planar and rigid. Inversion then has to be achieved by motion of the most distant methylene through the plane defined by the double bond and neighboring group, c.f. Figure 1. This motion is a true inversion and requires a high activation energy. By contrast, the 4-cyclohexenyl radical, 4-methylenecyclohexene, and 3-cyclohexenone have inversion barriers that are significantly less than that in cyclohexene. In these cases, a methylene separates the planar group and the double bond and leaves two adjacent methylenes in the remainder of the structure. These molecules are far less rigid than those of the first group and "inversion" can be achieved by low-energy twisting or pseudorotation pathways.

Conclusion. The ring inversions of the 3- and 4-cyclohexenyl radicals bear a close relationship to inversions of the related cyclohexenones and methylenecyclohexenes.

Acknowledgment. This work was supported in part by a grant (GM 30787) from the National Institutes of Health.

Palladium-Catalyzed Reactions in the Synthesis of 3- and 4-Substituted Indoles. 3.[1] Total Synthesis of (±)-Aurantioclavine

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Received January 15, 1987

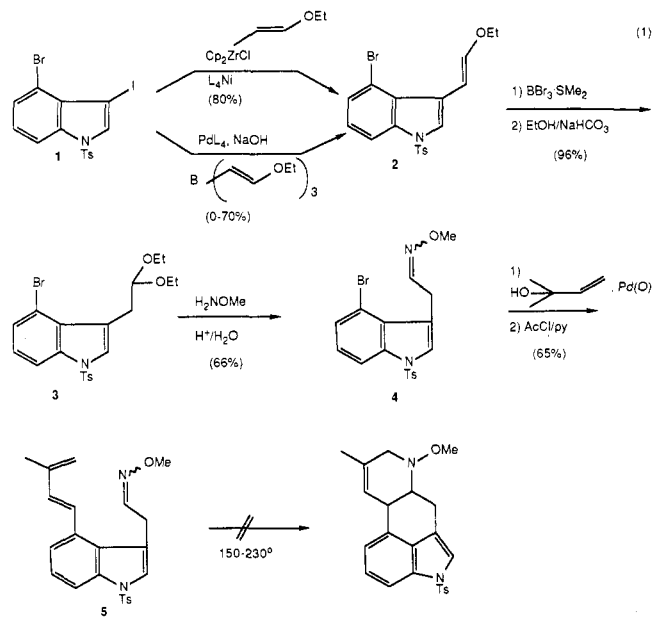
(±)-Aurantioclavine (**9**) was synthesized in overall 23% yield and 13 steps from commercially available starting materials. The synthesis involved palladium(II)-catalyzed indole ring formation, nickel(0)/zirconium(IV)-assisted introduction of one side chain, palladium(0)-catalyzed introduction of the other side chain, acid-catalyzed cyclization to form the seven-membered ring, and photolytic reductive detosylation to produce **9**.

Introduction

A general approach to the synthesis of 3,4-disubstituted indoles involving palladium(II)-catalyzed formation of 3-iodo-4-bromoindole **1** and sequential introduction of carbon side chains at the 3- and 4-positions using palladium(0) catalysis has recently been developed in these laboratories.[1] The use of this chemistry in the synthesis of derivatives of the ergot alkaloid clavicipitic acid has recently been reported.[2] The ease of introduction of highly functionalized side chains at the 3- and 4-positions of the indole nucleus suggested that this methodology would provide efficient routes to substrates suitable for intramolecular heteroatom Diels–Alder cyclizations to produce tetracyclic ergot alkaloid ring systems.[3] The results of studies directed toward this end are detailed herein.

Results and Discussion

The planned approach to the ergot alkaloid ring system involves synthesis of the requisite diene–aldehyde via palladium(0)-catalyzed chemistry, conversion of the aldehyde to an electron-deficient imine, and finally a reverse-electron-demand intramolecular heteroatom Diels-Alder reaction. The first attempt, patterned directly after Oppolzer's synthesis of lysergic acid methyl ester[3] is outlined in eq 1. The most direct route from **1** to **2**—palladium(0)-catalyzed alkylation of the 3-position by oxidative addition/insertion of methyl vinyl ether[4]—gave the undersired regioisomer (alkylation α to the methoxy group) as the major product. Palladium(0)-catalyzed oxidative addition–transmetalation from boron[5] was next attempted. For some reason this process was very sensitive to the purity of the boron reagent and to the freshness of the catalyst and yields were variable from run to run. The most reliable method proved to be nickel(0)-catalyzed oxidative addition–transmetalation from zirconium,[6] which consistently gave **2** in yields of 75–80%. Since the enol ether was somewhat resistant to hydrolysis and since the aldehyde was somewhat sensitive, hydrolysis using $BBr_3 \cdot SMe_2$ was immediately followed by acetalization to give **3** in excellent yield. Treatment with *O*-methylhydroxylamine under acidic conditions gave oxime **4** as a



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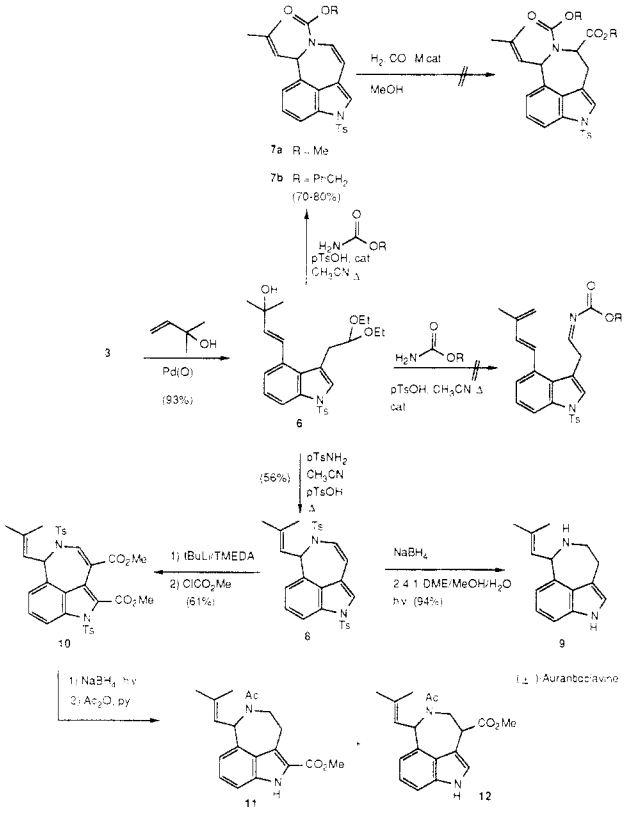

Figure 1.

3:2 mixture of syn and anti isomers. Introduction of the diene side chain was accomplished by using previously developed[1] palladium(0) chemistry to give **5** in fair yield. Attempted thermal cyclization resulted only in the recovery of starting materials at lower temperatures (150–190 °C in tetraglyme dimethyl ether) and decomposition at higher temperatures (225–230 °C). A more electron-deficient heterodienophile was judged necessary[7] to overcome this lack of reactivity. Hence, the synthesis of *N*-methoxycarbonyl and *N*-tosyl imines was attempted as in Figure 1.

Introduction of the tertiary allylic alcohol side chain (Figure 1) was quite efficient, giving high yields of **6**. Condensation of **6** with methyl or benzyl carbamate in the presence of 10% *p*-toluenesulfonic acid led not to the expected acylimine–diene but rather to tricyclic compound **7** in excellent yield. This same cyclization occurred when *p*-toluenesulfonamide was used as the amine component, producing **8** in fair yield. The sequence of steps leading from **6** to **7** or **8** is unknown at the present time but is likely to involve acid-catalyzed N-alkylation of the intermediate enamine by the tertiary allylic alcohol, probably via the delocalized allylic–benzylic cation.[8]

Compounds **7** and **8** have the complete skeleton of the ergot alkaloid clavicipitic acid[2,9] and only lack a carboxyl group β to the indole ring. However, numerous attempts to hydrocarboxylate[10] these compounds using a variety of catalysts (Pt, Pd, Rh, Co) under a wide range of conditions failed. Under most conditions, no reaction occurred. Under severe conditions overreduction of the exocyclic double bond or complete decomposition of the substrate was observed. In one case ($Co_2(CO)_8$, MeOH solvent, 1400 psi H_2/CO, 70 °C, 36 h) a minor amount (~8% by NMR spectroscopy) of the desired hydrocarboxylated product was obtained. However the yield could not be improved, and clavicipitic acid remains inaccessible from **7** or **8** by this route.

N-Tosylindoles undergo tosyl-group directed lithiation at the 2-position, permiting subsequent introduction of electrophiles at that position.[11] In an attempt to lithiate **8** at positions adjacent to each tosyl group, it was treated with excess *tert*-butyllithium/TMEDA at low temperatures, and the resulting dilithio species was treated with methyl chloroformate. Diester **10** was produced in fair yield. The positions of the carboxy groups were not assignable in compound **10**. Thus it was reduced with sodium borohydride under photochemical conditions[12] (see below) and N-acylated to give a mixture of monoesters **11** and **12**. These were not separated but were identified by 500-MHz NMR spectroscopy with complete spin decoupling. Compound **11** had already been synthesized by monolithiation/carboxylation of **8** and was readily identified. Compound **12** had the downfield methine signals typical for all the compounds having the =CHCHN array (**6-11**) as the left side of the molecule but had an ABX pattern distinctly different from either diastereoisomer of clavicipitic acid.[2,12] Hence the ester group occupies the seven-membered ring position α to the indole ring, not β to it. This is an unusual substitution pattern for the ring system. Factors controlling the site of lithiation in **12** are under study.

Although the 3,4,5,6-tetrahydro-6-(2-methyl-1-propenyl)azepino[5,4,3-*cd*]indole tricyclic ring system common to **7–12** was first encountered with the isolation of the clavicipitic acids from several varieties of *Claviceps*,[9] it has more recently been isolated from *Penicillium aurantio-virens* in the form of aurantioclavine, **9**.[13] Reductive detosylation of **8** using sodium borohydride under photolytic conditions[12] removed both tosylate groups and reduced the olefin, producing (±)-aurantioclavine in excellent yield. The physical and spectroscopic data for synthetic **9** were identical in all respects with those reported for natural[13] and synthetic[8] material. Thus, (±)-aurantioclavine (**9**) was synthesized in five steps from **1** in overall 37.6% yield and in 13 steps from commercially available 6-bromo-2-nitrotoluene in overall 23% yield. (This is not as efficient as the first-reported total synthesis of **9**, which involved five steps in overall 31% yield, starting from commercially available 3-formylindole.[8])

Experimental Section

General Methods. All melting points are uncorrected. ^1H NMR spectra were measured with an IBM-WP 270 NMR and a Bruker 500 NMR for the 270-MHz and 500-MHz ^1H NMR spectra, respectively, using Me_4Si as internal standard and are reported in δ. Infrared spectra were measured on a Beckman 4230 spectrophotometer. Analytical TLC was performed on Merck 60F254 silica gel. Products were visualized by UV light. Analyses were performed by M-H-W Laboratories, Phoenix, AZ.

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Materials. Silica gel, Baker analyzed reagent grade (60–200 mesh), and silica gel, EM Reagents (230–400 mesh), were used for column chromatography. Pyridine was fractionally distilled from CaH_2 under argon. Acetonitrile was fractionally distilled from CaH_2 under argon. *p*-Benzoquinone was sublimed at 60 °C, 10 mmHg, and then stored in an amber glass bottle at 0 °C under argon. Tetrahydrofuran was distilled from Na under N_2. Other materials were obtained from commercial suppliers and used without further purification.

4-Bromo-3-(2-ethoxyethen-1-yl)-1-tosylindole (2). Ethoxyacetylene (0.67 mL, 7.7 mmol) was added to dicyclopentadienylzirconium hydrogen chloride[6] (2.00 g, 7.7 mmol) in freshly distilled benzene (25 mL) in a 50-mL airless flask. The system was degassed, purged with argon (4×), and allowed to stir at room temperature for 2 h. The solvent was removed on a rotary evaporator and the complex was redissolved in THF (10 mL). $Ni(PPh_3)_4$, prepared by addition of DIBAL (0.73 mL, 1.0 M, 0.73 mmol) to $Ni(acac)_2$ (0.157 g, 0.7 mmol) and triphenylphosphine (0.734 g, 2.8 mmol) in THF (8.4 mL), was added to the zirconium complex via cannula. 4-Bromo-3-iodo-1-tosylindole (1.58 g, 3.5 mmol) was then added to the flask, and the flask was degassed and purged with argon (4×). The reaction mixture was stirred for 48 h at room temperature. The reaction mixture was taken up in diethyl ether (100 mL) and washed with H_2O (3 × 75 mL) and the organic layer was dried over $MgSO_4$, filtered, and concentrated to dryness on a rotary evaporator to afford a deep red oil. Purification by column chromatography (silica gel, 75:25 hexane/benzene to elute PPh_3 plus starting material, then 4:1 hexane/EtOAc afforded the vinyl ether tosylindole **2**, 1.17 g (80%) as a yellow oil. For consistent high yields in this reaction, the zirconium hydride complex must be freshly prepared.

^1H NMR (270 MHz) ($CDCl_3$): δ 7.93 (d, *J* = 7.8 Hz, 1 H, indole 7 H), 7.73 (d, *J* = 8.7 Hz, 2 H, tosyl Ar H), 7.45 (s, 1 H, indole 2 H), 7.36 (d, 1 H, *J* = 8.3 Hz, indole 5 H), 7.22 (d, *J* = 8.1 Hz, 2 H, tosyl Ar H), 7.11 (t, *J* = 7.8 Hz, 1 H, indole 6 H), 6.71 (d, *J* = 12.7 Hz, 1 H, C*H*=CHOEt), 6.36 (d, *J*= 12.2 Hz, 1 H, CH=C*H*OEt), 3.93 (q, *J* = 7.0 Hz, 2 H, OCH_2), 2.34 (s, 3 H, CH_3Ar), 1.36 (t, *J* = 7.0 Hz, 3 H, OCH_2CH_3). IR ($CDCl_3$): 3140, 2980, 1640, 1590, 1460, 1405, 1370, 1170 cm^{-1}. Anal. Calcd for $C_{19}H_{18}NO_3SBr$: C, 54.29; H, 4.32; N, 3.33. Found: C, 54.09; H, 4.46; N, 3.05.

4-Bromo-3-(2,2-diethoxyethyl)-1-tosylindole (3). 4-Bromoindole **2** (1.17 g, 279 mmol) was dissolved in methylene chloride (75 mL) in a 250-mL round-bottom flask. To the flask was added BBr_3·SMe_2 (8.37 mL, 8.37 mmol, 1.0 M) via syringe and reaction mixture was allowed to stir at room temperature for exactly 5 min. The reaction mixture was slowly poured into 100 mL of a stock solution containing 1 M aqueous $NaHCO_3$/300 mL of EtOH. The mixture was allowed to stir for 2.5 h at room temperature. The crude mixture was transferred to a 500-mL separatory funnel and the organic layer was separated, dried over $MgSO_4$, filtered, and concentrated to dryness on a rotary evaporator to afford a light brown oil. Purification by column chromatography (silica gel, 4:1 hexane/EtOAc afforded 1.25 g (96%) of 4-bromo-3-(2,2-diethoxyethyl)-1-tosylindole (**3**) as a yellow oil.

^1H NMR (270 MHz) ($CDCl_3$): δ 8.03 (d, 1 H, *J* = 8.3 Hz, indole 7 H), 7.81 (d, 2 H, *J* = 8.0 Hz, tosyl Ar H), 7.61 (s, 1 H, indole 2H), 7.40 (d, 1 H, *J* = 7.8 Hz, indole 5H), 7.24 (d, 2 H, *J* = 7.6 Hz, tosyl Ar H), 7.15 (t, 1 H, *J* = 8.1 Hz, indole 6H), 4.92 (t, 1 H, *J* = 5.7 Hz, C*H*$(OEt)_2$), 3.71 (m, 2 H, OCH_2CH_3), 3.54 (m, 2 H, OCH_2CH_3), 3.34 (d, 2 H, *J* = 5.6 Hz, CH_2CH$(OEt)_2$), 2.36 (s, 3 H, CH_3Ar), 1.23 (t, 6 H, *J* = 7.1 Hz, OCH_2CH_3). IR ($CDCl_3$): 3050, 2970, 2920, 2880, 1595, 1445, 1435 (sh), 1370, 1300, 1270, 1185, 1170 cm^{-1}. Anal. Calcd for $C_{21}H_{24}NO_4SBr$: C, 54.08; H, 5.19; N, 3.00. Found: C, 53.95; H, 5.08; N, 3.26.

4-Bromo-3-[2-(methoxyimino)ethyl]-1-tosylindole (4). A mixture of 4-bromo-3-(2,2-diethoxyethyl)indole-1-tosamide (0.363 g, 0.78 mmol), molecular sieves (4 Å, 2 g), and *O*-methylhydroxylamine hydrochloride (0.100 g, 1.19 mmol) in pyridine (3 mL) was stirred at room temperature for 1 h in a 10-mL round-bottom flask. The crude reaction mixture was taken up in diethyl ether (25 mL) and washed with 0.5 N HCl (2 × 50 mL) and then saturated $NaHCO_3$ (25 mL), dried over $MgSO_4$, and concentrated in vacuo to afford 0.284 g of crude product. Purification by column chromatography (silica gel, 25:75 benzene/hexane increasing polarity to benzene) afforded **4**, 0.210 g (66%). This material was used without further purification.

^1H NMR (270 MHz) ($CDCl_3$): δ 7.95 (m, 1 H, indole 7 H), 7.73 (d, 2 H, *J* = 8.3 Hz, tosyl Ar H), 7.62 (t, *J* = 6 Hz, N=C*H*), 7.46 (s, 1 H, syn indole 2H), 7.44 (s, anti indole 2H), 7.36 (m, 1 H, indole 5H), 7.24 (d, *J* = 8.1 Hz, 2H, tosyl Ar H), 7.13 (m, 1 H, indole 6 H), 6.88 (t, *J* = 4.9 Hz, N=C*H*), 3.96 (dd, *J* = 1.0 Hz, 5.1 Hz, CH_2C=N), 3.94 (s, 3 H, OCH_3), 3.89 (dd, *J* = 1.3 Hz, 6.0 Hz, CH_2C=N), 3.87 (s, 3 H, OCH_3), 2.35 (s, 3 H, CH_3Ar).

4-(3-Methyl-1,3-butadien-1-yl)-3-[2-(methoxyimino)ethyl]-1-tosylindole (5). A mixture of oxime–ether **4** (0.210 g, 0.517 mmol), 2-methyl–3–buten–2–ol (0.078 mL, 0.064 g, 0.75 mmol), Et_3N (0.127 g, 0.175 mL, 1.25 mmol), $Pd(OAc)_2$ (0.011 g, 0.049 mmol), and (*o*-tolyl)$_3$P (0.061 g, 0.20 mmol) in CH_3CN (0.25 mL) was flushed with argon and then heated in a sealed tube at 100 °C for 5 h. After cooling to room temperature, the residue was taken up in 50 mL of CH_2Cl_2, washed with brine (2×), dried over $MgSO_4$, and concentrated in vacuo. Purification by column chromatography (silica gel, eluted first with benzene, then with 1:1 ether/benzene) afforded 0.181 g (85%) of the tertiary alcohol oxime ether. The tertiary alcohol oxime–ether was taken up in pyridine (0.042 mL, 0.043 g, 0.545 mmol) and acetyl chloride (0.040 mL, 0.036 g, 0.46 mmol) was added in benzene (5 mL). The reaction mixture was heated at reflux for 0.5 h and then cooled to room temperature. The crude reaction mixture was taken up in benzene (25 mL), washed with saturated $NaHCO_3$ (2 × 50 mL), dried over $MgSO_4$, and concentrated in vacuo to afford a light yellow oil. The crude oil was taken up in diethyl ether (10 mL) and filtered through a silica gel plug to afford **5**, 0.135 g (66%) as a fluffy yellow solid.

^1H NMR (270 MHz) ($CDCl_3$): δ 7.91 (d, 0.5 H, *J* = 7.8 Hz, indole 7H), 7.90 (d, *J* = 7.8 Hz, 0.5 H, indole 7H), 7.76 (d, *J* = 7.8 Hz, 1 H, tosyl Ar H), 7.75 (d, *J* = 7.8 Hz, tosyl Ar H), 7.5–7.2 (m), 7.13 (d, *J* = 16.1 Hz, 0.5 H, C*H*=CH), 6.93 (d, *J* = 15.6 Hz, 0.5 H, C*H*=CH), 6.76 (m, 1 H, CH=C*H*), 5.11 (m, 2 H, C=CH_2), 3.96 (s, 1.5 H, OCH_3), 3.86 (s, 1.5 H, OCH_3), 3.74 (d, *J* = 5.9 Hz, 1.0 H, CH_2C=N), 3.85 (d, *J* = 6.3 Hz, 1.0 H, CH_2C=N), 2.35 (s, 3 H, CH_3Ar), 2.03 (s, 1.5 H, =CCH_3), 1.96 (s, 1.5 H, =CCH_3).

3-(2,2-Diethoxyethyl)-4-(3-hydroxy-3-methyl-1-buten-1-yl)-1-tosylindole (6). A mixture of 4-bromo-3-(2,2-Diethoxyethyl)-1-tosylindole (**3**) (1.3 g, 2.79 mmol), 2-methyl-3-buten-2-ol (0.600 g, 6.98 mmol), $Pd(OAc)_2$ (0.063 g, 0.279 mmol), (*o*-tolyl)$_3$P (0.339 g, 1.12 mmol), and Et_3N (0.705 g, 6.98 mmol) in CH_3CN (8.4 mL) was flushed with argon and then heated in a sealed tube at 100 °C for 5 h. After cooling to room temperature, the residue was taken up in 100 mL of CH_2Cl_2, washed with brine (3×), dried over $MgSO_4$, filtered, and concentrated to dryness on a rotary evaporator. Purification by column chromatography (silica gel, 4:1 hexane/EtOAc to elute (*o*-tolyl)$_3$P, followed by 1:1 hexane/EtOAc to elute product) afforded 1.2 g (92%) of **3** as a light brown oil.

^1H NMR (270 MHz) ($CDCl_3$): δ 7.84 (d, 1 H, *J* = 8.0 Hz, indole 7H), 7.65 (d, 2 H, *J* = 8.3 Hz, tosyl Ar H), 7.36 (s, 1 H, indole 2 H), 7.18–7.10 (m, 5 H, indole 5H, 6H; tosyl Ar H, C*H*=CH), 6.08 (d, 1 H, *J* = 15.8 Hz, CH=C*H*), 4.68 (t, 1 H, *J* = 5.1 Hz, C*H*$(OEt)_2$), 3.56 (m, 2 H, OCH_2CH_3), 3.35 (m, 2 H, OCH_2CH_3), 3.04 (d, 2 H, *J* = 5.2 Hz, CH_2CH$(OEt)_2$), 2.24 (s, 3 H, CH_3Ar), 1.33 (s, 6 H, =C$(CH_3)_2$), 1.07 (t, 6 H, *J* = 7.1 Hz, OCH_2CH_3). IR ($CDCl_3$): 3600–3400 (br), 3140, 2975, 2920, 1730, 1600, 1530, 1495, 1480, 1415, 1370, 1190, 1180, 1160, 1135, 1090 cm^{-1}. Anal. Calcd for $C_{26}H_{33}NO_5S$: C, 66.21; H, 7.05; N, 2.97. Found: C, 66.44; H, 7.20; N, 2.89.

1-Tosyl-5,6-dihydro-5-carbomethoxy-6-(2-methyl-1-propenyl)azepino[5,4,3-*cd*]indole (7a). A mixture of tosylindole **6** (0.087 g, 0.18 mmol), methyl carbamate (0.056 g, 0.75 mmol), and *p*-toluenesulfonic acid (0.003 g, 0.018 mmol) in CH_3CN (2.61 mL) was heated to 90 °C for 4 h. After cooling to room temperature, the residue was taken up in 50 mL of CH_2Cl_2, washed with brine (3×), dried over $MgSO_4$, filtered, and concentrated to dryness on a rotary evaporator. Purification by column chromatography (silica gel, 4:1 hexane/EtOAc) afforded 60 mg (76%) of **7a** as a light yellow oil.

^1H NMR (270 MHz) ($CDCl_3$): δ 7.85 (d, 1 H, *J* = 8.3 Hz, indole 7H), 7.77 (d, 2H, *J* = 8.2 Hz, tosyl Ar H), 7.49 (s, 1 H, indole 2H), 7.28–7.07 (m, 4 H, tosyl Ar H, indole 5H, 6H), 6.48 (m, 2H, NC*H*=CH, CHC*H*=C$(CH_3)_2$), 6.08 (d, 1 H, *J* = 8.7 Hz, NCH=C*H*), 5.24 (d, 1 H, *J* = 8.9 Hz, $(CH_3)_2$CCHC*H*N), 3.73 (br s, 3 H,

OCH_3), 2.35 (s, 3 H, CH_3Ar), 1.85 (br s, 3 H, $(CH_3)_2C$), 1.59 (s, 3 H, $(CH_3)_2C$). IR ($CDCl_3$): 2960, 2920, 2860, 1700, 1650, 1600, 1440, 1370, 1315, 1230, 1190, 1175 cm^{-1}. Anal. Calcd for $C_{24}H_{24}N_2O_4S$: C, 66.03; H, 5.54. Found: C, 66.51; H, 5.32. MS, *m/e* (CI NH_3): M + 1 437 (17.1% P).

1-Tosyl-5,6-dihydro-5-carbobenzoxy-6-(2-methyl-1-propenyl)azepino[5,4,3-*cd*]indole (7b). A mixture of tosylindole **6** (0.087 g, 0.18 mmol), benzyl carbamate (0.112 g, 0.75 mmol), and *p*-toluenesulfonic acid (0.003 g, 0.018 mmol) in CH_3CN (2.61 mL) was heated to 90 °C for 4 h. After cooling to room temperature, the residue was taken up in 50 mL of CH_2Cl_2, washed with brine (3×), dried over $MgSO_4$, filtered, and concentrated to dryness on a rotary evaporator. Purification by column chromatography (silica gel, 4:1 hexane/EtOAc) afforded 0.064 g (72%) of **7b** as a light yellow oil.

^1H NMR (270 MHz, $CDCl_3$): δ 7.93 (d, 1 H, *J* = 8.3 Hz, indole 7H), 7.86 (d, 2 H, *J* = 8.1 Hz, tosyl Ar H), 7.48 (s, 1 H, indole 2H), 7.3–7.08 (m, 4H, tosyl Ar H, indole 5H, 6H), 6.52 (m, 2 H, $CHCH{=}C(CH_3)_2$, $NCH{=}CH$), 6.04 (d, 1 H, *J* = 8.4 Hz, $NCH{=}CH$), 5.27–5.11 (m, 3 H, $PhCH_2$, $(CH_3)_2CCHCHN$), 2.32 (s, 3H, $ArCH_3$), 1.84 (br s, 3 H, $C(CH_3)_2$), 1.58 (s, 3 H, $C(CH_3)_2$). IR ($CDCl_3$): 3360 (br), 3120, 3040, 2920, 2840, 1710, 1600, 1545, 1500, 1450, 1380 cm^{-1}.

1,5-Ditosyl-5,6-dihydro-6-(2-methyl-1-propenyl)azepino[5,4,3-*cd*]indole (8). A mixture of tosylindole **6** (0.214 g, 0.455 mmol), *p*-toluenesulfonamide (0.312 g, 1.82 mmol), and *p*-toluenesulfonic acid (0.0195 g, 0.102 mmol) in CH_3CN (7 mL) was heated to 90 °C for 4 h. After cooling to room temperature, the residue was taken up in 50 mL of CH_2Cl_2, washed with brine, dried over $MgSO_4$, filtered, and concentrated to dryness on a rotary evaporator. Purification by radial chromatography (silica gel, 2 mm, 4:1 hexane/EtOAc) afforded 0.135 g (56%) of **6** as a light yellow foam.

^1H NMR (270 MHz) ($CDCl_3$): δ 7.67 (m, 3 H, indole 7H, tosyl Ar H), 7.29 (s, 1 H, indole 2H), 7.25 (d, 1 H, *J* = 8.2 Hz, indole 5 H), 7.17 (d, 2 H, *J* = 8.25 Hz, tosyl Ar H), 7.07 (t, 1 H, *J* = 7.7 Hz, indole 6H), 6.88 (d, 2 H, *J* = 7.24 Hz, tosyl Ar H), 6.74 (d, 2 H, *J* = 8.1 Hz, tosyl ArH), 6.30 (d, 1 H, *J* = 8.2 Hz, $NCH{=}CH$), 6.14 (d, 1 H, *J* = 8.2 Hz, $NCH{=}CH$), 5.98 (d, 1 H, *J* = 8.9 Hz, $(CH_3)_2C{=}CH$), 5.0 (d, 1 H, *J* = 8.9 Hz, $(CH_3)_2{=}CHCHN$), 2.29 (s, 3 H, CH_3Ar), 2.12 (s, 3 H, CH_3Ar), 1.75 (s, 3 H, $(CH_3)_2C$), 1.46 (s, 3 H, $(CH_3)_2C$). IR (neat): 3105, 2910, 2840, 1595, 1425, 1370, 1340, 1180, 1170, 1155, 1130, 1090 cm^{-1}. Anal. Calcd for $C_{29}H_{28}N_2O_4S_2$: C, 65.39; H, 5.30; N, 5.26. Found: C, 64.98; H, 5.50; N, 4.92.

Synthesis of (±)-Aurantioclavine (9). A 10-mL test tube was charged with 1,5-ditosyl-5,6-dihydro-6-(2-methyl-1-propenyl)azepino[5,4,3-*cd*]indole (**8**) (0.05 g, 0.094 mmol). To the test tube were added 1,2-dimethoxyethane (2 mL), methanol (4 mL), and H_2O (1 mL) followed by the addition of $NaBH_4$ (excess >25 mmol). The test tube was sealed with a rubber septum and irradiated with a 450-W Hanovia lamp for 1 h. The crude reaction mixture was transferred to a 25-mL round-bottom flask and concentrated to near dryness on a rotary evaporator. The residue was taken up in CH_2Cl_2 (25 mL), washed with brine, dried over $MgSO_4$, filtered, and concentrated to dryness on a rotary evaporator. Purification by preparative thin layer chromatography (silica gel, 0.5 mm, $CHCl_3/CH_3OH/NH_4OH$ (concentrated), 75:25:1) afforded 0.018 g (85%) of (±)-aurantioclavine as an off-white powder: mp 194–195 °C (lit.[13] mp 194–196°C).

^1H NMR (270 MHz) ($CDCl_3$): δ 8.17 (br s, 1 H, indole 1H), 7.24 (d, 1 H, *J* = 7.3 Hz, indole 7H), 7.09 (t, 1 H, *J* = 7.7 Hz, indole 6H), 7.00 (s, 1 H, indole 2H), 6.84 (d, 1 H, *J* = 7.2 Hz, indole 5H), 5.46 (br d, 1 H, *J* = 9.0 Hz, $(CH_3)_2CCH$), 4.96 (d, 1 H, *J* = 9.1 Hz, $(CH_3)_2CCHCHN$), 3.8–3.5 (m, 2 H, $HNCH_2CH_2$), 3.2–2.95 (m, 2 H, $HNCH_2CH_2$), 2.81 (br s, 1 H, NH), 1.84 (s, 6 H, *gem*-dimethyl). IR (KBr): 3400, 3290, 2920, 1610, 1565, 1440, 1415, 1330, 1250, 1110, 870, 770, 725 cm^{-1}. MS, *m/e* CI(NH_3): M + 1, M + 2; 227, 228 (49.9% P).

The physical and spectroscopic data for this compound were identical in all respects with those of both natural[13] and synthetic[8] material.

^{13}C NMR (270 MHz) ($CDCl_3$): δ 18.17 [$(CH_3)_2C$], 25.62 [$(CH_3)_2C$], 30.7 (NCH_2CH_2), 48.5 (NCH_2CH_2), 62.30 ($CHNHCH_2CH_2$), 109.2 (indole 3C), 109.3 (indole 7C), 115.9 (indole 6C), 117.85 (indole 5C), 117.9 (indole 4C), 120.8 (indole 2C), 121.6 [$(CH_3)_2CCH$], 127.6 (indole 3aC), 130.8 [$(CH_3)_2CCH$], 133.1 (indole 7aC).

2,3-Dicarbomethoxy-1,5-ditosyl-5,6-dihydro-6-(2-methyl-1-propenyl)azepino[5,4,3-*cd*]indole (10). 1,5-Ditosyl-5,6-dihydro-6-(2-methyl-1-propenyl)azepino[5,4,3-*cd*]indole (**8**) (0.015 g, 0.028 mmol) was dissolved in distilled THF (2 mL) and cooled to −78 °C. To this solution was added tetramethylethylenediamine (0.0195 g, 0.168 mmol) and *tert*-butyllithium [(105 μL, 1.6 M), 0.168 mmol], and after being allowed to stir for exactly 5 min, the solution turned reddish orange. To this solution was added methyl chloroformate (0.0212 g, 0.224 mmol), and the solution was allowed to warm to room temperature and turned a bright yellow color. The crude reaction mixture was concentrated to dryness on a rotary evaporator. The residue was taken up in CH_2Cl_2 (25 mL), washed with brine (2×), dried over $MgSO_4$, filtered, and concentrated to dryness on a rotary evaporator. Purification by radial chromatography (silica gel, 1 mm, 4:1 hexane/EtOAc) afforded 0.011 g (61%) of **7** as a yellow oil.

^1H NMR (270 MHz) ($CDCl_3$): δ 7.86–6.92 (m, 9 H, tosyl ArH, indole H's), 6.72 (d, 1 H, *J* = 8.88 Hz, tosyl Ar H), 6.36 (d, 1 H, *J* = 8.85 Hz, tosyl Ar H), 6.03 (d, 1 H, *J* = 9.2 Hz, $(CH_3)_2CCH$), 5.16 (d, 1 H, *J* = 9.2 Hz, $(CH_3)_2CCHCHN$), 4.0 (s, 3 H, OCH_3), 3.87 (s, 3 H, OCH_3), 2.37 (s, 3 H, CH_3Ar), 2.28 (s, 3 H, CH_3Ar), 1.73 (s, 3 H, $(CH_3)_2C$), 1.53 (s, 3 H, $(CH_3)_2C$). IR ($CDCl_3$): 2950, 2920, 1740, 1640, 1600, 1440, 1375, 1350, 1305, 1260, 1170, 1120 cm^{-1}. MS, *m/e* (rel intensity) EI: 648 (0.2% P).

2-Carbomethoxy-5-acetyl-3,4,5,6-tetrahydro-6-(2-methyl-1-propenyl)azepino[5,4,3-*cd*]indole (11) and 3-Carbomethoxy-5-acetyl-3,4,5,6-tetrahydro-6-(2-methyl-1-propenyl)-azepino[5,4,3-*cd*]indole (12). 2,3-Dicarbomethoxy-1,5-ditosyl-5,6-dihydro-6-(2-methyl-1-propenyl)azepino[5,4,3-*cd*]indole (**10**) (0.049 g, 0.076 mmol) was charged into a 10-mL test tube and dissolved in MeOH/DME/H_2O (4:2:1 mL). To the solution was added $NaBH_4$ (0.0285 g, 0.76 mmol), and the test tube was sealed with a rubber septum and irradiated with a 450-W Hanovia lamp for exactly 10 min. The crude reaction mixture was transferred to a 25-mL round-bottom flask and concentrated in vacuo. The residue was taken up in CH_2Cl_2 (25 mL), washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was taken up in pyridine (0.25 mL) and acetic anhydride (0.005 g, 0.047 mmol) and allowed to stir at room temperature for 3 h. The crude reaction mixture was taken up in CH_2Cl_2 (25 mL), washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. Purification by radial chromatography (silica gel, 1.0 mm, hexane/EtOAc 3:2) afforded 10 mg (65%) of **9** and **10** as an inseparable mixture.

^1H NMR (500 MHz, $CDCl_3$) **11**: δ 8.75 (br s, 1 H, indole NH), 7.34–7.19 (m, 3 H, indole 2, 6, 7H), 6.95 (d, 1 H, *J* = 8.14 Hz, $(CH_3)_2CCH$), 6.93 (d, 1 H, *J* = 6.78 Hz, indole 5H), 5.33 (d, 1 H, *J* = 8.0 Hz, $(CH_3)_2CCHCHNAc$), 3.98 (s, 3 H, OCH_3), 3.87 (dd, 2H, *J* = 2.5, 9.3 Hz, NCH_2CH_2), 3.66 (dt, 1 H, *J* = 2.6, 17.9 Hz, NCH_2CH_2), 3.27 (dt, 1 H, *J* = 9.0, 17.9 Hz), 2.22 (s, 3 H, $NCOCH_3$), 1.83 (s, 3 H, $(CH_3)_2$, 1.71 (s, 3 H, $(CH_3)_2C$). **12**: δ 8.81 (br s, 1 H, indole NH), 7.34–7.19 (m, 3 H, indole 2, 6, 7H), 6.84 (d, 1 H, *J* = 6.53 Hz, indole 5H), 5.85 (d, 1 H, *J* = 7.6 Hz, $(CH_3)_2CCH$), 5.38 (d, 1 H, *J* = 7.5 Hz, $(CH_3)_2CCHCHN$), 4.34 (dd, 1 H, *J* = 3.46, 9.8 Hz, $CHCO_2CH_3$), 3.49 (m, 2 H, $AcNCH_2CHCO_2CH_3$), 2.19 (s, 3 H, CH_3CON), 1.83 (s, 3 H, $(CH_3)_2C$), 1.74 (s, 3 H, $(CH_3)_2C$). IR ($CDCl_3$): 3300, 2920, 2840, 1740 (sh), 1700, 1620, 1570, 1540, 1430, 1370, 1330, 1250, 1180, 1165, 1145, 1100 cm^{-1}. MS, *m/e* EI: 326 (9.4% P).

Acknowledgment. Support for this research under Grant No. 2RO1GM26178-06 from the National Institutes of General Medical Sciences is gratefully acknowledged. High field NMR spectra were obtained in the Colorado State University Regional NMR Center funded by National Science Foundation Grant No. CHE 78-18581.