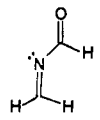
its eventual conversion to *epi*-lupinine (**1**, vide infra). We have been unable to detect any compound with the lupinine stereochemistry.

Methylol acetate **17** undoubtedly loses the elements of acetic acid upon being heated to form the intermediate unstable *N*-acyl imine **4** (Scheme I, R = CH_2Ph). Recently, Ripoll and co-workers[8] have actually isolated and characterized *N*-acylmethanimines of this type at low temperatures and have shown their involvement in imino Diels–Alder reactions. However, the general instability of acyl imines has to date precluded detailed studies of structure and conformation in these molecules.

Houk and Paddon-Row have calculated that in the simple *N*-formyl imine series the *s*-cis conformer **19** is



19



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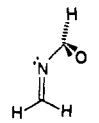


21

about 3 kcal/mol more stable than the *s*-trans form **20** and approximately 4 kcal/mol more stable than the nonplanar conformer **21**.[9,10] In addition, their calculations show that the nonplanar acyl imine should be considerably less reactive as a dienophile than either **19** or **20**. Interestingly, these conclusions are in line with the reported ability of acyl imines to act as *dienes* in 1,4-cycloaddition reactions.[10]

Inspection of a molecular model of acyl imine **4** indicates that several reasonable Diels–Alder transition states are available possessing the *s*-cis conformation and which have the carbonyl group either exo or endo to the diene moiety. Since it now seems quite clear that there is a strong driving force for the carbonyl group on nitrogen in N-acyl imines to be endo in both inter- and intramolecular Diels–Alder cycloadditions,[1,3,11] we can confidently eliminate exo transition states from consideration in explaining formation of **18**. It should also be noted that bridging restraints in **4** preclude any unstrained planar *s-trans*-acyl imine transition states (cf. **20**), although some nonplanar forms are possible (cf. **21**).

With these considerations in mind, it would appear that Diels–Alder cyclization of **4** should occur via transition state **22** and/or **23**. Both transition states contain an *s-cis*-acyl imine with the carbonyl group endo, and both have the large (benzyloxy)methyl group in an equatorial position. However, only transition state **22** can lead to the observed cycloadduct **18**, whereas **23** would give the lupinine stereochemistry shown in **24**, which was not detected. At first glance, one might anticipate that **23** is of lower energy than **22**. In the former transition state the

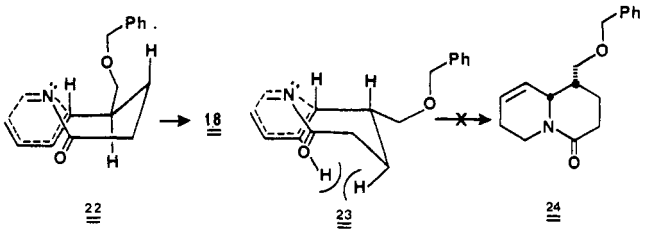
(7) Stevens, R. V.; Cherpeck, R. E.; Harrison, B. L.; Lai, J.; Lapalme, R. *J. Am. Chem. Soc.* **1976**, *98*, 6317.

(8) Lasne, M. C.; Ripoll, J. L.; Thuiller, A. *J. Chem. Res. Synop.* **1982**, 214.

(9) Houk, K. N.; Paddon-Row, M. N., unpublished results.

(10) (a) Ben-Ishai, D.; Hirsch, S. *Tetrahedron. Lett.* **1983**, *24*, 955. Schmidt, R. R. *Synthesis* **1972**, 333. (b) For recent similar calculations which give a somewhat different prediction see: Wurthwein, E. U.; Kupfer, R.; Kaliba, C. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 252.

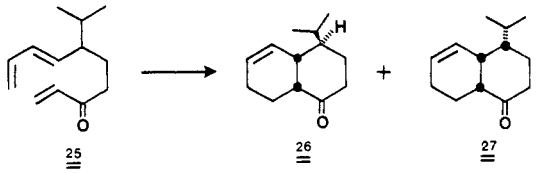
(11) There is as yet no good theoretical reationale for these experimental observations.



22 18 23 24

bridging chain is a quasi-chair, vs. the latter which has this chain in a quasi-boat conformation. However, transition state **23** is destabilized by a nonbonded flagpole type of interaction between a diene vinyl hydrogen and one in the bridging chain as shown. In **22**, the only such flagpole interaction is between the nitrogen lone pair and a bridge-carbon proton.

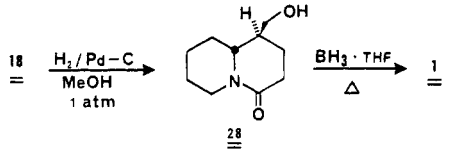
Taber has recently used a similar argument to rationalize the cyclization of **25** to a 9:1 mixture of **26** and **27**, re-



25 26 27

spectively.[12] Adduct **26** is derived from a transition state like **22** (N: = C—H), and product **27** is formed from one similar to **23**. The increased stereoselectivity in our imino case is probably due to the lower energy of the nitrogen lone pair/hydrogen interaction in **22** compared to a corresponding hydrogen/hydrogen interaction.[13] It is difficult to believe that in either of the above cyclizations the high stereoselectivity is due exclusively to the aforementioned nonbonded interactions. Selectivity here may result from the summation of several relatively small, subtle interactions in the transition states.[14]

Diels–Alder adduct **18** was converted into *epi*-lupinine (**1**) in two steps. Catalytic hydrogenation of **18** both sat-

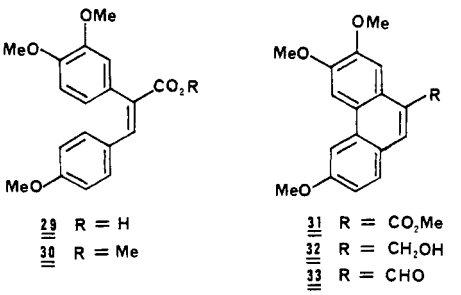


18 H_2/Pd–C, MeOH, 1 atm; $BH_3 \cdot THF$, Δ → 1

28

urated the double bond and removed the *O*-benzyl protecting group to give bicyclic lactam alcohol **28** (94%). Borane reduction of the carbonyl group of **28** provided racemic *epi*-lupinine (57%) which had spectra identical with those of an authentic sample.[15]

The synthesis of cryptopleurine (**2**) began with homoveratric acid and *p*-anisaldehyde which were condensed with acetic anhydride/triethylamine to afford stilbene acid **29** (58%).[1d] This compound was esterified with methanolic HCl to yield **30** (44%) which upon vanadium oxytrifluoride promoted cyclization[16] provided phenanthrene ester **31** (100%).[17] Lithium aluminum hydride reduction of **31** gave alcohol **32** (96%) which was oxidized to aldehyde

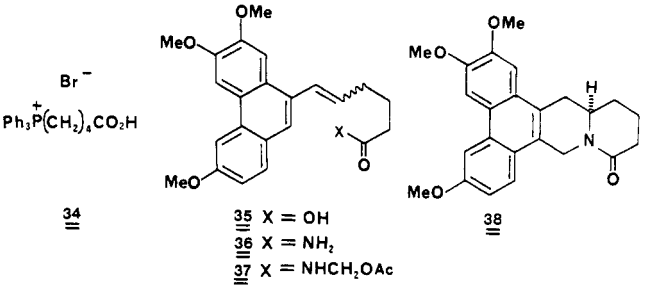


29 R = H
30 R = Me

31 R = CO_2Me
32 R = CH_2OH
33 R = CHO

33 with pyridinium chlorochromate[18] in methylene chloride (85%).

Wittig reaction of aldehyde **33** with the dianion derived from phosphonium salt **34**[19] gave acid **35** as an inseparable



34

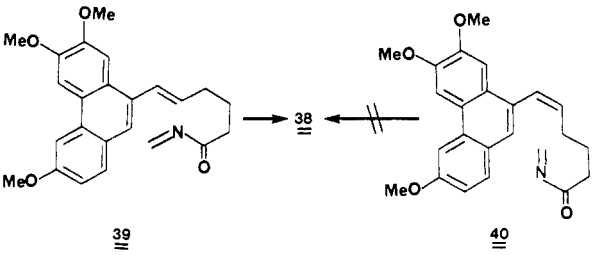
35 X = OH
36 X = NH_2
37 X = $NHCH_2OAc$

38

3:1 mixture of *E* and *Z* isomers in 60% yield. This acid was transformed to the amide **36** by using standard methodology, and our cesium carbonate/paraformaldehyde procedure was again used to convert **36** to methylol acetate **37** (46% from acid **35**).

When a 3:1 mixture of *E*/*Z* isomers of **37** was heated for 70 min in *o*-dichlorobenzene at 210 °C, pentacyclic lactam **38** was isolated in 66% yield. In addition, we recovered 30% of amide **36** which was found to be very highly enriched in the *Z* double bond isomer. Methylol acetate **37** prepared from this recovered *Z* isomer gave no lactam **38** on attempted thermal cyclization.

From molecular models, it is clear that the (*E*)-acyl imine **39** can readily attain a Diels–Alder transition state



39 38 40

having a *s*-cis conformation and the carbonyl group endo to the diene system. On the other hand, (*Z*)-acyl imine **40** can only cyclize via a transition state in which the acyl imine conformation is nonplanar as in **21**. Thus, these results are also consistent with the aforementioned calculations.

To complete the alkaloid synthesis, we reduced lactam **38** with lithium aluminum hydride to afford racemic cryptopleurine (**2**), identical with an authentic sample.[20]

Experimental Section

Melting points were taken on a Thomas-Hoover Uni-melt capillary melting point apparatus equipped with a calibrated

(12) Taber, D. F.; Gunn, B. P. *J. Am. Chem. Soc.* **1979**, *101*, 3992. See also: Wilson, S. F.; Mao, D. T. *Ibid.* **1978**, *100*, 6289.
(13) Riddell, F. G. "The Conformational Analysis of Heterocyclic Compounds"; Academic Press: New York, 1980.
(14) See for example: Boeckman, R. K.; Ku, S. S. *J. Am. Chem. Soc.* **1982**, *104*, 1033.
(15) We are grateful to Professor J. J. Tufariello for spectra of *epi*-lupinine and lupinine.
(16) Liepa, A. J.; Summons, R. E. *J. Chem. Soc., Chem. Commun.* **1977**, 826.
(17) Govindachari, T. R.; Ragade, I. S.; Viswanathan, N. *J. Chem. Soc.* **1962**, 1357.
(18) Corey, E. J.; Suggs, J. W. *Tetrahedron Lett.* **1975**, 2647.
(19) Corey, E. J.; Weinshenker, N. M.; Schaaf, T. K.; Huber, W. *J. Am. Chem. Soc.* **1969**, *91*, 5675. See also: Maryanoff, B. E.; Reitz, A. B.; Duhl-Emsweiler, B. A. *Tetrahedron Lett.* **1983**, *24*, 2477.
(20) We thank Dr. John Douros of NCI for a sample of natural cryptopleurine.

thermometer. Infrared spectra were recorded on a Perkin-Elmer Model 197 spectrophotometer. Proton magnetic resonance spectra (60 MHz) were recorded on a Varian EM-360 NMR spectrometer. ^{1}H NMR spectra at 200 MHz were obtained on a Bruker WP-200 Fourier transform spectrometer and at 360 MHz on a Bruker WM-360 instrument. Chemical shifts are reported in δ units with tetramethylsilane as an internal standard. High- and low-resolution mass spectra were recorded by electron impact on an Associated Electrical Industries, Ltd., MS-902 double-focusing mass spectrometer. Chemical-ionization mass spectra were determined on a Finnigan 3200 quadrupole instrument using methane as a carrier gas.

Anhydrous tetrahydrofuran was freshly distilled from sodium benzophenone ketyl. *o*-Dichlorobenzene and toluene were distilled from calcium hydride. Diisopropylamine was distilled from calcium hydride and stored over 4-Å molecular sieves. Methanol was distilled from $Mg(OCH_3)_2$.

Analytical and preparative thin-layer chromatography were performed on silica gel 60 PF_{254} (EM Reagents). Visualization was effectd by basic aqueous permanganate spray. Liquid column chromatography was carried out on 70–230-mesh silica gel 60 (EM Reagents) or 80–200-mesh basic alumina (Brockman Activity 1, Fisher) as the stationary phase.

Synthesis of Acetal Ester 10 by Alkylation of Methyl Sorbate. To a solution of diisopropylamine (10 mL, 0.071 mol) in THF (80 mL) at −40 °C was added 41.0 mL (0.059 mol) of *n*-butyllithium (1.46 M in hexane). The solution was cooled to −78 °C, and HMPA (10.0 mL) was added slowly. The mixture was stirred for 0.5 h and methyl sorbate (**6**; 6.30 g, 0.050 mol) in THF (15 mL) was added over a period of 20 min. The resulting dark red solution was stirred for 1 h at −78 °C and was added to 25.4 g (0.139 mol) of neat β-bromopropionaldehyde dimethyl acetal at 0 °C. The dark red solution was stirred for 4 h at room temperature, was poured into 200 mL of 5% acetic acid, and was extracted with hexane. The organic extract was washed with brine, dried over Na_2SO_4, and evaporated in vacuo. The oily residue was purified by column chromatography on silica gel (500 g), eluting with hexane/ethyl acetate (9:1) to give acetal ester **10**: 4.99 g (44%); oil; IR (film) 3040, 2950, 2840, 1710, 1640, 1610, 1440, 1380, 1300, 1240, 1220, 1195, 1170, 1130, 1070, 975, 920, 880, 840, 800, 765 cm^{-1}; ^{1}H NMR (360 MHz, $CDCl_3$) δ 7.15 (d, 1 H, J = 11 Hz), 6.4 (m, 1 H), 6.1 (m, 1 H), 4.33 (t, 1 H, J = 6 Hz), 3.73 (s, 3 H), 3.30 (s, 6 H), 2.43 (t, 2 H, J = 8 Hz), 1.85 (m, 3 H), 1.72 (m, 2 H); mass spectrum (CI), m/z 229 (M + H$^+$).

Deconjugation of Diene Ester 10. To a solution of diisopropylamine (4.52 mL, 0.032 mol) in dry THF (50 mL) at −40 °C was added 19 mL (0.029 mol) of *n*-butyllithium (1.55 M in hexane). The solution was cooled to −78 °C, and HMPA (5.1 mL, 0.028 mol) was added slowly. The solution was stirred for 0.5 h, and diene ester **10** (3.36 g, 0.015 mol) in THF (10 mL) was added dropwise over a period of 30 min. The dark red solution was stirred for 3 h at −78 °C and poured into 150 mL of 2% aqueous acetic acid, and the mixture was extracted with hexane. The extract was dried over Na_2SO_4 and evaporated in vacuo. The residue was purified by column chromatography on silica gel (200 g), eluting with hexane–ethyl acetate (9:1) to give the deconjugated diene ester **9**: 3.09 g (92%); viscous oil; IR (film) 3100, 2960, 2840, 1740, 1650, 1605, 1440, 1260, 1200, 1165, 1135, 1070, 1005, 975, 955, 910 cm^{-1}; ^{1}H NMR (360 MHz, $CDCl_3$) δ 6.32 (m, 1 H), 6.14 (m, 1 H), 5.66(m, 1 H), 5.09 (m, 2 H), 4.35 (t, 1 H, J = 5 Hz), 3.69 (s, 3 H), 3.30 (s, 6 H), 3.05 (t, 1 H, J = 7 Hz), 1.90–1.60 (m, 4 H); mass spectrum, m/z (relative intensity) 228 (M$^+$, 7.5), 197 (14.9), 165 (22.1), 137 (16.8), 105 (20.5), 75 (100.0); high-resolution mass spectrum, calcd for $C_{12}H_{20}O_4$ m/z 228.1361, found m/z 228.1377.

Preparation of Diene Alcohol 11. Acetal ester **9** (2.140 g, 9.38 mmol) was dissolved in ether (100 mL), and the solution was cooled to 0 °C. Lithium aluminum hydride (0.712 g, 18.8 mmol) was added slowly, and the reaction was monitored by TLC (ethyl acetate–hexane, 1:1) until all of the ester was consumed (0.5 h). Ethyl acetate (20 mL) was added slowly, followed by water (30 mL), and the mixture was extracted with ethyl acetate. The organic layer was dried over Na_2SO_4 and evaporated in vacuo. The residue was purified by column chromatography on 100 g of silica gel (ethyl acetate–hexane, 1:1) to give alcohol **11**: 1.27 g (68%); oil; IR (film) 3700–3100, 3090, 2950, 2840, 1645, 1600, 1450, 1395, 1125, 1060, 1005, 955, 900 cm^{-1}; ^{1}H NMR (360 MHz, $CDCl_3$) δ 6.32 (m, 1 H), 6.16 (m, 1 H), 5.47 (m, 1 H), 5.10 (dd, 1 H, J = 15, 1 Hz), 5.04 (dd, 1 H, J = 9, 1 Hz), 4.34 (t, 1 H, J = 6 Hz), 3.60 (m, 1 H), 3.46 (m, 1 H), 3.31 (s, 3 H), 3.30 (s, 3 H), 2.25 (m, 1 H), 1.80–1.25 (m, 5 H); mass spectrum, m/z (relative intensity) 200 (M$^+$, 0.4), 169 (6.4), 136 (15.2), 80 (44.4), 75 (58.7), 43 (68.6), 28 (100); high-resolution mass spectrum, calcd for $C_{11}H_{20}O_3$ m/z 200.1409, found m/z 200.1417.

Preparation of Benzyl Ether 13. To a solution of diene alcohol **11** (1.27 g, 6.35 mmol) and benzyl bromide (1.44 g, 8.4 mmol) in THF (80 mL) at 0 °C was slowly added 4 mL of KH (35% dispersion in mineral oil). The reaction was monitored by TLC (10% ethyl acetate–hexane) until the starting material was consumed (0.5 h). Methanol (5 mL) was added slowly, followed by water (50 mL), and the mixture was extracted with hexane. The organic extract was dried over Na_2SO_4 and evaporated in vacuo. The residue was purified by column chromatography on 100 g of silica gel, eluting with ethyl acetate–hexane (1:9) to give the benzyl ether **13**: 1.59 g (86%); clear oil; IR (film) 31008, 3045, 2950, 2900, 2860, 2840, 1650, 1605, 1455, 1390, 1365, 1200, 1130, 1080, 1010, 960, 900, 740, 700 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.32 (s, 5 H), 6.41–6.02 (m, 2 H), 5.60 (m, 1 H), 5.12 (dd, 1 H, J = 15, 1 Hz), 5.00 (dd, 1 H, J = 8, 1 Hz), 4.50 (s, 2 H), 4.36 (t, 1 H, J = 5 Hz), 3.39 (d, 2 H, J = 6 Hz), 3.29 (s, 6 H), 2.40–2.24 (m, 1 H), 1.81–1.26 (m, 4 H); mass spectrum, m/z (relative intensity) 290 (M$^+$, 0.1), 167 (13.3), 152 (7.4), 137 (16.3), 121 (20.6), 105 (25.0), 91 (100.0); high-resolution mass spectrum, calcd for $C_{18}H_{26}O_3$ m/z 290.1882, found m/z 290.1893.

Conversion of Ether Acetal 13 to Acid 15. To a solution of acetal **13** (0.766 g, 2.64 mmol) in acetone (50 mL) was added 20 mL of 5% HCl. The solution was stirred at room temperature for 5 min. Brine was added, and the mixture was extracted with hexane. The organic phase was dried over Na_2SO_4 and evaporated in vacuo. The crude aldehyde was dissolved in 50 mL of acetone and cooled to 0 °C. Jones reagent (4 mL) was added dropwise, and the resulting mixture was stirred for 15 min. Isopropyl alcohol (20 mL) and water (50 mL) were added, and the mixture was extracted with ethyl acetate. The organic layer was dried over Na_2SO_4 and evaporated in vacuo. The crude acid was purified by column chromatography on 100 g of silica gel, eluting with ethyl acetate/hexane (1:1) to give acid **15**: 0.766 g (85%); colorless oil; IR (film) 3700–2400, 3100, 3050, 2940, 2860, 1710, 1605, 1455, 1410, 1360, 1105, 1005, 905, 740, 700 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.32 (s, 5 H), 6.39–6.04 (m, 2 H), 5.5 (m, 1 H), 5.10 (dd, 1 H, J = 17, 1 Hz), 4.99 (dd, 1 H, J = 10, 1 Hz), 4.50 (s, 2 H), 3.40 (m, 2 H), 2.47–1.53 (m, 5 H); mass spectrum, m/z (relative intensity) 260 (M$^+$, 0.2), 154 (6.2), 121 (34.4), 91 (100.0); high-resolution mass spectrum, calcd for $C_{16}H_{20}O_3$ m/z 260.1412, found m/z 260.1409.

Synthesis of Amide 16. A solution of acid **15** (0.160 g, 0.615 mmol) in dry THF (15 mL) was cooled to 0 °C and was treated with pyridine (0.5 mL) and ethyl chloroformate (0.5 mL). The mixture was stirred under nitrogen at 0 °C for 0.5 h, and concentrated ammonia (2 mL) and water (10 mL) were added. The mixture was extracted with ethyl acetate. The organic phase was dried over Na_2SO_4 and evaporated in vacuo. The residue was purified by preparative TLC on silica gel (hexane–ethyl acetate, 1:1) to give amide **16**: 0.155 g (97%); waxy solid; IR ($CHCl_3$) 3540, 3420, 3000, 2940, 2860, 1680, 1595, 1455, 1390, 1100, 1005, 955, 905, 700, 660 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.33 (s, 5 H), 6.41–6.05 (m, 2 H), 5.58 (m, 2 H), 5.1 (dd, 1 H, J = 17, 1 Hz), 5.00 (dd, 1 H, J = 9, 1 Hz), 4.50 (s, 2 H), 3.40 (m, 2 H), 2.50–1.50 (m, 5 H); mass spectrum, m/z (relative intensity) 168 (M$^+$ − C_7H_7, 0.7), 151 (17.7), 138 (6.1), 121 (21.2), 91 (56.4), 79 (21.2), 28 (100); high-resolution mass spectrum, calcd for $C_{16}H_{21}O_2N$ m/z 259.1572, found m/z 25.1573.

Preparation of Methylol Acetate 17. A mixture of amide **16** (0.120 g, 0.463 mmol), paraformaldehyde (14 mg, 0.47 mmol), and cesium carbonate (0.300 g) in dry THF (3 mL) was stirred at room temperature under nitrogen for 12 h.[1f] The reaction mixture was added dropwise to a solution of pyridine (0.25 mL) in acetic anhydride (2 mL), and stirring was continued for 15 min. The volatiles were removed in vacuo, and the residue was purified by preparative TLC on silica gel (hexane–ethyl acetate, 1:1) to give the methylol acetate **17**: 0.102 g (66%); viscous oil; IR (film) 3700–3200, 3050, 2950, 2860, 1740, 1680, 1605, 1535, 1455, 1370, 1230, 1100, 1020, 960, 910, 740, 700 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.33 (s, 5 H), 6.62 (br, 1 H), 6.40–6.02 (m, 2 H), 5.56–5.44

(m, 1 H), 5.20 (d, 2 H, J = 7 Hz), 5.1 (dd, 1 H, J = 15, 1 Hz), 5.0 (dd, 1 H, J = 10, 1 Hz), 4.50 (s, 2 H), 3.40 (m, 2 H), 2.47–1.52 (m, 5 H), 2.06 (s, 3 H); mass spectrum, m/z (relative intensity) 331 ($M^+ - C_2H_3O_2$, 0.5), 180 (24.2), 150 (10.3), 91 (100); high-resolution mass spectrum, calcd for $C_{17}H_{22}NO_2$ ($M^+ - C_2H_3O_2$) m/z 272.1650, found m/z 272.1634.

Diels–Alder Cyclization of Methyol Acetate 17. Methylol acetate **17** (102 mg, 0.31 mmol) was dissolved in *o*-dichlorobenzene (25 mL), and the solution was refluxed under nitrogen for 2 h. The solvent was removed by vacuum distillation, and the residue was purified on silica gel (5 g), eluting with 1:1 ethyl acetate/hexane to give oily lactam **18**: 78 mg (93%); IR ($CHCl_3$) 3005, 2940, 2880, 1955, 1880, 1820, 1630, 1470, 1420, 1370, 1280, 1240–1200, 1120, 1100, 700–660 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 7.38–7.29 (5 H), 5.85 (m, 1 H), 5.75 (m, 1 H), 4.80 (m, 1 H), 4.52 (d, 2 H, J = 3 Hz), 3.93 (m, 1 H), 3.56 (d, 2 H, J = 5 Hz), 2.64–1.65 (m, 8 H); mass spectrum, m/z (relative intensity) 271 (M^+, 14.3), 180 (100), 150 (14.6), 108 (0.1), 91 (85.9), 82 (37.8); high-resolution mass spectrum, calcd for $C_{17}H_{21}NO_2$ m/z 271.1573, found m/z 271.1576.

Hydrogenation of Cycloadduct 18. Lactam **18** (41 mg, 0.15 mmol) in methanol (10 mL) containing 10% Pd/C (10 mg) was stirred under 1 atm of hydrogen for 1.5 h. The mixture was filtered through Celite 545, and the solvent was removed in vacuo to afford essentially pure hydroxy lactam **18**: 26 mg (94%); oil; IR ($CHCl_3$) 3630, 3600–3200, 3000, 2950, 2860, 1620, 1470, 1445, 1420, 1280, 1240–1200, 1055 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 4.80 (m, 1 H), 3.76–3.60 (m, 2 H), 3.15 (m, 1 H), 2.50–2.24 (m, 4 H), 1.95–1.1 (m, 9 H); mass spectrum, m/z (relative intensity) 183 (M^+, 47.9), 125 (49.8), 97 (100), 84 (67.8), 55 (41.3); high-resolution mass spectrum, calcd for $C_{10}H_{17}NO_2$ m/z 183.1259, found m/z 183.1260.

(±)-*epi*-Lupinine (1). Lactam alcohol **28** (19 mg, 0.10 mmol) was dissolved in dry THF (10 mL), and 0.5 mL of 1 M BH_3-THF complex was added. The solution was refluxed under nitrogen for 45 min. Water (2 mL) was added followed by 5% HCl (2 mL) and concentrated HCl (2 mL). The resulting solution was refluxed for 0.5 h and made strongly basic with concentrated NaOH. The solution was extracted with ethyl acetate. The organic layer was dried over Na_2SO_4 and evaporated in vacuo. The residue was purified by column chromatography on alumina (15 g), eluting with 20% methanol–ethyl acetate to give racemic *epi*-lupinine (1; 10 mg, 57%) having spectral data (IR, NMR, MS) identical with those of an authentic sample:[5,15] IR ($CHCl_3$) 3640, 2950, 2775, 2820, 1600, 1450, 1300, 1280–1170, 1115, 1095, 1010 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 3.71–3.55 (m, 2 H), 2.91–2.82 (m, 3 H), 2.11–1.18 (m, 4 H); mass spectrum, m/z (relative intensity) 169 (M^+, 7.5), 152 (10.0), 138 (7.9), 97 (8.9), 88 (8.2), 83 (9.5), 70 (11.9), 61 (13.3), 43 (100); high-resolution mass spectrum, calcd for $C_{10}H_{19}ON$ m/z 169.1467, found m/z 169.1462.

Synthesis of Stilbene Acid 29. A solution of homoveratric acid (12.96 g, 0.066 mol), *p*-anisaldehyde (8.0 mL, 8.9 g, 0.066 mol), acetic anhydride (25 mL), and triethylamine (12 mL) was refluxed under nitrogen for 3 h. The solution was cooled to room temperature, and 100 mL of 5% NaOH was added. The basic solution was extracted with ethyl ether (50 mL) and neutralized with glacial acetic acid, and the aqueous layer was extracted with ethyl acetate. The organic extract was washed with brine, dried over $MgSO_4$, and concentrated in vacuo to give 12.08 g (58%) of stilbene acid **29** sufficiently pure for the next step: mp 207–208 °C (on recrystallization from methanol); IR ($CHCl_3$) 3510, 3400–2200, 1680, 1600, 1510, 1460, 1410, 1250, 1175, 1140, 1030, 830 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 7.78 (s, 1 H), 6.99 (s, 1 H), 6.97 (s, 1 H), 6.81 (d, 1 H, J = 9 Hz), 6.74 (dd, 1 H, J = 8, 2 Hz), 6.70 (d, 1 H, J = 2 Hz), 6.66 (s, 1 H), 1.64 (s, 1 H), 3.86 (s, 3 H), 3.73 (s, 3 H), 3.71 (s, 3 H); mass spectrum, m/z (relative intensity 314 (M^+, 100), 299 (6.2); high-resolution mass spectrum, calcd for $C_{18}H_{18}O_5$ m/z 314.1154, found m/z 314.1147.

Esterification of Acid 29. Acid **29** (12.08 g, 38.5 mmol) was dissolved in 300 mL of methanol containing 0.5 mL of concentrated HCl, and the solution was refluxed under nitrogen for 24 h. The solvent was evaporated in vacuo, and the crude ester was purified by column chromatography on silica gel (500 g), eluting with $CHCl_3$ to give methyl ester **30**: 5.57 g (44%); mp 111–112 °C (on recrystallization from methanol); IR ($CHCl_3$) 3000, 2960, 2850, 1700, 1600, 1510, 1460, 1435, 1320, 1305, 1250, 1180, 1140, 1025, 890, 830 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 7.78 (s, 1 H), 7.04 (s, 1 H), 7.03 (s, 1 H), 6.89 (d, 1 H, J = 8 Hz), 6.78 (dd, 1 H, J = 8, 2 Hz), 6.74 (d, 1 H, J = 2 Hz), 6.71 (s, 1 H), 6.68 (s, 1 H), 3.92 (s, 3 H), 3.84 (s, 3 H), 3.79 (s, 3 H), 3.76 (s, 3H); mass spectrum, m/z (relative intensity) 328 (M^+, 80.0), 313 (2.2), 151 (100); high-resolution mass spectrum, calcd for $C_{19}H_{20}O_5$ m/z 328.1310, found m/z 328.1302.

Methyl 3,6,7-Trimethoxyphenanthrene-9-carboxylate (31). To a solution of stilbene ester **30** (5.52 g, 16.8 mmol) in 50 mL of dry CH_2Cl_2 containing 2 drops of trifluoroacetic anhydride was added dropwise a solution of vanadium oxytrifluoride (4.58 g, 37 mmol) dissolved in 50 mL of CH_2Cl_2 and 25 mL of ethyl acetate containing 2 mL of trifluoroacetic acid and 2 drops of trifluoroacetic anhydride. The reaction mixture was cooled in an ice–salt bath throughout the addition (0.5 h). The dark brown mixture was stirred for an additional 0.5 h in an ice-salt bath, was poured onto crushed ice, and was extracted with CH_2Cl_2. The organic extract was washed with brine and dried over $MgSO_4$. The solvent was evaporated in vacuo, and the residue was purified on silica gel (400 g), eluting $CHCl_3$ to give phenanthrene ester 31: 5.5 g (100%); mp 151–152 °C (on recrystallization from methanol) (lit.[16] mp 155 °C); IR ($CHCl_3$) 3110, 3000, 2950, 2840, 1705, 1620, 1510, 1465, 1440, 1300, 1270, 1150, 1110, 1030, 975, 870, 835 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 8.64 (s, 1 H), 8.42 (s, 1 H), 7.83 (m, 2 H), 7.77 (d, 1 H, J = 2 Hz), 7.20 (dd, 1 H, J = 9, 2 Hz), 4.10 (s. 3 H), 4.08 (s, 3 H), 4.02 (s, 3 H), 4.01 (s, 3 H); mass spectrum, m/z (relative intensity) 326 (M^+, 100.0), 311 (5.0); high-resolution mass spectrum, calcd for $C_{19}H_{18}O_5$ m/z 326.1155, found m/z 326.1158.

9-(Hydroxymethyl)-3,6,7-trimethoxyphenanthrene (32). To a suspension of $LiAlH_4$ (1.4 g, 0.037 mol) in 50 mL of dry THF was added a solution of ester **31** (4.0 g, 0.012 mol) in 80 mL of dry THF. The reaction mixture was stirred under nitrogen for 2 h and quenched by sequential addition of 2 mL of water, 2 mL of 15% NaOH, and 6 mL of water. The mixture was filtered, and the filtrate was concentrated in vacuo. The residue was dissolved in $CHCl_3$ (100 mL), and the solution was washed with brine, dried over $MgSO_4$, and evaporated in vacuo to afford 3.53 g (96%) of phenanthrene alcohol **32** sufficiently pure for the next step: mp 155–156 °C (on recrystallization from methanol) (lit.[16] mp 157–158 °C); IR ($CHCl_3$) 3610, 3000, 2950, 2850, 1620, 1600, 1500, 1470, 1260, 1160, 1120, 1060, 960, 910, 880 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 7.81 (s, 1 H), 7.75 (d, 1 H, J = 2 Hz), 7.70 (d, 1 H, J = 9 Hz), 7.53 (s, 1 H), 7.46 (s, 1 H), 7.15 (dd, 1 H, J = 9, 2 Hz), 5.03 (s, 2 H), 4.07 (s, 3 H), 4.02 (s, 3 H), 3.99 (s, 3 H); chemical-ionization mass spectrum, m/z 299 ($M + H^+$); high-resolution mass spectrum, calcd for $C_{18}H_{18}O_4$ m/z 298.1205, found m/z 298.1216.

3,6,7-Trimethoxyphenanthrene-9-carboxaldehyde (33). To a suspension of pyridinium chlorochromate (3.77 g, 0.017 mol) in 40 mL of dry CH_2Cl_2 at 0 °C was added in one portion 3.48 g (0.012 mol) of phenanthrene alcohol **32** dissolved in 100 mL of dry CH_2Cl_2. The reaction mixture was stirred at room temperature under nitrogen for 2 h. The mixture was diluted with 150 mL of ether and filtered. The solids were washed with $CHCl_3$, and the combined organic phase was concentrated in vacuo. The residue was purified by column chromatography on silica gel (220 g, $CHCl_3$) to give aldehyde **33**: 2.93 g (85%); mp 136–144 °C (on recrystallization from methanol); IR ($CHCl_3$) 3100–3050, 3005, 2975, 2950, 2850, 2740, 1680, 1620, 1515, 1470, 1430, 1300, 1275, 1075, 1035, 890 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 8.84 (s, 1 H), 7.89 (s, 1 H), 7.80 (d, 1 H, J = 9 Hz), 7.65 (s, 1 H), 7.62 (d, 1 H, J = 2 Hz), 7.16 (dd, 2 H, J = 9, 2 Hz), 4.06 (s, 3 H), 4.05 (s, 3 H), 4.00 (s, 3 H); mass spectrum, m/z (relative intensity) 296 (M^+, 51.0), 281 (43.0), 253 (13.0), 28 (100); high-resolution mass spectrum, calcd for $C_{18}H_{16}O_4$ m/z 296.1049, found m/z 296.1039.

Preparation of Acid 35. To a mixture of phosphonium salt **34**[19] (2.24 g, 5 mmol) and tetramethylethylenediamine (7.5 mL) in dry THF (25 mL) at 0 °C was added 10.8 mL (10 mmol) of 0.92 M lithium diisopropylamide in THF. The dark red-orange solution was stirred at 0 °C for 1 h, and 3,6,7-trimethoxyphenanthrene-9-carboxaldehyde (**33**; 0.50 g, 1.7 mmol) in THF (30 mL) was added dropwise over 20 min. The reaction mixture was stirred at room temperature overnight, was quenched with 130 mL of 5% HCl, and was extracted with ethyl acetate. The extract was dried over Na_2SO_4 and was concentrated in vacuo. The residue was washed with ethyl acetate and was filtered through Celite 545. Evaporation of the filtrate in vacuo and

purification of the residue by column chromatography on silica gel (200 g, ethyl acetate) afforded 0.40 g (60%) of phananthrene acid **35** as a viscous oil. The product was an inseparable mixture of geometric isomers with an E/Z ratio of approximately 3:1: IR ($CHCl_3$) 3520, 3400–2400, 3005, 2950, 2840, 1710, 1620, 1505, 1470, 1440, 1420, 1385, 1300, 1270, 1240–1200, 1160, 1035, 970, 890, 855 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.92–7.16 (6 H), 7.03 (major isomer, trans, d, 1 H, J = 15 Hz), 6.95 (minor isomer, cis, d, 1 H, J = 10 Hz), 6.22 (unsymmetrical dt, major isomer, 1 H, J = 15 Hz), 6.0 (m, minor isomer, 1 H), 4.12–4.02 (3 s, 9 H), 2.64–2.19 (m, 4 H), 1.97–1.82 (2 H, m); mass spectrum, m/z (relative intensity) 380 (M^+, 2.0), 277 (100.0), 199 (14.0), 183 (22.3); high-resolution mass spectrum, calcd for $C_{23}H_{24}O_5$ m/z 380.1624, found m/z 380.1610.

Conversion of Acid 35 to Amide 36. Acid **35** (55 mg, 0.14 mmol) was dissolved in dry THF (10 mL), cooled to 0 °C, and treated with 3 drops of pyridine and 4 drops of ethyl chloroformate. The reaction mixture was stirred for 1 h under nitrogen, and 0.5 mL of concentrated NH_4OH was added. The THF was removed in vacuo, and the remaining aqueous layer was diluted with 5 mL of water and was extracted with ethyl acetate. The organic extract was dried over Na_2SO_4 and was evaporated in vacuo to give 49 mg (89%) of amide **36** as a light yellow solid which was an inseparable mixture of double bond isomers: IR ($CHCl_3$) 3530, 3410, 3060, 3025, 3000, 2950, 2840, 1680, 1620, 1600, 1500, 1465, 1440, 1420, 1380, 1260, 1240–1200, 1160, 1030, 960, 920, 880 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.92–7.16 (6 H), 7.04 (d, major isomer, 1 H, J = 15 Hz), 6.87 (d, minor isomer, 1 H, J = 11 Hz), 6.23 (dt, 1 H, major isomer, J = 17, 4 Hz), 5.94 (dt, 1 H, minor isomer, J = 11, 5 Hz), 5.5 (br, 2 H), 4.12–4.02 (3 s, 9 H), 2.48–2.22 (4 H), 1.94 (m, 2 H); mass spectrum, m/z (relative intensity) 379 (M^+, (100.0); high-resolution mass spectrum, calcd for $C_{23}H_{25}NO_4$ m/z 379.1784, found m/z 379.1766.

Synthesis of Methylol Acetate 37. A mixture of amide **36** (55 mg, 0.15 mmol), paraformaldehyde (4.3 mg, 0.14 mmol), and anhydrous cesium carbonate (300 mg, 1.6 mmol) in dry THF (2 mL) was stirred under nitrogen for 2 h. The reaction mixture was added dropwise to acetic anhydride (1 mL) containing pyridine (3 drops). The resulting mixture was stirred for 10 min at room temperature, and the solvent was removed in vacuo. The residue was purified by preparative TLC on silica gel, eluting with ethyl acetate to give 34 mg (52%) of the methylol acetate as a viscous oil. The product was a mixture of geometric isomers with a E/Z ratio of approximately 3:1: IR ($CHCl_3$) 3450, 3100–3025, 3000, 2950, 2840, 1735, 1690, 1620, 1600, 1500, 1460, 1440, 1370, 1300, 1260, 1240–1200, 1160, 1025, 960 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 7.92–7.17 (6 H), 7.02 (d, 1 H, major isomer, J = 15 Hz), 6.86 (d, 1 H, minor isomer, J = 11 Hz), 6.60 (br t, 1 H), 6.22 (dt, 1 H, major isomer, J = 15, 7 Hz), 6.10 (m, 1 H, minor isomer) 5.24 (d, 2 H, J = 7 Hz), 4.12–4.02 (3 s, 9 H), 2.43–2.24 (4 H), 2.04 (s, 3 H, major isomer), 1.96 (s, 3 H, minor isomer), 1.90–1.75 (m, 2 H); mass spectrum, m/z (relative intensity) 451 (M^+, 2.7), 391 (36.8), 361 (14.0), 277 (100.0); high-resolution mass spectrum, calcd for $C_{26}H_{29}NO_6$ m/z 451.1994, found m/z 451.1999.

Phenanthrene Lactam 38. A solution of methylol acetate **37** (28 mg, 0.06 mmol) in *o*-dichlorobenzene (10 mL) was heated in a sealed tube at 210–212 °C for 70 min. The solvent was removed by vacuum distillation, and the residue was purified by preparative TLC on silica gel (4% CH_3OH/ethyl acetate) to give 16 mg (66%) of phenanthrene lactam **38** and 7 mg (30%) of amide **36**. For **38**: IR (film) 3100, 3075, 3010, 2950, 2840, 1640–1600, 1520, 1460, 1420, 1340, 1300, 1260, 1200, 1170, 1140, 1040, 940, 910, 840, 810, 780, 750, 660 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.95 (m, 3 H), 7.25 (m, 2 H), 5.94 (d, 1 H, J = 18 Hz), 4.49 (d, 1 H, J = 17 Hz), 4.12 (s, 3 H), 4.07 (s, 3 H), 4.03 (s, 3 H), 3.89 (m, 1 H), 3.13 (m, 2 H), 2.55 (m, 2 H), 2.36–1.86 (4 H); mass spectrum, m/z (relative intensity) 391 (M^+, 65.0), 294 (100.0), 2.79 (12.0), 251 (9.0), 236 (6.0); high-resolution mass spectrum, calcd for $C_{24}H_{25}NO_4$ m/z 391.1783, found m/z 391.1764.

(±)-Cryptopleurine (2). Phenanthrene lactam **38** (16 mg, 0.04 mmol) was dissolved in 5 mL of dry THF and treated with 10 mg (0.26 mmol) of lithium aluminum hydride at room temperature for 1.5 h. The reaction was quenched with saturated NH_4Cl (5 mL), and the mixture was extracted with ethyl acetate. The extract was dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by preparative TLC on silica gel (10% CH_3OH/ethyl acetate) to give 8 mg (53%) of racemic cryptopleurine (**2**), identical in spectral characteristics and TLC with natural material:[20] IR (film) 3025, 2950, 2860, 2840, 2750, 1615, 1515, 1470, 1420, 1310, 1260, 1235, 1205, 1170, 1130, 1040, 845, 810, 785, 760 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.89 (s, 2 H), 7.77 (d, 1 H, J = 9 Hz), 7.19 (m, 2 H), 4.46 (d, 1 H, J = 16 Hz), 4.12 (s, 3 H), 4.07 (s, 3 H), 4.02 (s, 3 H), 3.65 (d, 1 H, J = 16 Hz), 3.31 (d, 1 H, J = 11 Hz), 3.14–2.93 (m, 3 H), 2.44–2.32 (m, 2 H), 2.10–1.26 (5 H); mass spectrum, m/z (relative intensity) 377 (M^+, 23.3), 294 (100.0); high-resolution mass spectrum, calcd for $C_{24}H_{27}NO_3$ m/z 377.199, found m/z 377.1973.

Acknowledgment. We are grateful to the National Cancer Institute (Grant No. CA-25145) for financial support. We also thank Professors K. N. Houk and M. N. Paddon-Row for informing us of their calculations on acyl imines prior to publication and Dr. R. Minard for mass spectra. S.M.W. thanks the John Simon Guggenheim Foundation for a fellowship.

Registry No. (±)-**1**, 486-72-6; (±)-**2**, 23365-52-8; **8**, 36255-44-4; (±)-(*E*)-**9**, 85864-12-6; (*E*,*E*)-**10**, 85864-11-5; (±)-(*E*)-**11**, 87101-66-4; (±)-(*E*)-**13**, 85864-13-7; (±)-(*E*)-**15**, 85864-15-9; (±)-(*E*)-**16**, 85864-16-0; (±)-(*E*)-**17**, 85864-17-1; (±)-**18**, 85863-92-9; (*E*)-**29**, 87101-67-5; (*E*)-**30**, 87101-68-6; **31**, 4176-23-2; **32**, 87101-69-7; **33**, 87101-70-0; **34**, 17814-85-6; (*E*)-**35**, 87101-71-1; (*Z*)-**35**, 87101-72-2; (*E*)-**36**, 87101-73-3; (*Z*)-**36**, 87101-74-4; (*E*)-**37**, 87101-75-5; (*Z*)-**37**, 87101-76-6; (±)-**38**, 87101-77-7; methyl sorbate, 689-89-4; benzyl bromide, 100-39-0; homoveratric acid, 93-40-3; *p*-anisaldehyde, 123-11-5.