Syntheses of Strychnos and Aspidospermatan-Type Alkaloids. 8. Selective Total Syntheses of Mossambine and 14-*epi*-Mossambine by a Radical Cyclization Reaction[1]

Martin E. Kuehne,* Tiansheng Wang, and Denis Seraphin

Department of Chemistry, University of Vermont, Burlington, Vermont 05405

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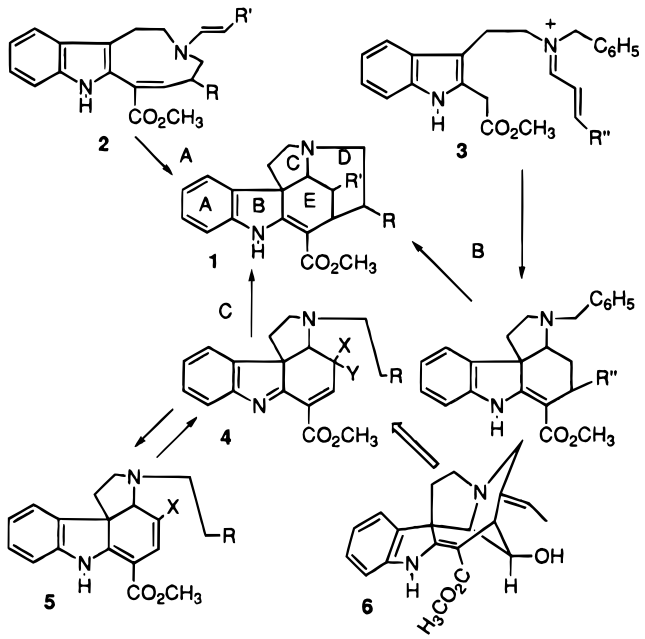
Mossambine (**6**) was obtained by a six-step reaction sequence from the indoloazepine ester **7**. Radical cyclization of the tetracyclic vinyl iodide **12a** provided a racemic pentacyclic ketone **16*E***, which could be converted to either enantiomer by condensation with (*S* or *R*)-*N*,*S*-dimethyl-*S*-phenylsulfoximine and selective pyrolysis of the resulting diastereomeric alcohols **18** and **19** or **20** and **21**. Selective reductions of the resolved (or racemic) ketone **16*E*** provided mossambine (**6**) and its hydroxy epimer **17**.

We have previously described two alternative strategies for the syntheses of strychnos alkaloids (**1**, R = alkyl, R′ = H), namely the intramolecular Diels−Alder cyclizations of indoloacrylate enamines (**2**, path A, Scheme 1), which could also be applied to syntheses of aspidospermatan alkaloids (**1**, R = H, R′ = alkyl), and a tandem cyclization−sigmatropic rearrangement sequence (**3**, path B). The key consideration in these reaction sequences was a direct generation of the vinylogous urethane function that is ubiquitous to the majority of the pentacyclic alkaloids of these classes. Thus, we were able to synthesize dihydroakuammicine and its C-20 epimer (**1**, R = Et, R′ = H),[2] tubotaiwine (**1**, R = H, R′ = Et),[2] echitamidine and its C-20 and C-19 epimers (**1**, R = CH(OH)CH_3, R′ = H),[3] lagunamine (**1**, R = H, R′ = CH(OH)CH_3),[4] and condylocarpine (**1**, R = H, R′ = $CHCH_3$)[4] by path A and echitamidine and akuammicine (**1**, R = $CHCH_3$, R′ = H)[5] by path B, and we could also obtain a total synthesis of strychnine[6,7] by subsequent reduction of the vinylogous urethane function derived from path B.

Before embarking on these syntheses, we had explored an alternative formation of the pentacyclic strychnos alkaloid skeleton, which was based on cyclization of ring D *seco* precursors **4**. This concept has since provided very successful syntheses of strychnine by Stork[8] and Rawal,[9] when applied to corresponding dihydro compounds (dihydro **4**, X = Y = H, amine in place of imine). However, to satisfy our goal of maintaining the vinylogous urethane function of the pentacycle **1**, it seemed clear that at the imine oxidation level **4**, a tautomerization to a conjugated enamine **5** had to be avoided (e.g., **4**, X = Y ≠ H). A carbonyl, or masked carbonyl group at C-14, suggested itself as a suitable blocking group for maintaining the imine and acrylate functionalities of a cyclization precursor **4**, and mossambine (**6**),[10] a C-14 hydroxylated pentacyclic alkaloid, albeit of uncertain stereochemistry, seemed an interesting target for testing this synthetic strategy. While syntheses of strychnos alkaloids have received much recent attention,[11] there have been no other entries into C-14-oxygenated structures.

Scheme 1



N^b-Alkylation of the indoloazepine **7** (Scheme 2),[12] which was obtained in three steps from tryptamine (43% overall yield), with (*Z*)-1-bromo-2-iodo-2-butene[13] provided a 70% yield of the allylic amine **8a**. Pyrolysis of this azepine in refluxing toluene, in the presence of 2-acetoxyacetaldehyde, led to transient generation of an enamine acrylate **9a** and its cyclization, with stereose-

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(1) Preliminary communication: Kuehne, M. E.; Wang, T.; Seraphin, D. *Synlett* **1995**, 557.

(2) Kuehne, M. E.; Frasier, D. A.; Spitzer, T. D. *J. Org. Chem.* **1991**, *56*, 2696.

(3) Kuehne, M. E.; Brook, C. S.; Frasier, D. A.; Xu, F. *J. Org. Chem.* **1994**, *59*, 5977.

(4) Kuehne, M. E.; Brook, C. S.; Frasier, D. A.; Xu, F. *J. Org. Chem.* **1995**, *60*, 1864.

(5) Kuehne, M. E.; Xu, F.; Brook, C. S. *J. Org. Chem.* **1994**, *59*, 7803.

(6) Parsons, R. L.; Berk, J. D.; Kuehne, M. E. *J. Org. Chem.* **1993**, *58*, 7482.

(7) Kuehne, M. E.; Xu, F. *J. Org. Chem.* **1993**, *58*, 7490.

(8) Stork, G. Lecture at Ischia School of Organic Chemistry, Ischia Porto, Italy, Sept 21, 1992.

(9) Rawal, V. H.; Iwasa, S. *J. Org. Chem.* **1994**, *59*, 2685.

(10) (a) Stauffacher, D. *Helv. Chim. Acta* **1961**, *44*, 2006. (b) Monseur, X.; Goutarel, R.; LeMen, J.; Wilson, J.; Budzikiewicz, H.; Djerassi, C. *Bull. Soc. Chim. Fr.* **1962**, 1088.

(11) Bosch, J.; Bonjoch, J.; Amat, M. In *The Alkaloids*; Cordell, G. A., Ed.; Academic Press: New York, 1996; Vol. 48, p 75.

(12) Kuehne, M. E.; Bohnert, J. C.; Bornmann, W. G.; Kirkemo, C. L.; Kuehne, S. E.; Seaton, P. J.; Zebovitz, T. C. *J. Org. Chem.* **1985**, *50*, 919.

(13) (a) Ensley, H. E.; Buescher, R. R.; Lee, K. *J. Org. Chem.* **1982**, *47*, 404. (b) For methodology see: Corey, E. J.; Kirst, H. A.; Katzenellenbogen, J. A. *J. Am. Chem. Soc.* **1970**, *92*, 6314.

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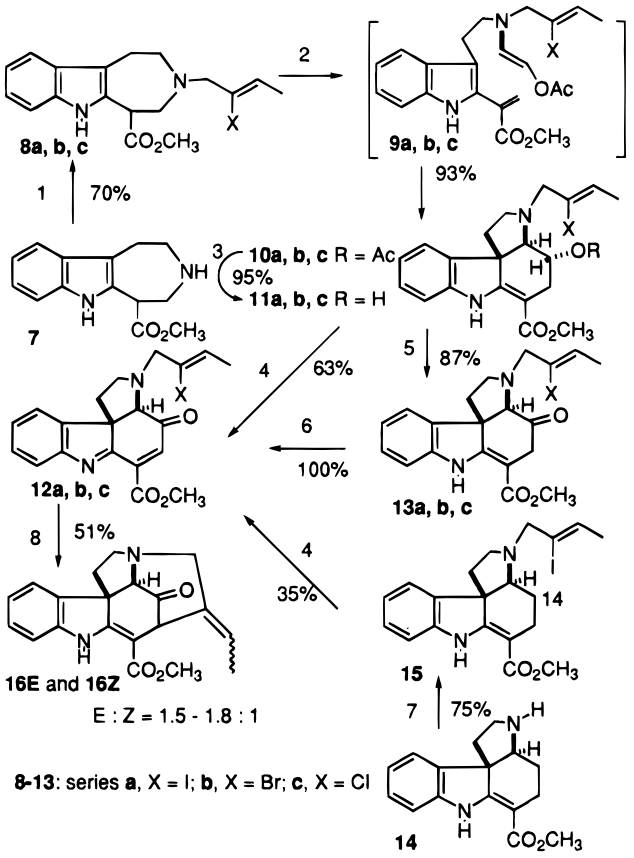
Scheme 2[a]



[a] For series **a**, X = I: (1) (*Z*)-1-bromo-2-iodo-2-butene, K_2CO_3, Et_3N, acetone, rt, 3 h; (2) $AcOCH_2CHO$, toluene, reflux, 2 h; (3) K_2CO_3, $MeOH/H_2O$; (4) $(PhSeO)_2O$, benzene, reflux, 30 min; (5) TFAA−DMSO−Et_3N, CH_2Cl_2, −70 °C; (6) *t*-BuOCl, Et_3N, CH_2Cl_2 0 °C; (7) (*Z*)-1-bromo-2-iodo-2-butene/THF; (8) Bu_3SNH, AIBN, benzene, 85 °C.

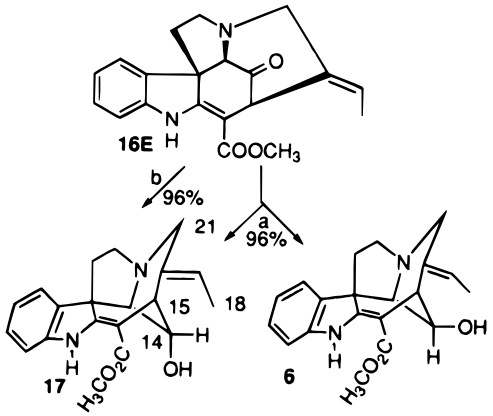
lective formation of the tetracyclic acetate **10a**, in 93% yield.[14] Hydrolysis of the acetate gave the corresponding alcohol **11a** (95%) and oxidation of this vinylogous urethane with phenylseleninic anhydride[15−17] then provided the imino enone **12a** (63%).

This key cyclization precursor could also be obtained, in better overall yield, by Swern oxidation of the alcohol **11a** (87%) and reaction of the resulting ketone **13a** with *tert*-butyl hypochlorite and triethylamine (100%).

In a third sequence to the imino enone **12a** the tetracyclic amine **14**[18] was alkylated with (*Z*)-1-bromo-2-iodo-2-butene (75%). The resulting vinylogous urethane **15a**, on reaction with phenylseleninic anhydride, then also led to oxygenation at C-14 and formation of the imino acrylate **12a** (35%).

A radical cyclization of the tetracyclic iodide **12a** could now be induced by its reaction with tri-*n*-butyltin hydride in refluxing benzene. The pentacyclic vinylogous urethane product was reproducibly obtained in at least 51% yield as a 1.5−1.8:1 *E*:*Z* mixture of olefin isomers **16*E*** and **16*Z***. Crystallization provided the pure *E* isomer from chromatographically enriched fractions.

Scheme 3[a]



[a] Key: (a) $NaBH_4$, $CeCl_3$, MeOH/THF (1:1), **6**:**17** (5:1), pure mossambine (**6**) was then obtained by crystallization from methanol; (b) L-Selectride/THF, 0 °C.

Attempted radical cyclizations of the bromo and chloro analogues **12b** and **12c**, prepared in analogy to formation of the iodo compound **12a**, did not yield more than traces of the pentacyclic products **16*E*** and **16*Z***.

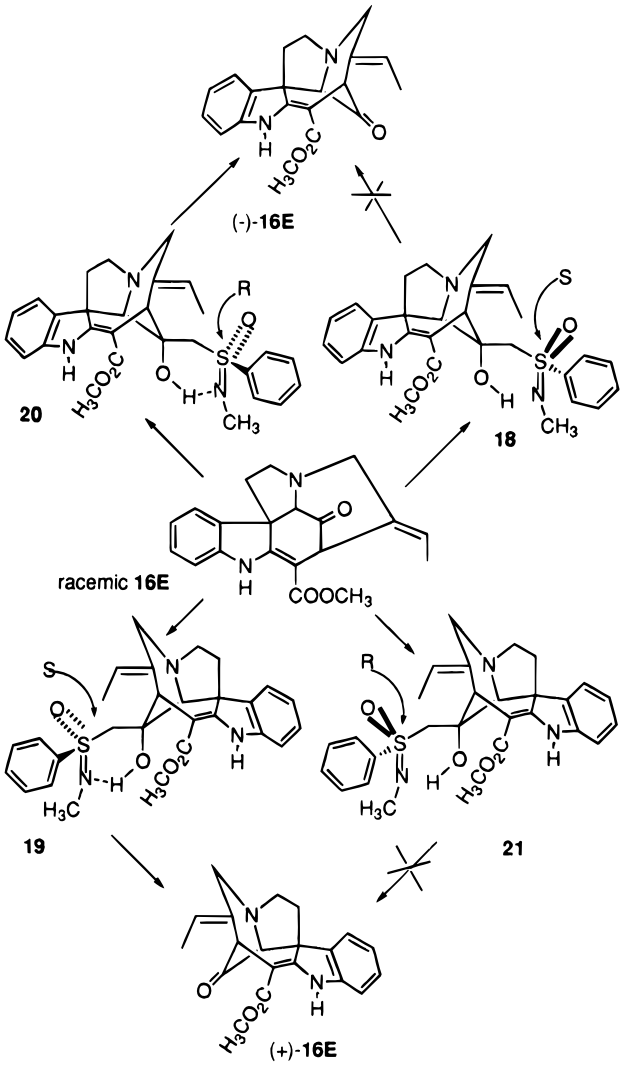
Reduction of the major ketonic olefin isomer **16*E*** with sodium borohydride and ceric chloride (Scheme 3) gave racemic mossambine ((±)-**6**) and its hydroxy epimer (±)-**17** in a ratio of 5:1 (96%). Alternatively, the epimer (±)-**17** could be formed exclusively (96%) with L-Selectride (Aldrich).

The relative stereochemistry of the hydroxyl function in the epimers (±)-**6** and (±)-**17** was established by NMR NOE experiments, which showed interaction of the hydrogens at C-14 β (δ 4.47) and C-21 α (δ 3.77) in 14-*epi*-mossambine (±**17**), but not in mossambine ((±)-**6**). NOE coupling of the C-18 methyl group (δ 1.78) with the C-15 methine hydrogen (δ 3.95 in (±)-**6** and δ 4.17 in (±)-**17**), expected for the *E*-olefins, was also observed as well as coupling of the olefinic C-19 hydrogen (δ 5.74) with the C-21 α hydrogen (δ 3.50) in mossambine ((±)-**6**). Comparison of an NMR spectrum of natural mossambine with spectra of the synthetic product (±)-**6** showed a good match, with the C-14 α hydrogen signal at δ 3.72, whereas the epimer (±)-**17** displayed the C-14 β hydrogen signal at δ 4.47. These NMR data allowed stereochemical assignment to the natural product.

In order to obtain a chiral resolution of the synthetic products, the racemic ketone **16*E*** was treated with [(*S* or *R*)-(*N*-methylphenylsulfonimidoyl)methyl]lithium at −78 °C.[19] The diastereomeric C-14 alcohol product pairs (1:1) **18** and **19** or **20** and **21**, respectively (Scheme 4), could be separated by chromatography. When they were heated at 150 °C under vacuum, the C-14 (*S*)−S (*S*) compound **19** reverted to the ketone (+)-**16*E*** with $[\alpha]^{24}_D$ +779°, while the C-14 (*R*)−S (*S*) diastereomer **18** was recovered unchanged. Analogously, the C-14 (*R*)−S (*R*) alcohol **20** decomposed to the ketone (−)-**16*E*** with $[\alpha]^{24}_D$ −783°, while its diastereomer **21** resisted cleavage. It was thus possible to selectively generate either pure natural ($[\alpha]^{25}_D$ −) or unnatural ($[\alpha]^{25}_D$ +) mossambine (**6**) by subsequent reduction of the ketone. This method allows the selective generation of either enantiomer of mossambine from the racemic ketone **16*E*** without separation of intermediate diastereomers by chromatography or crystallization.

(14) For methodology see: Kuehne, M. E.; Kuehne, S. E. *J. Org. Chem.* **1993**, *58*, 4147.
(15) Danieli, B.; Lesma, G.; Palmisano, G.; Riva, R. *J. Chem. Soc., Chem. Commun.* **1984**, 909.
(16) Kuehne, M. E.; Podhorez, D. E.; Mulamba, T.; Bornmann, W. G. *J. Org. Chem.* **1987**, *52*, 347.
(17) Danieli, B.; Lesma, G.; Palmisano, G.; Passarella, D.; Silvani, A. *Tetrahedron* **1994**, *50*, 6941.
(18) Kuehne, M. E.; Matsko, T. H.; Bohnert, J. C.; Motyka, L.; Oliver-Smith, D. *J. Org. Chem.* **1981**, *46*, 2002.
(19) (a) Johnson, C. R.; Zeller, J. R. *Tetrahedron* **1984**, *40*, 1225. (b) Johnson, C. R. *Aldrichim. Acta* **1985**, *18*, 3.

Scheme 4



The selective pyrolyses of iminosulfoxides **19** and **20** can be seen (Figure 1) as the result of a favored conformation with steric and stereoelectronic optimization of the C−C bond cleavage, if one considers the alternatives for relative orientation of the sulfoxide vs S-phenyl bonds.

For a possible alternative to the radical cyclization of the vinyl iodide enone **12a**, the ketone **13a** was converted to its trimethylsilyl enol ether derivative **22a** (Scheme 5). However, from treatment of this compound with tri-*n*-butyltin hydride only the tertiary alcohol *E* and *Z* olefin isomers **23** and **24** were obtained in low yield (10%). The corresponding vinyl bromide **22b** gave a somewhat higher yield (18%) of these products.

Still better yields of these cyclization products were obtained from reactions of bromo and chloro ketones **13b** and **13c** with bis(1,5-cyclooctadiene)nickel,[20,21] where **23** and **24** were obtained 1:1, in 72% yield, and 1:1.4, in 53% yield, respectively. These are the first examples of intramolecular reactions of vinyl halides with a ketone, induced by this nickel reagent. With $NiCl_2/CrCl_2$ and the iodide **13a** an 86% yield of the pure *Z*-isomer **24** was obtained.

(20) Bonjoch, J.; Solé, D.; Bosch, J. *J. Am. Chem. Soc.* **1995**, *117*, 11017.

(21) Solé, D.; Cancho, Y.; Llebaria, A.; Moreto, J. M.; Delgado, A. *J. Am. Chem. Soc.* **1994**, *116*, 12133.

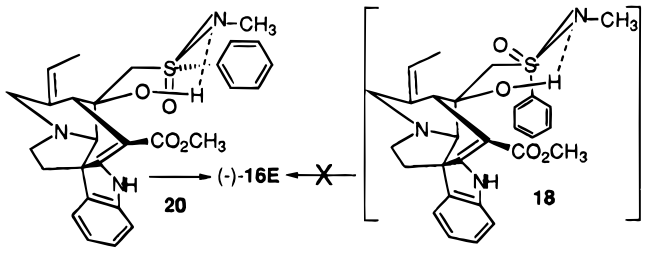
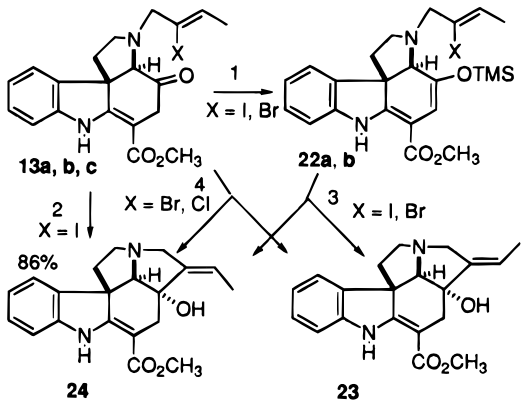


Figure 1.

Scheme 5[a]



[a] (1) TMSTfI, Et_3N, rt; (2) $NiCl_2/CrCl_2$, DMSO, rt; (3) Bu_3SnH, AIBN, 85 °C; (4) $(COD)_2Ni$, Et_3N, MeCN, rt.

Experimental Section

(±)-(3a*R,11b*R**)-Methyl 3-[(*Z*)-(2-Iodo-2-butenyl)]-2,3,3a,4,5,7-hexahydro-1*H*-pyrrolo[2,3-*d*]carbazole-6-carboxylate (15a).** A mixture of 10.31 g of 2-butyn-1-ol (0.147 mol), 20 mL of tri-*n*-butyltin hydride (74.35 mmol) and 0.3 g of AIBN was heated in an oil bath at 85 °C for 2 h. Distillation under vacuum then gave 21.45 g of (*Z*)-2-(tri-*n*-butylstannyl)-2-buten-1-ol (80%): bp 130−133 °C/0.2 mm.[13a]

To 10.0 g of (Z)-2-(tri-*n*-butylstannyl)-2-buten-1-ol (27.7 mmol) in 200 mL of carbon tetrachloride in an ice bath was added 8.5 g of iodine (67 mmol) in one portion. After the mixture was stirred for 10 min, 50 mL of 10% sodium bisulfite was added. The aqueous layer was extracted with 2 × 100 mL of ether. The combined organic layers were washed with brine, dried (Na_2SO_4), and concentrated under vacuum. The residue was purified on a SiO_2 flash column (20% to 50% ether/hexane) to give 4.13 g of pure (*Z*)-2-iodobuten-1-ol[13a] followed by 0.657 g of a 2:1 *Z*/*E* mixture (the ratio was determined by integration of the well-resolved vinylic proton in the ^1H NMR spectrum). Total 4.787 g (87%) of *Z*-isomer: TLC (ethyl ether/hexane, 1:1) $R_f = 0.46$; ^1H NMR (500 MHz, $CDCl_3$) δ 5.97 (qt, $J = 6.5$, 1.5 Hz, 1 H), 4.25 (dt, $J = 6.5$, 1 Hz, 2 H), 1.84 (t, $J = 6.7$ Hz, 1 H), 1.80 (dt, $J = 6$, 1 Hz, 3 H).

To a solution of 1.268 g (6.40 mmol) of (*Z*)-2-iodo-2-buten-1-ol in 15 mL of dry ethyl ether was added 0.24 mL (2.5 mmol) of phosphorus tribromide at 0 °C. The mixture was stirred for 22 h. Then 30 mL of cold aqueous potassium carbonate was added. After separation and extraction with 2 × 30 mL of ether, the combined ether layers were washed with brine and dried (Na_2SO_4). Concentration under vacuum then gave 1.241 g of the bromoiodide.[13b] It was directly used in the following alkylation.

A mixture of 0.578 g (2.14 mmol) of the tetracyclic amine **14**[18] and 0.649 g (2.40 mmol) of the above bromoiodide, in 20 mL of THF, was stirred at rt for 24 h and at 50 °C for 5 h. After addition of 0.5 g of potassium carbonate and 0.5 mL of water, stirring was continued at rt overnight. Removal of THF under vacuum gave a residue, which was partitioned between 50 mL of water and 50 mL of dichloromethane. The water layer was extracted with 2 × 20 mL of dichloromethane, and the combined dichloromethane solutions were dried (Na_2SO_4) and concentrated. Column chromatography on silica gel with

9:1 hexane/ethyl acetate then gave 0.718 g of the N^b-alkylated product as a white foam (75%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.93 (br s, 1 H), 7.20 (d, J = 7.4 Hz, 1 H), 7.15 (t, J = 7.7 Hz, 1 H), 6.87 (t, J = 7.4 Hz, 1 H), 6.81 (d, J = 7.7 Hz, 1 H), 5.95 (q, J = 6.3 Hz, 1 H), 3.77 (s, 3 H), 3.71 (br d, J = 13.8 Hz, 1 H), 3.45 (d, J = 13.8 Hz, 1 H), 3.22 (d, J = 4.6 Hz, 1 H), 2.98 (dd, J = 8.7, 6.6 Hz, 1 H), 2.64−2.56 (m, 2 H), 2.35 (td, J = 13.8, 2.8 Hz, 1 H), 2.02 (td, J = 11.9, 6.5 Hz, 1 H), 1.90 (br d, J = 13.3 Hz, 1 H), 1.81 (d, J = 6.3 Hz, 3 H), 1.74 (dd, J = 11.8, 4.7 Hz, 1 H), 1.04 (dt, J = 13.2, 4.2 Hz, 1 H; ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.31, 164.94, 143.13, 137.27, 130.89, 127.64, 211.94, 120.21, 110.03, 108.97, 95.56, 65.59, 65.30, 55.48, 50.69, 49.80, 42.69, 29.26, 21.55, 18.49; IR (film) ν_{max} 3377, 3053, 2945, 2914, 2853, 2793, 1733, 1677, 1477, 1465, 1438, 1302, 1276, 1248, 1241, 1190, 1087, 1058, 782, 745 cm^{-1}; UV (EtOH) λ_{max} 210, 226, 298, 328 nm; MS *m/z* (rel intens) 450 (12), 351 (3), 323 (4), 254 (2), 237 (4), 236 (43), 228 (25), 227 (100), 214 (11), 210 (5), 209 (6), 194 (5), 182 (8), 181 (12), 168 (10), 167 (13), 154 (16), 143 (6), 127 (5), 98 (5); high-resolution MS, EI ionization, calcd for $C_{20}H_{23}N_2O_2I$ 450.0804, found 450.0807.

Methyl 3-(2-Iodobut-2-en-1-yl)-1,2,3,4,5,6-hexahydroazepino[4,5-*b*]indole-5-carboxylate (8a). To 3.50 g (14.3 mmol) of the indoloazepine **7** in 80 mL of acetone were added 4.60 g of 1-bromo-2-iodo-2-butene (see above, 17 mmol), 6 g of potassium carbonate, and 6 mL of triethylamine. After vigorous stirring at room temperature for 3 h, the reaction mixture was filtered and the residue washed with acetone. The filtrate was concentrated and purified by flash silica gel chromatography, eluting with 1:1 ethyl ether/hexane to give 4.23 g of the alkylated azepine **8a** (70%) as a white powder. An analytical sample, crystallized from methanol, had mp 130−131 °C: TLC (SiO_2, 2:1 ethyl ether/hexane) R_f = 0.40 (CAS spray, blue); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.32 (br s, 1 H), 7.47 (d, J = 7.7 Hz, 1 H), 7.26 (d, J = 7.7 Hz, 1 H), 7.12 (t, J = 7.5 Hz, 1 H), 7.08 (t, J = 7.5 Hz, 1 H), 5.89 (q, J = 6.4 Hz, 1 H), 4.01 (dd, J = 7, 2.4 Hz, 1 H), 3.76 (s, 3 H), 3.52−3.45 (m, 2 H), 3.40 (dd, J = 13.2, 7.1 Hz, 1 H), 3.17 (dd, J = 13.2, 2.6 Hz, 1 H), 3.02−2.98 (m, 1 H), 2.94−2.91 (m, 2 H), 2.81−2.77 (m, 1 H), 1.82 (d, J = 6.4 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.46, 134.83, 131.96, 128.53, 121.52, 119.22, 117.99, 114.03, 110.67, 109.59, 68.69, 56.00, 54.30, 52.46, 45.77, 24.17, 21.71; IR (film) ν_{max} 3396, 3057, 2948, 2913, 2825, 1730, 1645, 1491, 1462, 1434, 1374, 1341, 1251, 1207, 1163, 1139, 1029, 917, 813, 745, 720 cm^{-1}; UV (EtOH) λ_{max} 208, 228, 284, 294 nm; MS *m/z* (rel intens) 424 (5), 298 (3), 297 (20), 265 (1), 243 (2), 229 (1), 228 (8), 223 (3), 216 (4), 215 (8), 214 (12), 202 (19), 183 (11), 181 (13), 170 (10), 169 (32), 156 (30), 155 (14), 154 (42), 128 (20), 127 (22), 115 (13), 96 (69), 69 (16), 54 (65), 53 (100). Anal. Calcd for $C_{18}H_{21}N_2O_2I$: C, 50.96; H, 4.99; N, 6.60; I, 29.91. Found: C, 51.02; H, 4.96; N, 6.49; I, 29.74.

(±)-(3a*R,4*R**,11b*R**)-Methyl 3-((*Z*)-2-Iodobut-2-en-1-yl)-2,3,3a,4,5,7-hexahydro-4-acetoxy-1*H*-pyrrolo[2,3-*d*]-carbazole-6-carboxylate (10a).** The indoloazepine (**8a**) (3.78 g, 8.91 mmol) and 6.8 mL of a 1.45 N acetoxyacetaldehyde[22] solution in dichloromethane (9.86 mmol, 1.1 equiv) were mixed with 70 mL of dry toluene. After being connected to a Dean−Stark trap filled with 4 Å molecule sieves, the mixture was heated at reflux for 2 h. Cooling, and removal of solvents under vacuum, gave a residue, which was triturated with ether to give 2.337 g of product as a white powder. The ether filtrate was concentrated and the residue was flash chromatographed on silica gel, eluting with 1:1 ethyl ether/hexane to afford another 1.881 g of pure product: total product 4.218 g; yield 93%; mp 165−165.5 °C (needles from ethanol); TLC (SiO_2, ethyl ether/hexane, 2:1) R_f = 0.44 (CAS, blue); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.00 (br s, 1 H), 7.18 (t, J = 7.7 Hz, 1 H), 7.15 (d, J = 7.3 Hz, 1 H), 6.90 (t, J = 7.4 Hz, 1 H), 6.85 (d, J = 7.7 Hz, 1 H), 5.95 (q, J = 6.4 Hz, 1 H), 5.05 (bs, 1 H), 4.03 (d, J = 13.9 Hz, 1 H), 3.78 (s, 3 H), 3.52 (d, J = 13.9 Hz, 1 H), 3.14 (br s, 1 H), 3.04−2.98 (m, 2 H), 2.70−2.64 (m, 2 H), 2.08 (td, J = 12.0, 6.6 Hz, 1 H), 1.84 (s, 3 H), 1.81 (d, J = 6.4 Hz, 3 H), 1.75 (dd, J = 12.0, 4.8 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.74, 168.89, 163.90, 143.21, 137.04, 131.67, 128.05, 122.21, 120.62, 109.52, 109.35, 89.06, 71.21, 70.06, 65.27, 54.79, 50.98, 49.93, 41.75, 23.75, 21.68, 21.32; IR (film) ν_{max} 3374, 2949, 2851, 1729, 1681, 1613, 1482, 1466, 1375, 1279, 1251, 1213, 1200, 1134, 1089, 1029, 799, 746 cm^{-1}; UV (EtOH) λ_{max} 206, 226, 298, 326 nm; MS *m/z* (rel intens) 509 (4.8, M + 1), 508 (21, M), 449 (10), 448 (43), 422 (19), 322 (11), 321 (49), 295 (9), 294 (84), 289 (8), 286 (28), 285 (25), 267 (8), 264 (14), 259 (12), 253 (7), 252 (63), 243 (11), 235 (9), 228 (29), 227 (21), 226 (77), 225 (52), 224 (66), 217 (28), 214 (20), 207 (17), 206 (14), 196 (18), 195 (27), 194 (28), 193 (34), 182 (20), 181 (35), 180 (40), 169 (24), 168 (67), 167 (77), 166 (10), 165 (11), 155 (15), 154 (68), 128 (18), 127 (34), 124 (19), 115 (20), 114 (24), 96 (78), 84 (26), 82 (18), 72 (78), 70 (18), 69 (22), 55 (21), 54 (75), 53 (100). Anal. Calcd for $C_{22}H_{25}N_2O_4I$: C, 51.98; H, 4.96; N, 5.51; I, 24.96. Found: C, 52.11; H, 4.90; N, 5.38; I, 25.30.

(±)-(3a*R,4*R**,11b*R**)-Methyl 3-((*Z*)-2-Iodobut-2-en-1-yl)-2,3,3a,4,5,7-hexahydro-4-hydroxy-1*H*-pyrrolo[2,3-*d*]-carbazole-6-carboxylate (11a).** A mixture of 1.39 g of the acetate **10a** (2.73 mmol), 0.400 g of potassium carbonate (2.89 mmol), 40 mL of methanol, and 2.5 mL of water was heated at reflux for 30 min. The reaction mixture was cooled and concentrated. To the residue was added 50 mL of water. After extraction with 3 × 50 mL of dichloromethane, drying (Na_2SO_4), and concentration, the residue was purified on a flash SiO_2 column, eluting with 4:1 ethyl ether:hexane. Thus, 1.212 g of pure alcohol **11a** was obtained (yield 95%), with mp 173−174 °C, from ethanol: TLC (ethyl ether/hexane, 5:1) R_f = 0.31 (CAS, blue); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.02 (br s, 1 H), 7.16−7.13 (m, 2 H), 6.89 (t, J = 7.4 Hz, 1 H), 6.82 (d, J = 8.1 Hz, 1 H), 5.95 (q, J = 6.3 Hz, 1 H), 4.01 (br s, 1 H), 3.78 (d, J = 13.8 Hz, 1 H), 3.74 (s, 3 H), 3.51 (d, J = 13.8 Hz, 1 H), 3.09 (s, 1 H), 3.01 (dd, J = 8.7, 6.5 Hz, 1 H), 2.94 (ddd, J = 16, 3.2, 2 Hz, 1 H), 2.69 (dd, J = 16, 2 Hz, 1 H), 2.66−2.61 (m, 1 H), 2.05 (ddd, J = 12.1, 12.1, 6.5 Hz, 1 H), 1.81 (d, J = 6.3 Hz, 3 H), 1.71 (dd, J = 11.9, 4.7 Hz, 1 H), 1.60 (br d, J = 6.0 Hz, 1 H, OH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.03, 164.51, 142.95, 137.19, 131.51, 127.90, 122.05, 120.71, 109.68, 109.39, 87.30, 72.78, 68.32, 66.03, 54.68, 50.93, 50.37, 41.67, 26.31, 21.60; IR (film) ν_{max} 3452, 3383, 2976, 2941, 2850, 2788, 1675, 1610, 1482, 1469, 1439, 1386, 1348, 1290, 1249, 1214, 1121, 1088, 1061, 1023, 750 cm^{-1}; UV (EtOH) λ_{max} 206, 228, 300, 326 nm; MS *m/z* (rel intens) 467 (M+1, 2), 466 (M, 5), 448 (7), 422 (8), 339 (4), 321 (6), 253 (9), 252 (100), 244 (10), 243 (47), 226 (16), 195 (12), 181 (16), 180 (13), 169 (14), 168 (30), 167 (25), 154 (47), 128 (10), 127 (18), 115 (18), 96 (23), 72 (45), 70 (17), 54 (44), 53 (77). Anal. Calcd for $C_{20}H_{23}N_2O_3I$: C, 51.51; H, 4.97; N, 6.01. Found: C, 51.54; H, 4.94; N, 5.93.

(±)-(3a*R,11b*R**)-Methyl 3-((*Z*)-2-Iodobut-2-en-1-yl)-2,3,3a,4-tetrahydro-4-oxo-1*H*-pyrrolo[2,3-*d*]carbazole-6-carboxylate (12a).** a. A mixture of 0.415 g of the alcohol **11a** (0.89 mmol) and 0.332 g of benzeneseleninic anhydride (0.92 mmol, 1.04 equiv) in 15 mL of dry benzene was heated at reflux for 15 min. After cooling and evaporation, the residue was purified by flash SiO_2 column, eluting with 1:1 ethyl ether/hexane, to afford 0.257 g of the product **12a** as a brown foam; yield 63%.

b. To a solution of 0.913 g of the tetracyclic ketone **13a** (1.966 mmol) and 0.384 mL of triethylamine (2.76 mmol, 1.4 equiv) in 65 mL of dichloromethane, in an ice bath, was added dropwise 0.282 mL of *tert*-butyl hypochlorite (2.36 mmol, 1.2 equiv). The reaction mixture was stirred at 0 °C for 10 min and then brought to room temperature, diluted with 80 mL of dichloromethane, and washed with brine. After the solution was dried and evaporated under vacuum, 0.987 g of product was obtained. TLC (silica gel, ethyl ether/hexane, 3:1) showed only one spot. The product **12a** was used directly in the next step without further purification.

c. A mixture of 0.197 g (0.44 mmol) of the tetracycle **15** and 0.252 g (0.70 mmol) of phenylseleninic anhydride in 30 mL of dry benzene was stirred at 70 °C for 35 min. After cooling, benzene was removed under vacuum, the residue was dissolved in 15 mL of dichloromethane, and the solution washed twice with saturated aqueous potassium bicarbonate, dried (Na_2SO_4), and concentrated. The residue was flash chromatographed (SiO_2, ethyl acetate/hexane, 1:3) to give 0.070 g (35%) of the imino ketone **12a**.

For **12a**: TLC (ethyl ether/hexane, 3:1) R_f = 0.38 (CAS, blue faded to greenish yellow); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97

(22) Nagasawa, J.; Araki, Y.; Ishido, Y. *J. Org. Chem.* **1981**, *46*, 1734.

(d, J = 7.5 Hz, 1 H), 7.82 (d, J = 7.6 Hz, 1 H), 7.43 (t, J = 7.6 Hz, 1 H), 7.33 (t, J = 7.5 Hz, 1 H), 6.84 (s, 1 H), 6.01 (q, J = 6 Hz, 1 H), 4.24 (d, J = 14 Hz, 1 H), 3.98 (s, 3 H), 3.97 (d, J = 14 Hz, 1 H), 3.49 (s, 1 H), 2.93−2.88 (m, 1 H), 2.46−2.40 (m, 1 H), 2.05−2.00 (m, 1 H), 1.79 (d, J = 6 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.74, 172.86, 164.15, 154.68, 144.42, 138.68, 135.59, 133.02, 128.65, 127.51, 124.09, 122.74, 108.17, 71.03, 64.13, 63.74, 53.19, 47.96, 34.73, 21.65; IR (film) ν_{max} 2949, 2850, 2831, 1737, 1678, 1607, 1467, 1438, 1264, 1208, 1142, 912, 771, 733 cm^{-1}; UV (EtOH) λ_{max} 208, 244, 274, 338 nm; MS m/z (rel intens) 463 (M + 1, 3), 462 (M, 14), 351 (3), 335 (13), 279 (5), 254 (25), 253 (14), 222 (30), 221 (22), 195 (16), 194 (22), 193 (14), 181 (10), 180 (16), 168 (17), 167 (24), 166 (23), 154 (15), 127 (23), 115 (49), 89 (13), 55 (13), 54 (60), 53 (100); high-resolution MS, EI ionization, calcd for $C_{20}H_{19}N_2O_3I$ 462.0440, found 462.0428.

(±)-(3a*R,11b*R**)-Methyl 3-((*Z*)-2-Iodobut-2-en-1-yl)-2,3,3a,4,5,7-hexahydro-4-oxo-1*H*-pyrrolo[2,3-*d*]carbazole-6-carboxylate (13a).** To a solution of 0.52 mL of DMSO (7.33 mmol, 3.6 equiv) in 50 mL of dichloromethane, at −70 °C, was added dropwise 0.863 mL of trifluoroacetic anhydride (6.11 mmol, 3 eq). After 20 min, 0.950 g of the tetracyclic alcohol **11a** (2.04 mmol) in 20 mL of dichloromethane was added at −65 to −70 °C. Stirring was continued at the same temperature for 1 h before addition of 2.84 mL of triethylamine (20.1 mmol, 10 equiv). After being stirred for 2 h, the reaction mixture was gradually warmed to rt. The mixture was diluted with 100 mL of dichloromethane, washed with saturated aqueous sodium bicarbonate, and dried (Na_2SO_4). Removal of solvents under vacuum gave a residue, which was purified by flash SiO_2 column (2:1 hexane/ethyl ether) to give 0.824 g of the ketone **13a** (87%). Continuing elution with ether/hexane (4:1) gave 0.099 g of the starting material **11a** (10% recovery). For the ketone **13a**, mp 134−135 °C (ether/hexane): TLC (ethyl ether/hexane, 1:1) R_f = 0.43 (CAS, greenish blue); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.14 (br s, 1 H), 7.44 (d, J = 7.4 Hz, 1 H), 7.16 (t, J = 7.7 Hz, 1 H), 6.91 (t, J = 7.5 Hz, 1 H), 6.80 (d, J = 7.7 Hz, 1 H), 5.95 (q, J = 6.4 Hz, 1 H), 3.77 (d, J = 14 Hz, 1 H), 3.74 (s, 3 H), 3.72 (dd, J = 14, 1 Hz, 1 H), 3.51 (d, J = 17.1 Hz, 1 H), 3.32 (dd, J = 17.1, 1.7 Hz, 1 H), 3.20 (d, J = 1 Hz, 1 H), 3.06−2.98 (m, 2 H), 2.55 (dt, J = 12.6, 8.6 Hz, 1 H), 2.04 (ddd, J = 12.6, 12.6, 2.9 Hz, 1 H), 1.79 (d, J = 6.4 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 206.00, 167.65, 162.34, 143.41, 135.68, 132.49, 128.36, 123.03, 121.36, 109.28, 108.01, 87.80, 67.92, 63.69, 57.57, 51.06, 50.28, 40.14, 35.85, 21.61; IR (film) ν_{max} 3373, 3056, 3019, 2980, 2949, 2913, 2851, 2809, 2252, 1714, 1690, 1683, 1635, 1617, 1597, 1480, 1469, 1436, 1385, 1244, 1137, 1045, 910, 733 cm^{-1}. UV (EtOH) λ_{max} 206, 226, 300, 330 nm; MS m/z (rel intens) 465 (M + 1, 7), 464 (M, 17), 437 (14), 436 (90), 377 (9), 376 (13), 352 (3), 351 (28), 349 (10), 309 (23), 256 (10), 255 (72), 249 (13), 228 (25), 227 (50), 224 (6), 223 (20), 221 (7), 214 (49), 209 (7), 197 (6), 196 (28), 195 (50), 194 (50), 182 (16), 181 (46), 180 (15), 170 (14), 169 (38), 168 (91), 167 (100), 166 (19), 160 (13), 155 (12), 154 (75), 143 (15), 142 (12), 141 (18), 140 (45), 128 (19), 127 (35), 115 (43), 96 (18), 89 (14), 86 (12), 84 (26), 82 (12), 77 (24), 63 (11); high-resolution MS, EI ionization, calcd for $C_{20}H_{21}N_2O_3I$ 464.0597, found 464.0587.

(±)-(19,20*E* and -*Z*)-14-Oxoakuammicine (16*E* and 16*Z*). A solution of 0.987 g of the imino ketone **12a**, obtained from the above hypochlorite procedure, and 10 mg of AIBN, in 131 mL of dry benzene, was degassed with argon for 10 min and then immersed into an oil bath at 85 °C. A solution of 1.85 mL of tri-*n*-butyltin hydride (6.88 mmol, 3.5 eq) and 240 mg of AIBN in 12 mL of benzene was added to the above solution by a syringe pump over 12 h. After cooling, the solvent was removed under reduced pressure and the residue was purified by flash SiO_2 column, eluting with 75:25:0.5 ethyl acetate/hexane/triethylamine. Collection of the appropriate fractions gave two fractions: the first fraction, 0.145 g, *E*-isomer/*Z*-isomer 1:2.5 (determined by ^{1}H NMR) and the second fraction, 0.193 g, *E*-isomer/*Z*-isomer 5.5:1. Total 0.338 g (51% over last two steps). Crystallization of the second fraction from methanol gave 58 mg of pure *E*-isomer, which had mp 215−216 °C: TLC (ethyl acetate/hexane/triethylamine, 9:1:0.5) R_f = 0.40 (CAS, blue); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.09 (br s, 1 H), 7.17−7.14 (m, 2 H), 6.90 (t, J = 7.5 Hz, 1 H), 6.79 (d, J = 7.8 Hz, 1 H), 5.57 (qt, J = 6.9, 2 Hz, 1 H), 4.21 (br s, 1 H), 3.84 (d, J = 2 Hz, 1 H), 3.78 (s, 3 H), 3.74 (dd, J = 15, 2 Hz, 1 H), 3.44−3.38 (m, 1 H), 3.30−3.25 (m, 1 H), 3.20 (d, J = 15 Hz, 1 H), 3.08−3.02 (m, 1 H), 2.06−2.02 (m, 1 H), 1.63 (dt, J = 6.9, 1.8 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 211.08, 167.33, 166.03, 143.67, 138.86, 135.56, 128.53, 123.08, 121.81, 121.00, 109.96, 95.39, 66.99, 63.85, 59.10, 57.67, 51.37, 47.99, 46.51, 12.91; IR (film) ν_{max} 3353, 2951, 2855, 1743, 1727, 1675, 1596, 1476, 1465, 1435, 1384, 1282, 1239, 1198, 1169, 1095, 1061, 1038, 955, 909, 781, 763, 740, 663 cm^{-1}; UV (EtOH) λ_{max} 206, 230, 300, 316, 340 nm; MS m/z (rel intens) 337 (M + 1, 14), 336 (M, 61), 308 (65), 307 (33), 293 (50), 277 (17), 276 (18), 275 (29), 261 (30), 252 (24), 250 (14), 249 (63), 248 (25), 247 (41), 241 (19), 238 (16), 235 (58), 234 (26), 233 (23), 232 (18), 231 (13), 221 (29), 220 (37), 219 (26), 206 (48), 205 (32), 204 (42), 194 (35), 193 (33), 192 (30), 191 (38), 180 (38), 154 (69), 149 (84), 139 (46), 138 (35), 128 (31), 121 (100), 115 (47), 111 (90), 108 (84), 84 (95), 77 (48), 71 (47), 69 (40); high-resolution MS, EI ionization, calcd for $C_{20}H_{20}N_2O_3$ 336.1474, found 336.1481.

A pure *Z*-isomer sample was obtained by flash chromatographic purification (SiO_2, 30:70:0.5, hexane/ethyl acetate/triethylamine): TLC (ethyl acetate/hexane/triethylamine, 90:10:0.5) R_f = 0.48 (CAS, blue); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.87 (br s, 1 H), 7.16−7.12 (m, 2 H), 6.89 (t, J = 7.5 Hz, 1 H), 6.78 (d, J = 7.7 Hz, 1 H), 5.70 (q, J = 6.9 Hz, 1 H), 4.04 (br s, 1 H), 3.95 (d, J = 2.3 Hz, 1 H), 3.80 (s, 3 H), 3.65 (d, J = 15.6 Hz, 1 H), 3.43 (br d, J = 15.6 Hz, 1 H), 3.32−3.27 (m, 1 H), 3.20−3.15 (m, 1 H), 2.78−2.73 (m, 1 H), 2.08−2.03 (m, 1 H), 1.67 (d, J = 6.9 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 212.21, 167.66, 164.77, 144.11, 138.45, 133.91, 128.49, 123.06, 121.62, 121.01, 110.03, 98.32, 66.48, 64.34, 54.97, 51.41, 49.94, 48.37, 46.59, 13.17; IR (film) ν_{max} 3357, 2949, 2921, 2854, 1744, 1675, 1604, 1465, 1437, 1381, 1314, 1242, 1200, 1101, 1062, 744 cm^{-1}; UV (EtOH) λ_{max} 206, 234, 298, 334 nm; MS m/z (rel intens) 337 (18), 336 (53), 334 (8), 309 (20), 308 (98), 307 (25), 294 (15), 293 (100), 278 (10), 277 (18), 276 (19), 275 (35), 262 (11), 261 (44), 252 (15), 250 (17), 249 (84), 248 (26), 247 (39), 241 (25), 235 (73), 234 (26), 233 (29), 221 (25), 220 (30), 219 (22), 206 (40), 205 (23), 204 (30), 194 (31), 193 (33), 192 (30), 191 (27), 181 (22), 180 (28), 169 (26), 168 (34), 167 (52), 166 (45), 154 (43), 149 (49), 138 (36), 127 (22), 123 (23), 121 (55), 116 (20), 115 (22), 111 (49), 110 (20), 109 (21), 108 (39), 103 (21), 97 (22), 91 (46), 86 (28), 85 (20), 84 (56), 83 (21), 71 (33), 69 (22), 57 (29), 56 (26), 54 (31).

(±)-Mossambine (6) and Its Enantiomers. To a stirred solution of 15 mg of the *E*-ketone **16*E*** (0.045 mmol) and 22 mg of $CeCl_3$ in 3 mL of methanol and 3 mL of THF, cooled in an ice bath, was added 40 mg of sodium borohydride, by portions, over 30 min. The reaction was brought to room temperature, and 30 mL of saturated aqueous sodium bicarbonate solution was added. Extraction with 4 × 15 mL of chloroform, followed by drying (Na_2SO_4) and evaporation, gave the crude product, which was purified by flash SiO_2 column (70:30:0.5 ethyl acetate/methanol/triethylamine) to afford 14.5 mg of product as a mixture of 1:5 α/β-hydroxy epimers, as determined by ^{1}H NMR (96%). Crystallization of the mixture from methanol then gave 9.3 mg (62%) of pure mossambine as white crystals: mp 219−220 °C; TLC (ethyl acetate/methanol, 1:1) R_f = 0.24 (CAS, blue); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.83 (br s, 1 H), 7.19 (d, J = 7.4 Hz, 1 H), 7.14 (t, J = 7.7 Hz, 1 H), 6.91 (t, J = 7.4 Hz, 1 H), 6.81 (d, J = 7.7 Hz, 1 H), 5.74 (q, J = 6.7 Hz, 1 H), 3.95 (d, J = 3.1 Hz, 1 H), 3.84 (t, J = 2.4 Hz, 1 H), 3.77 (s, 3 H), 3.72 (t, J = 3.1 Hz, 1 H), 3.50 (d, J = 13.2 Hz, 1 H), 3.15 (d, J = 13.2 Hz, 1 H), 2.98 (dd, J = 14.7, 7.1 Hz, 1 H), 2.93−2.86 (m, 2 H), 1.86 (dd, J = 11.9, 5.9 Hz, 1 H), 1.78 (dd, J = 6.7 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.54, 167.88, 144.49, 135.47, 132.21, 127.88, 123.90, 121.26, 120.01, 109.78, 97.91, 70.49, 65.25, 58.67, 54.69, 53.97, 51.20, 44.69, 36.32, 12.66; IR (film) ν_{max} 3350, 2948, 2915, 2902, 2864, 1660, 1604, 1478, 1467, 1433, 1310, 1254, 1232, 1209, 1199, 1122, 1102, 1063, 1035, 840, 747, 665 cm^{-1}; UV (EtOH) λ_{max} 206, 230, 300, 330 nm; MS m/z (rel intens) 339 (M + 1, 5), 338 (M, 29), 309 (4), 293 (3), 279 (5), 277 (4), 266 (4), 263 (3), 261 (4), 252 (11), 249 (3), 247 (3), 238 (5), 235 (5), 234 (8), 222 (4), 221 (6), 220 (13), 216 (6), 208 (7), 207 (7), 206 (19), 204 (7), 194 (8), 193 (9), 192 (8), 191 (12), 181 (7), 180 (15),

178 (6), 169 (6), 168 (6), 167 (11), 166 (6), 165 (9), 154 (17), 149 (6), 144 (8), 139 (9), 137 (12), 130 (6), 128 (7), 127 (9), 122 (20), 121 (100), 108 (7), 106 (7), 95 (9), 91 (8), 86 (14), 84 (15), 80 (11), 77 (11); high-resolution MS, EI ionization calcd for $C_{20}H_{22}N_2O_3$ 338.1630, found 338.1627; FAB (+H) calcd 339.17, found 339.17; (+Li) calcd 345.18, found 345.18.

The same sodium borohydride reduction procedure was repeated with 7 mg of the (+)-ketone **16*E***, resulting in 4 mg of (+)-mossambine: mp 236−237 °C (MeOH); $[\alpha]^{24}_D = +480°$ ($c = 0.015$, $CHCl_3$); high-resolution MS, FAB ionization, calcd for $C_{20}H_{23}N_2O_3$ 339.17, found 339.17.

Repetition of the same reduction procedure with 4 mg of the (−)-ketone **16*E*** gave 2.1 mg of (−)-mossambine after crystallization from methanol: mp 238−239 °C; $[\alpha]^{22.4}_D = -482°$ ($c = 0.021$, $CHCl_3$); high-resolution MS, FAB ionization, calcd for $C_{20}H_{23}N_2O_3$ 339.17, found 339.17; EI ionization, calcd for $C_{20}H_{22}N_2O_3$ 338.1630, found 338.1629.

(±)-14-*epi*-Mossambine (17). To an ice-cooled solution of the *E*-ketone **16*E*** (12 mg, 0.036 mmol) in 2 mL of THF was added, dropwise, 0.50 mL of a 1 M L-Selectride (Aldrich) in THF solution (14 equiv). Stirring was continued for 20 min, when TLC showed absence of starting material. Then 0.3 mL of water was added, and the resulting mixture was concentrated under reduced pressure and partitioned between 30 mL of saturated aqueous sodium bicarbonate solution and 20 mL of chloroform. After separation of the two layers, the aqueous layer was extracted with 3 × 15 mL of chloroform. The combined organic layers were dried (Na_2SO_4) and concentrated. The residue was purified by flash SiO_2 column, eluting with 75:25:0.1 ethyl acetate/methanol/triethylamine to provide 11.6 mg of the product **17** (96%): mp 200−202 °C (MeOH); TLC (ethyl acetate/methanol, 1:1) $R_f = 0.33$ (CAS, blue); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.06 (br s, 1 H), 7.20 (d, $J = 7.5$ Hz, 1 H), 7.13 (t, $J = 7.7$ Hz, 1 H), 6.89 (t, $J = 7.5$ Hz, 1 H), 6.83 (d, $J = 7.7$ Hz, 1 H), 5.41 (q, $J = 7$ Hz, 1 H), 4.47 (dd, $J = 4$, 3 Hz, 1 H), 4.15 (br s, 1 H), 3.95 (t, $J = 2.2$ Hz, 1 H), 3.79 (s, 3 H), 3.77 (d, $J = 15.0$ Hz, 1 H), 3.29−3.23 (m, 1 H), 2.98 (dd, $J = 13$, 6.6 Hz, 1 H), 2.95 (d, $J = 15$ Hz, 1 H), 2.60−2.54 (m, 1 H), 1.81 (dd, $J = 13$, 5.6 Hz, 1 H), 1.67 (d, $J = 7$ Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.68, 168.36, 143.05, 137.18, 137.05, 127.72, 121.64, 121.32, 120.51, 109.73, 92.43, 68.04, 67.03, 56.58, 55.88, 55.66, 51.09, 45.19, 37.51, 12.90; IR (film) ν_{max} 3428, 3366, 3357, 2949, 2921, 2869, 1670, 1605, 1479, 1469, 1438, 1384, 1308, 1279, 1241, 1206, 1166, 1105, 1059, 1037, 914, 748 cm^{-1}; UV (EtOH) λ_{max} 206, 230, 300, 330 nm; MS *m*/*z* (rel intens) 339 (M + 1, 3), 338 (M, 11), 309 (2), 307 (2), 293 (1), 279 (3), 277 (2), 266 (3), 263 (2), 252 (6), 249 (1), 247 (2), 238 (3), 235 (3), 234 (5), 220 (6), 216 (3), 208 (4), 207 (3), 206 (10), 204 (3), 194 (4), 193 (4), 192 (5), 191 (6), 180 (7), 178 (3), 167 (7), 165 (4), 154 (8), 139 (5), 137 (10), 130 (3), 123 (3), 122 (20), 121 (100), 115 (5), 109 (4), 108 (5), 106 (4), 103 (4), 97 (4), 95 (4), 91 (4), 86 (10), 84 (13), 82 (5), 77 (5), 71 (6), 69 (7).

Resolution of (±)-14-Oxoakuammicine (16*E*). To 0.240 g (1.42 mmol) of (*S*)-(+)-*N*,*S*-dimethyl-*S*-phenylsulfoximine[19] in 3 mL of THF at 0 °C was added, dropwise, 0.50 mL of 2.5 N *n*-butyllithium (1.2 mmol). The resulting solution was stirred at rt for 15 min and then cooled to −75 °C. At −75 °C was added 31 mg of the racemic ketone **16*E*** in 5 mL of THF. After 30 min saturated aqueous ammonium chloride solution was added. The mixture was brought to rt, and most of the solvent was evaporated to give a residue, which was mixed with aqueous ammonium hydroxide and ammonium chloride solution and extracted with 4 × 15 mL of chloroform. The combined chloroform layers were dried over sodium sulfate and evaporated on a rotary evaporator. The crude diastereomeric mixture was carefully separated by flash chromatography (9:1:0.5 ethyl acetate/hexane/triethyl amine). Attempted pyrolysis of the less polar isomer at 190 °C, under vacuum for 12 h, showed only 3% of the ketone in the reaction mixture; all the rest was still the unreacted adduct. If the pyrolysis temperature rose above 200 °C, the mixture went to a black tar. Pyrolysis of the more polar isomer at 150 °C for 12 h gave, after flash chromatographic purification (8:2:0.5 ethyl acetate/hexane/triethylamine), 10 mg (32% yield, 64% of theoretical) of the (+)-ketone: $[\alpha]^{26.6}_D = +778°$ ($c = 0.095$, $CDCl_3$). The spectroscopic data matched those of the racemic sample.

The same procedure was repeated, starting with 26.3 mg of the racemic ketone **16*E*** and the *R*-sulfonimine. Thus, 7.9 mg (30%, 60% of theoretical) of the (−)-ketone was obtained, $[\alpha]^{24}_D = -783°$. The spectroscopic data of the chiral ketone were identical to those of the racemic sample.

Determination of the Ee Value by Chiral Shift Reagent. An enantiomeric excess >99.5% for the resolved ketone **16*E*** was determined by ^{1}H-NMR shift studies using a gradual addition of a 0.1 M solution of Eu(hfc)$_3$, [tris[3-(heptafluoropropylhydroxymethylene)-*d*-camphorato]europium(III)] in chloroform-*d* to the pentacyclic racemate or to the chiral ketone **16*E***. The allylic methyl proton signal at δ 1.63 was split to give signals at δ 2.05 and 1.97 for the (−)- and the (+)-ketone, and the indole proton signal at δ 9.09 was split to give signals at δ 9.84 and δ 9.71 for the (−)- and the (+)-ketone.

Separation and Characterization of the Two Diastereomeric Sulfoximine and Ketone Adducts. Following the above procedure, starting from 30 mg of the ketone **16*E*** and 10 equiv of (*R*)-(−)-*N*,*S*-dimethyl-*S*-phenylsulfoximine and 8 equiv of *n*-butyllithium, a mixture of the adducts, contaminated with the starting sulfoximine, was obtained after workup. Washing of the mixture with ether−hexane (4×) then gave a white solid, which was the pure, less polar diastereomer (by TLC). The washings were concentrated and purified by flash chromatography (SiO_2, 0.5:10:90 triethylamine/hexane/ethyl acetate) to afford the pure polar diastereomer.

For the less polar diastereomer: TLC (0.5% triethylamine in ethyl acetate) $R_f = 0.25$ (CAS, blue); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.94 (br s, 1 H), 7.86 (d, $J = 7.7$ Hz, 2 H), 7.64−7.49 (m, 3 H), 7.16−7.08 (m, 2 H), 6.90 (t, $J = 7.5$ Hz, 1 H), 6.82 (d, $J = 7.7$ Hz, 1 H), 5.53 (br q, $J = 6.5$ Hz, 1 H), 4.57 (br s, 1 H), 3.78 (s, 3 H), 3.67 (br s, 1 H), 3.66 (br s, 2 H), 3.23 (br d, $J = 13.9$ Hz, 1 H), 3.15 (br d, $J = 13.9$ Hz, 1 H), 2.94−2.75 (m, 3 H), 2.57 (s, 3 H), 1.93 (dd, $J = 6.5$, 2 Hz, 3 H), 1.80 (dd, $J = 12.8$, 5.7 Hz, 1 H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 170.99, 168.59, 143.63, 139.14, 137.33, 133.17, 129.49, 129.02, 127.17, 122.31, 121.25, 119.11, 109.96, 94.46, 72.33, 70.66, 60.69, 56.73, 53.97, 52.38, 51.02, 42.83, 40.84, 28.87, 13.34 (one carbon was not observed); IR (film) ν_{max} 3357, 2947, 2918, 2875, 2808, 1683, 1675, 1671, 1653, 1602, 1475, 1463, 1436, 1386, 1239, 1203, 1149, 1101, 1081, 912, 816, 734 cm^{-1}; UV (EtOH) λ_{max} 196, 206, 220, 298, 328 nm; MS *m*/*z* (rel intens) 508 (0.57), 507 (7), 506 (21), 477 (1), 460 (2), 459 (1), 381 (2), 380 (3), 352 (52), 351 (57), 349 (2), 336 (5), 335 (7), 334 (30), 322 (16), 321 (9), 308 (11), 307 (9), 291 (21), 280 (18), 276 (8), 275 (9), 266 (14), 265 (27), 263 (14), 253 (24), 252 (100), 249 (10), 248 (19), 247 (16), 238 (17), 235 (11), 234 (16), 233 (11), 222 (13), 221 (18), 220 (35), 219 (12), 206 (18), 194 (24), 193 (25), 192 (21), 180 (17), 168 (15), 167 (21), 154 (17), 144 (16), 125 (18), 109 (15), 98 (88), 97 (31), 86 (15), 84 (20), 77 (23), 57 (23), 55 (21); high-resolution MS, FAB ionization, calcd for $C_{28}H_{31}N_3O_4S$ + H 506.2113, found 506.2122.

For the more polar diastereomer: TLC (0.5% triethylamine in ethyl acetate) $R_f = 0.14$ (CAS, blue); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.90 (br s, 1 H), 7.89 (d, $J = 7.5$ Hz, 2 H), 7.64−7.55 (m, 3 H), 7.27 (d, $J = 7.5$ Hz, 1 H), 7.12 (t, $J = 7.7$ Hz, 1 H), 6.93 (t, $J = 7.5$ Hz, 1 H), 6.83 (d, $J = 7.7$ Hz, 1 H), 5.44 (br q, $J = 6.3$ Hz, 1 H), 4.67 (br s, 1 H), 3.86 (br s, 1 H), 3.84 (d, $J = 13.8$ Hz, 1 H), 3.71 (s, 3 H), 3.29 (br d, $J = 13.9$ Hz, 1 H), 3.18 (d, $J = 13.8$ Hz, 1 H), 3,16−3.10 (m, 2 H), 3.00−2.89 (m, 2 H), 2.53 (s, 3 H), 1.86 (dd, $J = 12.8$, 6.4 Hz, 1 H), 1.64 (dd, $J = 6.3$, 2 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.07, 168.39, 143.78, 138.67, 138.06, 133.45, 133.24, 129.57, 129.28, 126.97, 121.27, 121.10, 119.31, 109.84, 92.93, 72.27, 68.16, 60.04, 57.36, 54.42, 52.55, 50.90, 42.98, 42.42, 28.76, 12.54; IR (film) ν_{max} 3355, 3054, 2948, 2926, 2875, 2808, 1675, 1601, 1475, 1463, 1382, 1359, 1305, 1278, 1239, 1162, 1130, 1100, 1081, 1058, 1012, 845, 810, 786, 746, 689 cm^{-1}; UV (EtOH) λ_{max} 194, 210, 224, 296, 328 nm; MS *m*/*z* (rel intens) 507 (3), 506 (22), 381 (4), 380 (1), 353 (1), 352 (18), 351 (35), 350 (12), 336 (1), 335 (2), 334 (1), 333 (5), 323 (3), 322 (8), 321 (3), 319 (5), 318 (1), 309 (3), 308 (7), 307 (9), 305 (1), 293 (5), 292 (9), 291 (13), 290 (4), 289 (3), 279 (8), 280 (16), 275 (8), 266 (11), 265 (25), 253 (17), 252 (87), 248 (14), 247 (13), 238 (15), 234 (13), 221 (15), 220 (27), 206 (23), 205 (11), 194 (18), 193 (20), 192 (19), 180 (14), 167 (17), 144 (12), 125 (18), 109 (11), 98 (100), 97 (21), 86 (13), 84 (21), 77 (24), 56 (27), 55 (19), 54 (18); high-

resolution MS, FAB ionization, calcd for $C_{28}H_{31}N_3O_4S$ + H 506.2113, found 506.2110.

Methyl 3-(2-Bromobut-2-en-1-yl)-1,2,3,4,5,6-hexahydroazepino[4,5-*b*]indole-5-carboxylate (8b). To 1.50 g of (*Z*)-2-bromo-2-buten-1-ol[23] (9.93 mmol) in 20 mL of dry ethyl ether at 0 °C, was added, dropwise, 0.38 mL (4 mmol) of phosphorus tribromide. The resulting solution was stirred at room temperature for 18 h and then diluted with 50 mL of ether. The ether was washed with saturated aqueous sodium bicarbonate and brine and dried. Evaporation of the solvent gave crude (*Z*)-1,2-dibromo-2-butene, which was used directly in the next step.

To the above crude dibromide, in 50 mL of acetone, was added 1.60 g of indoloazepine **7** (6.55 mmol), 2.72 g of potassium carbonate (3 equiv), and 2.74 mL of triethylamine (3 equiv). After being stirred vigorously at rt for 3 h, the reaction mixture was filtered and the residual solid was washed with acetone. The filtrate was concentrated under vacuum and purified by flash silica gel column (1/2 hexane: ethyl ether) to give 1.962 g of the alkylated azepine **8b** (79%): mp 122−124 °C (MeOH); TLC (SiO_2, 3:1 ethyl ether/hexane) R_f = 0.41 (CAS, greyish blue); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.36 (br s, 1 H), 7.48 (d, J = 7.8 Hz, 1 H), 7.30 (d, J = 7.8 Hz, 1 H), 7.14 (t, J = 7.5 Hz, 1 H), 7.09 (t, J = 7.5 Hz, 1 H), 6.02 (q, J = 6.5 Hz, 1 H), 4.07 (dd, J = 7.3, 2.6 Hz, 1 H), 3.77 (s, 3 H), 3.57 (br s, 2 H), 4.44 (dd, J = 13.3, 7.4 Hz, 1 H), 3.24 (dd, J = 13.3, 2.6 Hz, 1 H), 3.07−3.02 (m, 1 H), 2.96−2.87 (m, 3 H), 1.81 (d, J = 6.5 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.44, 134.88, 131.98, 128.57, 126.58, 125.94, 121.61, 119.31, 118.03, 114.05, 110.69, 65.74, 56.92, 54.61, 52.38, 45.67, 24.11, 16.64; IR (film) ν_{max} 3377, 3353, 2945, 2913, 2852, 2792, 1733, 1677, 1610, 1477, 1465, 1438, 1302, 1276, 1249, 1241, 1212, 1190, 1087, 1057, 1041, 782, 745 cm^{-1}; UV (EtOH) λ_{max} 208, 228, 284, 292 nm; MS *m*/*z* (relative intensity) 378 (16), 376 (14), 320 (6), 318 (6), 298 (4), 297 (24), 243 (3), 239 (6), 238 (8), 237 (5), 228 (3), 223 (3), 216 (6), 215 (18), 214 (20), 210 (6), 203 (6), 202 (55), 184 (7), 183 (21), 182 (6), 178 (7), 177 (6), 176 (14), 174 (8), 170 (10), 169 (17), 168 (13), 162 (10), 160 (6), 158 (6), 157 (21), 156 (100), 155 (6), 154 (33), 144 (29), 143 (18), 140 (6), 131 (7), 130 (15), 129 (17), 128 (19), 127 (12), 115 (12), 99 (16), 97 (8), 96 (92), 86 (31), 84 (83), 82 (17), 77 (10), 55 (11), 53 (47), 51 (17). Anal. Calcd for $C_{18}H_{21}N_2O_2Br$: C, 57.30; H, 5.61; N, 7.43; Br, 21.18. Found: C, 57.37; H, 5.57; N, 7.30; Br, 21.13.

(±)-(3a*R,4*R**,11b*R**)-Methyl 3-((*Z*)-2-Bromobut-2-en-1-yl)-2,3,3a,4,5,7-hexahydro-4-acetoxy-1*H*-pyrrolo[2,3-*d*]-carbazole-6-carboxylate (10b).** A mixture of 1.908 g of the azepine **8b** (5.06 mmol) and 4 mL of a 1.45 N solution of acetyloxyacetaldehyde in dichloromethane (1.15 eq) in 40 mL of toluene was heated under a Dean−Stark trap at reflux overnight. Cooling to rt and removal of solvents gave a residue, which was purified by flash SiO_2 column (1/1 ethyl ether:hexane), to afford 1.968 g of the acetate **10b** (84%): mp 157−157.5 °C (needles from ethanol); TLC (SiO_2, 2:1 ethyl ether/hexane) R_f = 0.43 (CAS, blue); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.00 (br s, 1 H), 7.18 (t, J = 7.7 Hz, 1 H), 7.15 (d, J = 7.4 Hz, 1 H), 6.90 (t, J = 7.4 Hz, 1 H), 6.85 (d, J = 7.7 Hz, 1 H), 6.06 (q, J = 6.5 Hz, 1 H), 5.00 (br s, 1 H), 4.00 (d, J = 14.4 Hz, 1 H), 3.78 (s, 3 H), 3.64 (d, J = 14.4 Hz, 1 H), 3.15 (br s, 1 H), 3.07 (dd, J = 8.9, 6.5 Hz, 1 H), 2.99−2.92 (m, 1 H), 2.83−2.78 (m, 1 H), 2.62 (dd, J = 15.8, 2.3 Hz, 1 H), 2.11−2.05 (m, 1 H), 1.84 (s, 3 H), 1.79 (d, J = 6.5 Hz, 3 H), 1.75 (dd, J = 12, 4.8 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.73, 168.92, 163.90, 143.28, 137.06, 128.07, 126.40, 126.01, 122.30, 120.66, 109.35, 89.05, 71.40, 70.05, 62.07, 54.77, 50.99, 50.12, 41.65, 23.68, 21.33, 16.66; IR (film) ν_{max} 3372, 2946, 2855, 2803, 1729, 1681, 1611, 1478, 1468, 1437, 1374, 1282, 1249, 1202, 1130, 1090, 1034, 913, 800, 746 cm^{-1}; UV (ethanol) λ_{max} 208, 226, 298, 326 nm; MS *m*/*z* (rel intens) 378 (16), 376 (14), 320 (6), 318 (6), 298 (4), 297 (24), 239 (6), 238 (8), 237 (5), 216 (6), 215 (18), 214 (20), 210 (6), 203 (6), 202 (55), 184 (7), 183 (21), 176 (14), 170 (10), 169 (17), 168 (13), 162 (10), 157 (21), 156 (100), 154 (33), 144 (29), 143 (18), 130 (15), 129 (17), 128 (19), 127 (12), 116 (12), 99 (16), 86 (31), 84 (83), 82 (17), 77 (10), 55 (11), 53 (47), 51 (17). Anal. Calcd for $C_{22}H_{25}N_2O_4Br$: C, 57.28; H, 5.46; N, 6.07; Br, 17.32. Found: C, 57.32; H, 5.47; N, 5.96; Br, 17.34.

(±)-(3a*R,4*R**,11b*R**)-Methyl 3-((*Z*)-2-Bromobut-2-en-1-yl)-2,3,3a,4,5,7-hexahydro-4-hydroxy-1*H*-pyrrolo[2,3-*d*]-carbazole-6-carboxylate (11b).** To 1.886 g of the acetate **10b** (4.09 mmol) in 35 mL of methanol and 2 mL of water was added 0.565 g of potassium carbonate (1 equiv). After being heated at reflux for 45 min, the reaction mixture was concentrated and the residue was dissolved in 120 mL of dichloromethane and washed with 40 mL of brine. After drying and concentration, the crude product was flash chromatographed on silica gel (1:3 hexane/ethyl ether) to provide 1.448 g of the alcohol **11b** (85%): mp 159−160 °C (ethanol); TLC (SiO_2, ethyl ether/hexane, 3:1) R_f = 0.12 (CAS, blue); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.04 (br s, 1 H), 7.18−7.15 (m, 2 H), 6.90 (t, J = 7.5 Hz, 1 H), 6.84 (d, J = 7.9 Hz, 1 H), 6.07 (q, J = 6.5 Hz, 1 H), 3.98 (br s, 1 H), 3.79 (d, J = 14.1 Hz, 1 H), 3.77 (s, 3 H), 3.61 (d, J = 14.1 Hz, 1 H), 3.11 (s, 1 H), 3.07 (dd, J = 8.8, 6.5 Hz, 1 H), 2.94 (ddd, J = 15.7, 2.4, 2.0 Hz, 1 H), 2.75 (ddd, J = 13, 8.8, 4.8 Hz, 1 H), 2.65 (dd, J = 15.7, 2.0 Hz, 1 H), 2.07 (td, J = 12.1, 6.5, 1 H), 1.80 (d, J = 6.4, 3H), 1.73 (dd, J = 12.0, 4.7 Hz, 1 H), 1.38 (d, J = 7.3 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.13, 164.63, 143.00, 137.26, 128.02, 126.60, 125.87, 122.25, 120.87, 109.45, 87.29, 72.96, 68.69, 63.06, 54.74, 51.03, 50.75, 41.64, 26.30, 16.64; IR (film) ν_{max} 3452, 3385, 2966, 2915, 2852, 2801, 1673, 1608, 1465, 1437, 1283, 1248, 1199, 1122, 745 cm^{-1}; UV (ethanol) λ_{max} 206, 228, 300, 324 nm; MS *m*/*z* (rel intens) 420 (9), 418 (7), 402 (8), 400 (7), 391 (3), 389 (4), 376 (10), 374 (9), 339 (7), 321 (9), 305 (3), 303 (3), 244 (12), 243 (41), 228 (6), 227 (4), 226 (10), 225 (10), 217 (9), 214 (7), 207 (7), 206 (94), 204 (100), 202 (10), 196 (5), 195 (6), 184 (6), 183 (6), 182 (7), 181 (6), 180 (8), 169 (10), 168 (19), 167 (25), 154 (32), 135 (15), 133 (15), 115 (10), 96 (15), 72 (34), 70 (13), 53 (57). Anal. Calcd for $C_{20}H_{23}N_2O_3Br$: C, 57.58; H, 5.07; N, 6.71; Br, 19.15. Found: C, 57.51; H, 5.12; N, 6.62; Br, 19.33.

(±)-(3a*R,11b*R**)-Methyl 3-((*Z*)-2-Bromobut-2-en-1-yl)-2,3,3a,4,5,7-hexahydro-4-oxo-1*H*-pyrrolo[2,3-*d*]carbazole-6-carboxylate (13b).** To 0.383 mL of DMSO in 50 mL of dichloromethane at −75 °C was added dropwise 0.572 mL of trifluoroacetic anhydride. After 20 min, 1.134 g of the alcohol **11b** in 10 mL of dichloromethane was added, dropwise. Stirring was continued at −70 °C for 1 h before adding 4.7 mL of *N*,*N*-diisopropylethylamine (10 eq). The reaction mixture was stirred at −70 °C for 1 h, and the dry ice−acetone bath was removed. When the mixture had gradually warmed to rt, it was diluted with 50 mL of dichloromethane, washed with saturated sodium bicarbonate, and dried. Concentration and flash SiO_2 column chromatography (1/1 ethyl ether: hexane) gave 0.963 g of the ketone **13b** (86%). Continued elution with 3:1 ether/hexane gave 0.123 g of recovered starting alcohol **11b** (11%).

For the ketone **13b**: mp 115 °C (needles from ethanol); TLC (SiO_2, ethyl ether/hexane, 2:1) R_f = 0.43 (CAS, greenish blue); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.11 (br s, 1 H), 7.41 (d, J = 7.4 Hz, 1 H), 7.18 (t, J = 7.7 Hz, 1 H), 6.93 (t, J = 7.4 Hz, 1 H), 6.82 (d, J = 7.7 Hz, 1 H), 6.06 (q, J = 6.5 Hz, 1 H), 3.83 (d, J = 14 Hz, 1 H), 3.76 (s, 3 H), 3.76 (d, J = 14 Hz, 1 H), 3.50 (d, J = 17.4 Hz, 1 H), 3.31 (dd, J = 17.4, 1.6 Hz, 1 H), 3.26 (s, 1 H), 3.18−3.13 (m, 1 H), 3.07−3.03 (m, 1 H), 2.58−2.52 (m, 1 H), 2.08−2.04 (m, 1 H), 1.78 (d, J = 6.5 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 206.57, 167.90, 162.52, 143.55, 135.82, 128.50, 126.89, 125.60, 123.08, 121.57, 109.38, 87.97, 67.72, 60.46, 57.63, 51.19, 50.36, 40.14, 35.79, 16.66; IR (film) ν_{max} 3367, 2947, 1717, 1683, 1610, 1467, 1437, 1243, 1208, 1136, 749 cm^{-1}; UV (ethanol) λ_{max} 206, 230, 298, 330 nm; MS *m*/*z* (rel intens) 418 (16), 416 (15), 391 (99), 390 (64), 388 (58), 331 (7), 330 (10), 329 (10), 328 (11), 310 (5), 309 (28), 305 (27), 303 (32), 301 (10), 256 (9), 255 (64), 249 (11), 228 (17), 227 (28), 226 (13), 214 (40), 196 (19), 195 (53), 194 (18), 182 (11), 181 (14), 180 (16), 169 (27), 168 (67), 167 (79), 166 (20), 154 (30), 140 (20), 115 (28), 96 (13), 86 (18), 84 (37), 53 (100), 51 (20). Anal. Calcd for $C_{20}H_{21}N_2O_3Br$: C, 57.56; H, 5.07; N, 6.71; Br, 19.15. Found: C, 57.51; H, 5.12; N, 6.62; Br, 19.33.

Methyl 3-(2-Chlorobut-2-en-1-yl)-1,2,3,4,5,6-hexahydroazepino[4,5-*b*]indole-5-carboxylate (8c). Chlorine gas was bubbled into 8.928 g (89.2 mmol) of methyl crotonate in

(23) Fevig, J. M.; Marquis, R. W., Jr.; Overman, L. E. *J. Am. Chem. Soc.* **1991**, *113*, 5085.

80 mL of dichloromethane for 40 min. The solution was purged with argon for 5 min before 25 mL of triethylamine in 200 mL of pentane was added dropwise. After being heated at reflux for 2 h and cooled to rt, the mixture was filtered, and the filtrate was dissolved in 300 mL of ether, washed with brine, and dried over sodium sulfate. Evaporation of solvents gave a residue, which was distilled to afford the 4.12 g (34%) of methyl (*Z*)-2-chlorocrotonate: bp 50−53 °C/12 mmHg.[24] ^{1}H NMR showed only one isomer.

To the chloro ester (3.58 g, 26.6 mmol) in 30 mL of dry THF was added 60 mL of 1 M DIBAL, dropwise, at −78 °C, over 1.5 h. The reaction mixture was brought to rt and stirred overnight. The reaction was quenched with 5 mL of methanol, and then 50 mL of 15% HCl was added. The layers were separated, and the aqueous phase was extracted with 2 × 50 mL of ether. The combined organic phases were washed with brine and dried (Na_2SO_4). After the solvents were removed under vacuum, the residue was distilled to give the 2.41 g of the pure alcohol (85%): bp 64−65 °C/12 mm; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.84 (q, J = 6.3 Hz, 1 H), 4.14 (s, 2 H), 2.37 (br s, 1 H), 1.75 (d, J = 6.3 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 134.06, 121.93, 66.73, 13.52; IR (film) ν_{max} 3326, 2922, 2863, 1667, 1447, 1381, 1299, 1223, 1149, 1087, 1047, 1013, 922, 813, 698, 646, 586 cm^{-1}; MS *m*/*z* (rel intens) 108 (14), 106 (42), 105 (5), 93 (6), 91 (25), 90 (5), 89 (11), 88 (9), 78 (5), 72 (5), 71 (100), 69 (14), 63 (5), 54 (10), 52 (33), 50 (7), 42 (37), 41 (67), 39 (33), 37 (10), 31 (18), 29 (15), 27 (23). Anal. Calcd for C_4H_7OCl: C, 45.09; H, 6.62; Cl, 33.27. Found: C, 45.30; H, 6.84; Cl, 33.04.

To an ice-cooled solution of 1.00 g of (*Z*)-2-chlorobuten-1-ol (9.39 mmol) in 20 mL of dry ether was added, dropwise, phosphorus tribromide (0.357 mL, 3.76 mmol). After being stirred at rt for 18 h, the reaction mixture was diluted with 50 mL of ether and washed with aqueous sodium bicarbonate solution and brine. Drying (Na_2SO_4) and concentration of the ether layer gave the crude chlorobromide, which was used directly for the following alkylation.

A mixture of 1.91 g of indoloazepine **7** (7.8 mmol), the above bromide, 3.3 g of potassium carbonate, and 3.3 mL of triethylamine in 50 mL of acetone was stirred vigorously at rt for 3 h. Filtration and concentration gave the crude product **8c**, which was purified by flash SiO_2 column (ethyl ether/hexane, 1:1) to afford 1.71 g of the alkylated azepine as a white powder (66%): mp 106−107 °C (from ethanol); TLC (ether/hexane, 2:1) R_f = 0.41 (CAS, blue); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.3 (s, 1 H), 7.46 (d, J = 7.5 Hz, 1 H), 7.22 (d, J = 7.7 Hz, 1 H), 7.11 (t, J = 7.5 Hz, 1 H), 7.07 (t, J = 7.7 Hz, 1 H), 5.78 (q, J = 6.6 Hz, 1 H), 3.94 (dd, J = 6.7, 2 Hz, 1 H), 3.73 (s, 3 H), 3.43 (s, 2 H), 3.43 (dd, J = 13.4, 6.7 Hz, 1 H), 13.3, 2 Hz, 1 H), 3.11 (dd, J = 13.3, 2.4 Hz, 1 H), 3.05−3.01 (m, 1 H), 2.95−2.78 (m, 3 H), 1.79 (d, J = 6.6 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.40, 134.73, 132.65, 132.01, 128.43, 122.94, 121.45, 119.16, 117.94, 113.85, 110.66, 64.38, 56.97, 54.83, 52.29, 45.63, 24.14, 13.82; IR (film) ν_{max} 3392, 3354, 2948, 2916, 2828, 1730, 1663, 1459, 1434, 1340, 1287, 1240, 1207, 1163, 1027, 963, 917, 818, 743, 723 cm^{-1}; UV (EtOH) λ_{max} 206, 228, 284 nm; MS *m*/*z* (rel intens) 335 (8), 334 (31), 333 (29), 332 (88), 301 (3), 297 (12), 296 (8), 273 (2), 259 (9), 243 (5), 237 (4), 216 (13), 215 (46), 214 (31), 203 (13), 202 (86), 201 (11), 184 (11), 183 (35), 182 (8), 170 (13), 169 (23), 168 (5), 157 (14), 156 (100), 155 (25), 154 (43), 144 (11), 143 (11), 142 (7), 133 (7), 132 (15), 131 (26), 130 (33), 129 (21), 128 (21), 127 (13), 118 (18), 116 (22), 115 (12), 96 (41), 89 (14). Anal. Calcd for $C_{18}H_{21}N_2O_2Cl$: C, 64.96; H, 6.36; N, 8.42; Cl, 10.68. Found: C, 65.24; H, 6.44; N, 8.28; Cl, 10.51.

(±)-(3a*R,4*R**,11b*R**)-Methyl 3-((*Z*)-2-Chlorobut-2-en-1-yl)-2,3,3a,4,5,7-hexahydro-4-acetoxy-1*H*-pyrrolo[2,3-*d*]-carbazole-6-carboxylate (10c).** The alkylated azepine **8c** (1.616 g, 4.86 mmol) and 3.7 mL of 1.45 N acetoxyacetaldehyde[22] in dichloromethane (5.365 mmol, 1.1 equiv) were mixed in 50 mL of dry toluene. With a Dean−Stark trap, the mixture was heated at reflux for 3 h. Removal of solvents with a rotary evaporator gave a residue, which was triturated with ether to afford 0.612 g of product, as a white solid. The mother liquor was concentrated and purified by flash SiO_2 column (ether/hexane, 1:1), giving an additional 1.027 g of product: total 1.639 g (81%); mp 146−147 °C (needles from ethanol); TLC (ether/hexane, 2:1) R_f = 0.48 (CAS, blue); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.03 (br s, 1 H), 7.17 (t, J = 7.7 Hz, 1 H), 7.15 (d, J = 7.4 Hz, 1 H), 6.89 (t, J = 7.3 Hz, 1 H), 6.84 (d, J = 7.7 Hz, 1 H), 5.86 (q, J = 6.5 Hz, 1 H), 4.98 (s, 1 H), 3.90 (d, J = 14.3 Hz, 1 H), 3.77 (s, 3 H), 3.59 (d, J = 14.3 Hz, 1 H), 3.16 (s, 1 H), 3.09−3.06 (m, 1 H), 2.97 (dd, J = 16, 2 Hz, 1 H), 2.88−2.83 (m, 1 H), 2.61 (dd, J = 16, 2 Hz, 1 H), 2.10−2.04 (m, 1 H), 1.83 (s, 3 H), 1.78 (d, J = 6.5 Hz, 3 H), 1.74 (dd, J = 12, 4.8 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.60, 168.75, 163.77, 143.16, 136.95, 132.61, 127.98, 123.02, 122.22, 120.59, 109.27, 88.93, 71.39, 69.89, 60.04, 54.68, 50.88, 50.12, 41.51, 23.58, 21.22, 13.79; IR (film) ν_{max} 3373, 2945, 2857, 2808, 1729, 1681, 1611, 1479, 1467, 1372, 1353, 1305, 1279, 1247, 1211, 1201, 1132, 1090, 1059, 1035, 969, 800, 747, 695 cm^{-1}; UV (EtOH) λ_{max} 206, 226, 298, 328 nm; MS *m*/*z* (rel intens) 420 (M + 2, 2), 419 (M + 1, (13), 418 (M, 20), 417 (38), 416 (38), 385 (5), 381 (8), 359 (10), 358 (31), 357 (34), 356 (78), 332 (9), 331 (6), 330 (30), 322 (8), 321 (43), 286 (22), 285 (19), 259 (9), 228 (12), 227 (12), 226 (34), 225 (20), 217 (8), 214 (11), 209 (9), 204 (32), 203 (12), 202 (100), 196 (9), 195 (12), 194 (11), 193 (3), 182 (10), 180 (13), 169 (12), 168 (30), 167 (24), 162 (18), 160 (59), 154 (19), 132 (19), 89 (13). Anal. Calcd for $C_{22}H_{25}N_2O_4Cl$: C, 63.38; H, 6.04; N, 8.72; Cl, 8.50. Found: C, 63.58; H, 6.13; N, 8.62; Cl, 8.42.

(±)-(3a*R,4*R**,11b*R**)-Methyl 3-((*Z*)-2-Chlorobut-2-en-1-yl)-2,3,3a,4,5,7-hexahydro-4-hydroxy-1*H*-pyrrolo[2,3-*d*]-carbazole-6-carboxylate (11c).** A mixture of the acetate **10c** (1.518 g, 3.64 mmol) and 0.53 g of potassium carbonate (3.83 mmol, 1.05 equiv) in 40 mL of methanol and 3 mL of water was heated to reflux for 40 min. After concentration, the residue was dissolved in 100 mL of dichloromethane and washed with 50 mL of brine. Drying (Na_2SO_4) and evaporation gave the crude product, which was purified by flash SiO_2 column (ether/hexane, 3:1) to give 1.315 g of the alcohol **11c** as a white solid: mp 137−138 °C (from methanol); TLC (ether/hexane, 3:1) R_f = 0.19 (CAS, blue); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.04 (s, 1 H), 7.19−7.16 (m, 2 H), 6.90 (t, J = 7.5 Hz, 1 H), 6.84 (d, J = 7.7 Hz, 1 H), 5.86 (q, J = 6.4 Hz, 1 H), 3.95 (br s, 1 H), 3.78 (s, 3 H), 3.70 (br d, J = 14.4 Hz, 1 H), 3.54 (d, J = 14.4 Hz, 1 H), 3.13 (s, 1 H), 3.09−3.06 (m, 1 H), 2.96−2.92 (m, 1 H), 2.82−2.77 (m, 1 H), 2.63 (d, J = 15.2 Hz, 1 H), 2.11−2.04 (m, 1 H), 1.80 (d, J = 6.4 Hz, 3 H), 1.73 (dd, J = 11.8, 4.9 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.65, 164.09, 142.78, 136.96, 132.57, 127.54, 122.36, 121.73, 120.30, 109.12, 87.20, 72.50, 68.22, 60.66, 54.37, 50.50, 50.33, 41.34, 25.89, 13.48; IR (film) ν_{max} 3431, 3384, 2945, 2917, 2850, 2804, 1674, 1634, 1610, 1479, 1466, 1438, 1383, 1348, 1305, 1283, 1250, 1211, 1200, 1125, 1088, 1062, 1046, 1020, 923, 874, 808, 772, 745, 695 cm^{-1}; UV (EtOH) λ_{max} 206, 230, 300, 326 nm; MS *m*/*z* (rel intens) 377 (3), 376 (8), 375 (12), 374 (16), 358 (6), 357 (5), 356 (17), 345 (6), 339 (6), 332 (7), 330 (18), 321 (6), 244 (10), 243 (27), 228 (5), 226 (8), 225 (4), 14 (4), 195 94), 182 (5), 169 (5), 168 (12), 167 (10), 162 (30), 161 (9), 160 (100), 158 (7), 155 (6), 154 (17), 128 (5), 127 (5), 115 (5), 89 (14). Anal. Calcd for $C_{20}H_{23}N_2O_3Cl$: C, 64.08; H, 6.18; N, 7.47; Cl, 9.46. Found: C, 64.36; H, 6.28; N, 7.45; Cl, 9.34.

(±)-(3a*R,11b*R**)-Methyl 3-((*Z*)-2-Chlorobut-2-en-1yl)-2,3,3a,4,5,7-hexahydro-4-oxo-1*H*-pyrrolo[2,3-*d*]carbazole-6-carboxylate (13c).** To 0.435 mL of DMSO (6.13 mmol) in 50 mL of dichloromethane at −70 °C was added dropwise 0.693 mL of trifluoroacetic anhydride (4.91 mmol). After 15 min, a precooled solution of the alcohol **11c** (1.15 g, 3.07 mmol) in 15 mL of dichloromethane was added. Stirring was continued at the same temperature for 45 min, and then 4.4 mL (25.3 mmol) of *N*,*N*-diisopropylethylamine was added. After 1 h, the reaction mixture was gradually warmed to rt, diluted with 100 mL of dichloromethane, washed with brine, and dried (Na_2SO_4). After concentration and flash silica gel column chromatography (ether/hexane, 1:2) 0.923 g of the ketone **13c** was obtained as a white powder (81%). Continuing elution of the column by ether/hexane (6:1) gave 0.151 g of the starting alcohol (13%). For the ketone **13c**: TLC (ether/hexane, 1:1) R_f = 0.48 (CAS, greenish blue); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.12 (br s, 1 H), 7.35 (d, J = 7.5 Hz, 1 H), 7.18 (t, J = 7.7 Hz,

(24) Kamigata, N.; Satoh, T.; Yoshida, M. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 449.

1 H), 6.92 (t, J = 7.5 Hz, 1 H), 6.81 (d, J = 7.7 Hz, 1 H), 5.85 (q, J = 6.6 Hz, 1 H), 3.75 (s, 3 H), 3.73 (d, J = 14.3 Hz, 1 H), 3.68 (d, J = 14.3 Hz, 1 H), 3.51 (d, J = 17.3 Hz, 1 H), 3.29 (dd, J = 17.3, 1.6 Hz, 1 H), 3.26 (s, 1 H), 3.20−3.15 (m, 1 H), 3.08−3.05 (m, 1 H), 2.57−2.51 (m, 1 H), 2.06−2.02 (m, 1 H), 1.78 (d, J = 6.6 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 206.51, 167.85, 162.48, 143.55, 135.79, 132.03, 128.47, 123.82, 122.90, 121.54, 109.37, 87.96, 67.54, 58.57, 57.64, 51.16, 50.43, 40.12, 35.49, 13.84; IR (film) ν_{max} 3373, 2948, 2916, 2856, 2817, 1710, 1682, 1611, 1479, 1467, 1438, 1384, 1318, 1280, 1244, 1210, 1190, 1137, 1101, 1044, 748 cm^{-1}; UV (EtOH) λ_{max} 206, 228, 298, 330 nm; MS m/z (rel intens) 375 (3), 374 (9), 373 (11), 372 (30), 347 (5), 346 (29), 345 (24), 344 (100), 343 (11), 315 (4), 310 (4), 309 (22), 286 (6), 285 (13), 284 (15), 261 (8), 260 (8), 259 (34), 257 (14), 256 (13), 255 (47), 249 (5), 228 (15), 227 (20), 226 (7), 223 (6), 214 (21), 196 (14), 195 (31), 194 (10), 182 (6), 181 (7), 180 (7), 170 (5), 169 (17), 168 (43), 167 (46), 166 (11), 154 (16), 143 (6), 141 (7), 140 (10), 128 (6), 127 (6), 115 (12), 89 (16); high-resolution MS, FAB ionization, calcd for $C_{20}H_{21}N_2O_3ClLi$ 379.14, found 379.14.

(±)-15-*nor*-(*E* and *Z*)-19,20-Didehydro-14-hydroxypseudovincadifformine (23 and 24). a. To a suspension of 0.128 g (1.04 mmol) of chromium(II) chloride and 0.003 g of nickel(II) chloride in 3 mL of DMSO was added a solution of 0.040 g (0.086 mmol) of the iodo ketone **13a** in 1 mL of DMSO, at rt. After 2 h, the reaction was quenched with water (20 mL) and the mixture extracted with 3 × 10 mL of chloroform. The combined extracts were washed with water, dried (Na_2SO_4), and concentrated. The residue was purified by flash chromatography (SiO_2, 0.5:20:80 triethylamine/methanol/ethyl acetate) to generate 0.025 g of the pure *Z*-isomer **24** (86%): TLC (triethylamine/methanol/ethyl acetate 0.5:10:90) R_f = 0.36 (CAS, blue); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.14 (br s, 1 H), 7.36 (d, J = 7.4 Hz, 1 H), 7.17 (td, J = 7.7, 1.2 Hz, 1 H), 6.92 (td, J = 7.4, 0.9 Hz, 1 H), 6.85 (d, J = 7.7 Hz, 1 H), 5.61 (qt, J = 7.2, 2 Hz, 1 H), 3.96 (br d, J = 14.4 Hz, 1 H), 3.79 (s, 3 H), 3.56 (d, J = 2 Hz, 1 H), 3.47 (dt, J = 14.4, 2 Hz, 1 H), 3.44−3.39 (m, 1 H), 3.36 (dd, J = 16, 2 Hz, 1 H), 2.81−2.76 (m, 1 H), 2.29−2.23 (m, 1 H), 2.27 (d, J = 16 Hz, 1 H), 1.97 (dd, J = 7.3, 5.2 Hz, 1 H), 1.95 (dt, J = 7.2, 1.8 Hz, 3 H), 1.81 (br s, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.94, 164.20, 143.35, 142.75, 137.42, 128.10, 122.64, 121.46, 120.30, 109.29, 88.66, 82.92, 78.77, 60.54, 56.56, 55.04, 51.13, 40.03, 33.92, 13.25; IR (film) ν_{max} 3369, 2947, 2920, 2854, 1676, 1609, 1480, 1467, 1437, 1387, 1288, 1249, 1201, 1125, 1043, 745 cm^{-1}; UV (EtOH) λ_{max} 208, 226, 296, 328 nm; MS m/z (relative intensity) 340 (M + 2, 1), 339 (M + 1, 11), 338 (5, M), 307 (1), 228 (1), 216 (1), 215 (2), 169 (1), 168 (3), 167 (3), 166 (1), 154 (3), 153 (2), 140 (1), 128 (1), 127 (1), 125 (7), 124 (100), 115 (1), 96 (1), 94 (1), 82 (1), 81 (1), 79 (1), 77 (1), 67 (1), 55 (1), 52 (1); high-resolution MS, EI ionization, calcd for $C_{20}H_{20}N_2O_3$ 338.1630, found 338.1627.

b. To 120 mg (0.44 mmol) of di(cycloocta-1,5-diene)nickel in 2 mL of dry acetonitrile was added 2 mL of an acetonitrile solution of 54 mg of the chloro ketone **13c** (0.145 mmol) and 0.061 mL of triethylamine. The mixture was stirred overnight at rt. Evaporation of solvent with a rotary evaporator gave a residue, which was purified by flash chromatography on silica gel. Elution with 1:1 ether/hexane gave 28 mg of unreacted ketone. Continuing elution with 30% methanol in ethyl acetate afforded the cyclized products **23** and **24** as a mixture of 1:1.4 *E*/*Z* geometric isomers (53%, based on consumed starting material).

c. To 100 mg (0.36 mmol) of di(cycloocta-1,5-diene)nickel in 3 mL of acetonitrile was added a solution of 50 mg (0.12 mmol) of bromo ketone **13b** and 0.05 mL (0.4 mmol) of triethylamine in 2 mL of acetonitrile. The reaction mixture was stirred at rt for 3 h. Evaporation gave a residue, which was purified by flash chromatography on silica gel (25% methanol in ethyl acetate) to afford 29 mg (72%) of the cyclized products **23** and **24** as a 1:1 *E*/*Z* mixture (by NMR).

d. To 0.257 g of the bromo ketone **13b** (0.616 mmol) and 0.258 mL of triethylamine (3 equiv) in 10 mL of dichloromethane, stirred in an ice bath, was added, dropwise, trimethylsilyl triflate (0.298 mL, 2.5 equiv). The reaction mixture was stirred at rt overnight. TLC then showed only a trace of the starting material. After removal of solvents under vacuum, the residue was dissolved in 1% triethylamine/ether. Filtration and concentration gave 0.275 g (91%) of the enol ether **22b**, which was directly used in the next step.

The silyl enol ether **22b** (0.275 g) was mixed with 0.226 mL of tri-*n*-butyltin hydride and 20 mg of AIBN in 40 mL of dry benzene. After being degassed with argon for 10 min, the mixture was immersed in an oil bath at 80−85 °C and stirred for 3 h. Further equal amounts of tin hydride and AIBN were added, and the reaction mixture was kept at 85 °C overnight. After cooling and concentration, the residue was dissolved in 10 mL of methanol and 8 mL of 20% hydrochloric acid, and stirred for 1 h. The methanol was evaporated, and concentrated ammonium hydroxide was added to make the mixture strongly basic. Extraction with 3 × 40 mL of dichloromethane, drying, concentration, followed by flash SiO_2 column chromatography (ethyl acetate/methanol/triethylamine 90:10:1) afforded 0.034 g of the pentacyclic alcohols **23** and **24** as a 1:2 *E*/*Z* mixture (18% over two steps). Careful flash chromatographic purification (SiO_2, 5−10% methanol in dichloromethane) of the mixture afforded the pure analytical *E*-isomer **23**: TLC (SiO_2, triethylamine/methanol/ethyl acetate 0.5:10:90) R_f = 0.41 (CAS, blue); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.13 (br s, 1 H), 7.36 (d, J = 7.4 Hz, 1 H), 7.17 (td, J = 7.7, 1 Hz, 1 H), 6.92 (td, J = 7.4, 0.8 Hz, 1 H), 6.85 (d, J = 7.7 Hz, 1 H), 5.77 (qt, J = 6.9, 2.3 Hz, 1 H), 4.12 (br d, J = 14.6 Hz, 1 H), 3.78 (s, 3 H), 3.54 (d, J = 1.7 Hz, 1 H), 3.51−3.46 (m, 1 H), 3.45 (br d, J = 14.6 Hz, 1 H), 2.94 (dd, J = 16, 2 Hz, 1 H), 2.86−2.82 (m, 1 H), 2.30−2.24 (m, 1 H), 2.25 (d, J = 16 Hz, 1 H), 1.96−1.91 (m, 1 H), 1.70 (d, J = 6.9 Hz, 3 H); ^{13}C NMR (125 MHz, methanol-d_4) δ 170.01, 163.12, 145.37, 144.49, 137.36, 129.67, 123.07, 122.15, 119.56, 110.83, 90.75, 80.37, 78.90, 57.77, 56.24, 54.95, 51.52, 40.17, 36.39, 14.57; IR (film) ν_{max} 3371, 3054, 2949, 2923, 2855, 1676, 1610, 1467, 1438, 1386, 1288, 1247, 1203, 1126, 911, 731 cm^{-1}; UV (ethanol) λ_{max} 208, 224, 298, 328 nm; MS m/z (rel intens) 340 (2, M + 2), 339 (10, M + 1), 338 (7, M), 307 (1), 228 (1), 216 (1), 215 (2), 214 (2), 196 (1), 195 (1), 194 (1), 183 (1), 182 (1), 170 (1), 169 (2), 168 (5), 167 (5), 154 (5), 153 (2), 149 (3), 140 (2), 128 (2), 127 (3), 125 (13), 124 (100), 115 (2), 96 (2), 56 (2), 55 (2), 54 (3).

e. The same procedure was repeated, starting with 0.232 g of the iodo ketone **13a** and 0.017 g (10%) of the cyclized products **23** and **24**, was isolated as a 1:1 *E*/*Z* mixture.

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Supporting Information Available: ^{1}H NMR and ^{13}C NMR spectra for compounds **6**, **8a**−**c**, **10a**−**c**, **11a**−**c**, **12a**, **13a**−**c**, **15**, **16*Z***, **16*E***, **17**, **20**, **21**, **23**, and **24** (57 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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