Notes

Syntheses of *Strychnos*- and *Aspidospermatan*-Type Alkaloids. 7. Total Syntheses of Lagunamine, Isolagunamine, Condylocarpine, and Isocondylocarpine

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In our earlier syntheses of *Aspidosperma* alkaloids by intramolecular Diels–Alder reactions of secodine-type indoloacrylate–enamine intermediates,[1] we had found that stabilization of the enamine moiety by conjugation with a carbonyl group allowed isolation of the Diels–Alder reaction substrates **1** and **2** (Scheme 1) and subsequent generation of C19- or C15-oxygenated *Aspidosperma* alkaloids **3** and **4**.[2–4] Extending this approach to our intramolecular Diels–Alder route to *Strychnos* and *Aspidospermatan* alkaloids,[5] for a synthesis of lagunamine (**5**), we alkylated the indoloazonine, derived from deprotection of its *N*-*t*-BOC derivative **6**,[5] with butyn-3-one to form the enaminone **7** (Scheme 2). On heating in toluene this intermediate formed a minor amount of the anticipated *Aspidospermatan*-type product **8** (19%) and a new enaminone **9** (72%). That the latter is probably not a primary product was indicated by monitoring the reaction mixture, which showed the initial generation of the Diels–Alder product **8**, followed by gradual formation of the enaminone **9**. Also, the isolated pentacyclic ketone **8** was quantitatively converted to the tetracyclic enaminone **9** on heating in toluene.

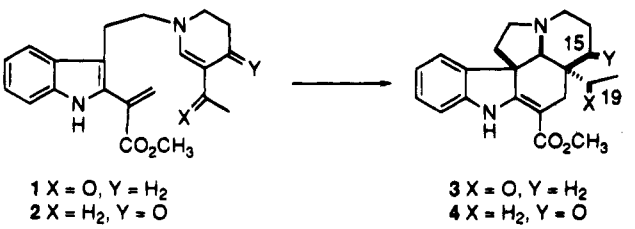
To overcome this gain in conjugative stabilization (indole and vinylogous amide in **9** *vs* vinylogous urethane in **8**), the tetracyclic enaminone **9** was heated with HCl in tetrahydrofuran. Thus, the more basic pentacyclic amine **8** (*vs* vinylogous amide **9**) was generated by formation of its hydrochloride salt.

The relative stereochemistry of the ketone **8** could be established by a NOESY NMR spectrum, which showed coupling of the C20 α and C14 β hydrogens (Figure 1). The trans relationship of C20 and C21 hydrogens in the ketone **8**, expected from the (*E*)-enamine **7** in the Diels–Alder cyclization, is also generated in the acid-catalyzed cyclization of the tetracyclic enaminone **9**.

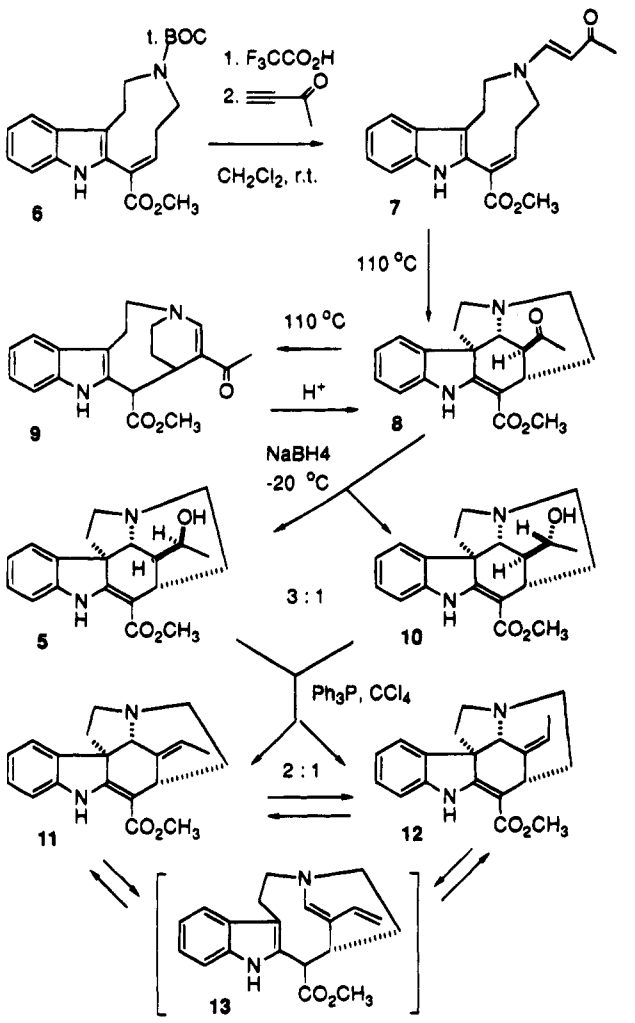
Reduction of the ketone **8** with sodium borohydride gave a 3:1 mixture of two alcohols **5** and **10**. Comparison of a 500 MHz ^{1}H NMR spectrum of the major synthetic isomer **5** with the spectra of natural lagunamine, and of the corresponding racemic compound obtained by a different synthesis,[6] showed identity. Similarly, the synthetic samples of 19-*epi*-lagunamine (**10**) had matching ^{1}H NMR and NOESY spectra.[6,7]

For a synthesis of condylocarpine (**11**), either lagunamine (**5**) or its C 19-epimer **10** were heated with triphenylphosphine and CCl_4 in acetonitrile (Scheme 2).[8] Condylocarpine (**11**) and isocondylocarpine (**12**) were obtained in a 2:1 ratio in each case. These dehydration

Scheme 1



Scheme 2



(1) For a review of early examples see: Kuehne, M. E.; Marko, I. *The Alkaloids*; Brossi, A., Ed.; Academic Press: New York, 1990; Vol. 37, p 133.

(2) The biogenetic numbering system for all compounds is that of: Le Men, J.; Taylor, W. I. *Experientia* **1965**, *21*, 508. Lettering of the fused ring systems follows the same implied principle.

(3) Kuehne, M. E.; Earley, W. G. *Tetrahedron* **1983**, *39*, 3713.

(4) Kuehne, M. E.; Bornmann, W. G.; Earley, W. G.; Marko, I. *J. Org. Chem.* **1986**, *51*, 2913.

(5) Kuehne, M. E.; Frasier, D. A.; Spitzer, T. D. *J. Org. Chem.* **1991**, *56*, 2697.

(6) Nkiliza, J.; Vercauteren, J.; Léger, J.-M. *Tetrahedron Lett.* **1991**, *32*, 1787.

(7) The NMR spectra of these compounds are very sensitive to traces of acid (DCl) in the solvent ($CDCl_3$), leading to a downfield shift of hydrogen signals adjacent to the amine nitrogen.

(8) Appel, R.; Wihler, H. D. *Chem. Ber.* **1976**, *109*, 3446.

0022-3263/95/1960-1864$09.00/0

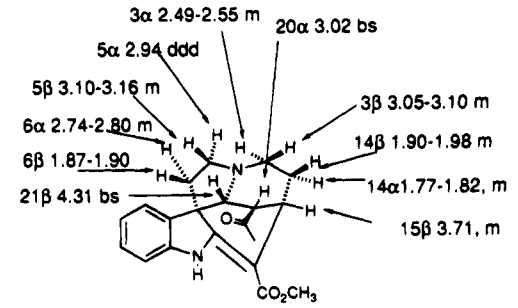


Figure 1. NOESY NMR correlations on ketone **8**: 14α–6α; 14β–20α; 14α–5α; 3α–5α; 3α–6α; 6β–21β; 5β–21β.

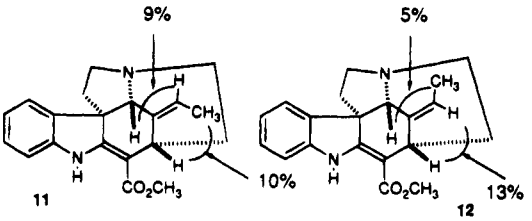


Figure 2. NOE NMR correlations on condylocarpine (**11**) and isocondylocarpine (**12**).

products could be separated by chromatography. Assignment of the *E* double bond configuration structure **11** to the major product was derived from NOE difference spectra, which showed coupling of C18 with C15 and C19 with C3 hydrogens (Figure 2).

Surprisingly, an old sample of natural condylocarpine was also found to contain both isomers (3.7:1).[9] It is not known if the previously unreported minor isomer **12** is present in the plant or if it was formed by isomerization during extraction with acid or on storage. Such an isomerization might be rationalized by protonation of C16, with reversible rupture of the C/E ring fusion, and reversible tautomerization of the resulting imonium species to a dienamine **13**. While condylocarpine (**11**) was not isomerized by stirring with trifluoroacetic acid in chloroform, it was found that both condylocarpine (**11**) and isocondylocarpine (**12**) generated the same 2:1 equilibrium mixture of double bond isomers at room temperature for 24 h in chloroform containing some acetic acid, as well as at reflux for 4 h in toluene, without acid.

Conclusions. By introduction of a carbonyl substituent at C19 in the present study, the resulting stabilization has allowed isolation of the presumed enamine diene intermediate in our intramolecular Diels–Alder reaction route to *Strychnos* and *Aspidospermatan* alkaloids.[5] This carbonyl substituent has also resulted in facile thermal cleavage of the resulting pentacyclic product to a briged indoloazonine structure. Such a cleavage is reminiscent of the reductive cleavages of *Aspidosperma* alkaloids (i.e., formation of quebrachamine and cleavamines) but has not previously been encountered in the *Aspidospermatan*-type alkaloids. Recyclization, under acidic conditions, to the initial pentacyclic ketone without epimerization of the ethyl substituent provides, overall, an exceptionally simple access to this class of natural products. It was also of interest to discover that the long known centerpiece of this alkaloid manifold, condylocarpine, naturally seems to be a mixture of *E*/*Z* double bond isomers (rather than the universally described *E* isomer) and to find the facility of this double bond isomerization.

(9) Dr. Bhupesh Das, CNRS Gif, France, has confirmed this isomeric ratio by HPLC in the condylocarpine sample that he had kindly provided for NMR comparison with our synthetic products.

Experimental Section

3-(4-Oxobut-1-en-4-yl)-7-(methoxycarbonyl)-1,2,4,5-tetrahydro-8*H*-[3,2-*d*]indoloazonine (7). To a solution of 0.184 g (0.497 mmol) of 3-(*tert*-butoxycarbonyl)-7-(methoxycarbonyl)-1,2,4,5-tetrahydro-8*H*-[3,2-*d*]indoloazonine (**6**)[5] in 20 mL of dichloromethane was added 0.5 mL of trifluoroacetic acid. The mixture was stirred at room temperature for 1 h and then partitioned between 10% aqueous potassium carbonate and three portions of dichloromethane. The organic extracts were dried over sodium sulfate and concentrated under vacuum. The residue was dissolved in 20 mL of dichloromethane and the solution cooled to 0 °C. Butyn-3-one (0.043 mL, 0.546 mmol) was added dropwise and the reaction mixture allowed to warm slowly to room temperature. TLC showed the reaction to be complete after 2 h. The mixture was concentrated under vacuum and the residue subjected to flash chromatography on silica gel, eluting with ethyl acetate:triethylamine, 10:0.4, to give 0.101 g (60%) of the title product. TLC (silica gel, dichloromethane:methanol, 95:5) R_f = 0.17 (CAS, green); 270-MHz NMR ($CDCl_3$) δ 8.50 (s, 1 H), 7.56–7.16 (m, 6 H), 5.10 (d, 1 H, J = 13 Hz), 3.74 (s, 3 H), 3.65 (m, 1 H), 3.48 (m, 2 H), 3.36 (m, 2 H), 2.91 (m, 2 H), 2.34 (m, 2 H), 2.13 (s, 3 H); IR (KBr) ν_{max} 3223, 3195, 1717, 1647, 1616, 1589, 1558, 1444, 1435, 1370, 1278 cm^{-1}; UV (ethanol) λ_{max} 302, 222, 202 nm; EIMS *m/e* (relative intensity) 339 ($(M + 1)^+$, 3), 338 (M^+, 5), 295 (5), 279 (3), 267 (7), 263 (3), 252 (3), 240 (5), 211 (27), 194 (17), 180 (32), 167 (22), 124 (17), 98 (52), 95 (57), 82 (12), 71 (100), 56 (14).

Methyl 5-Acetyl-3,6-ethano-1,6,7,8-tetrahydro-2*H*-azonino[5,4-*b*]indole-7-carboxylate (9) and 19-Oxotubotaiwine (8). (a) The *t*-BOC acrylate **6** (56.6 mg, 0.153 mmol) was dissolved in 5 mL of dry CH_2Cl_2. Triethylamine (70 μL, 0.504 mmol) was added, followed by trimethylsilyl triflate (88 μL, 0.458 mmol), and the mixture was stirred for 1 h at room temperature. The reaction mixture was poured over 10% aqueous sodium bicarbonate and extracted with CH_2Cl_2 (3 × 25 mL). The organic phase was dried over sodium sulfate and then concentrated to a residue by rotary evaporator.

The residue was dissolved in 5 mL of dry toluene, and the mixture was cooled to 0 °C. Butyn-3-one (14 μL, 0.183 mmol) was added, and the reaction mixture was stirred until TLC showed that the reaction was complete. The volume of toluene was then increased to 25 mL, and the reaction mixture was immersed in a 130 °C oil bath and heated for 36 h. The mixture was then cooled and concentrated by rotary evaporator. Flash chromatography on silica gel, eluting with ethyl acetate/ethanol/triethylamine (48:2:0.5), gave 37.1 mg (72%) of **9** and 10 mg (19%) of **8**, both as a colorless film.

For **9**: TLC (SiO_2, ethyl acetate/triethylamine = 10:0.4) R_f = 0.38 (CAS, blue-green); 500-MHz ^1H NMR ($CDCl_3$) δ 9.00 (s, 1 H), 7.45 (d, 1 H, J = 7.7 Hz), 7.26 (d, 1 H, J = 7.9 Hz), 7.11 (t, 1 H, J = 7.4 Hz), 7.06 (t, 1 H, J = 7.6 Hz), 6.24 (s, 1 H), 3.85 (s, 3 H), 3.79 (s, 1 H), 3.68 (d, 1 H, J = 3.5 Hz), 3.47 (m, 1 H), 3.40 (m, 1 H), 3.29 (m, 1 H), 3.08 (m, 2 H), 3.00 (m, 1 H), 2.41 (m, 1 H), 1.99 (m, 1 H), 1.57 (s, 3 H); 67.5-MHz ^{13}C NMR ($CDCl_3$) δ 191.1, 174.1, 151.0, 136.1, 135.5, 126.6, 122.0, 119.4, 117.0, 116.9, 110.9, 110.1, 55.1, 52.5, 47.3, 40.6, 36.8, 32.7, 23.4, 20.4; IR (film) ν_{max} 3425 (w), 3264 (w), 2947 (m), 2930 (m), 2872 (w), 1730 (s), 1616 (m), 1578 (s), 1485 (w), 1457 (s), 1433 (m), 1392 (m), 1345 (s), 1304 (m), 1276 (m), 1246 (m), 1197 (s), 1163 (s), 1054 (m), 1016 (m), 938 (m) cm^{-1}; UV (ethanol) λ_{max} 327, 292, 285, 224, 202 nm; MS *m/e* (relative intensity) 338 (M^+, 25), 265 (17), 216 (11), 211 (14), 202 (6), 149 (55), 144 (11), 137 (100), 121 (19), 94 (15), 67 (9); high-resolution MS, EI ionization, calcd for $C_{20}H_{22}N_2O_3$ 338.1630, found 338.1620.

For **8**: TLC (SiO_2, ethyl acetate/triethylamine = 10:0.4) R_f = 0.06 (CAS, dark blue); 500-MHz ^1H NMR ($CDCl_3$) δ 8.75 (s, 1 H), 7.24 (d, 1 H, J = 7.3 Hz), 7.10 (t, 1 H, J = 7.6 Hz), 6.92 (t, 1 H, J = 7.4 Hz), 6.77 (d, 1 H, J = 7.7 Hz), 4.32 (s, 1 H), 3.78 (s, 3 H), 3.71 (d, 1 H, J = 2.5 Hz), 3.13 (ddd, 1 H, J = 6.5, 12.0, 12.0 Hz), 3.08 (ddd, 1 H, J = 5.5, 5.5, 12.8 Hz), 3.02 (dd, 1 H, J = 2.3, 2.3 Hz), 2.92 (dd, 1 H, J = 7.1, 12.0 Hz), 2.78 (ddd, 1 H, J = 7.2, 12.8, 12.8 Hz), 2.53 (ddd, 1 H, J = 5.3, 9.8, 12.5 Hz), 1.98–1.87 (m, 2 H), 1.92 (s, 3 H), 1.81 (m, 1 H); 125-MHz ^{13}C

NMR δ ($CDCl_3$) 206.3, 169.3, 167.8, 142.8, 137.1, 127.1, 121.3, 119.7, 109.7, 95.9, 61.8, 55.9, 54.3, 51.9, 51.1, 45.8, 45.3, 28.6, 28.1, 27.5; IR (film) ν_{max} 3358 (w), 2947 (m), 2923 (m), 2868 (w), 1704 (s), 1673 (s), 1602 (s), 1475 (m), 1461 (m), 1433 (m), 1366 (w), 1299 (m), 1278 (m), 1234 (s), 1197 (m), 1160 (m), 1144 (m), 1102 (m), 1088 (m), 1069 (w), 1046 (w) cm^{-1}; UV (ethanol) λ_{max} 332, 299, 231, 201 nm; MS *m/e* (relative intensity) 339 ($(M + 1)^+$, 24), 338 (M^+, 67), 279 (18), 265 (35), 216 (18), 202 (14), 180 (12), 169 (42), 149 (100), 137 (53), 97 (21), 94 (34), 86 (19); high-resolution MS, EI ionization, calcd for $C_{20}H_{22}N_2O_3$ 338.1630, found 338.1621.

(b) The vinylogous amide **9** (20 mg) was dissolved in 5 mL of THF and 2 mL of 1% HCl. The reaction mixture was stirred at room temperature for 0.5 h. After this time, TLC showed complete conversion to the tetracyclic ketone **8**. The mixture was washed with saturated sodium bicarbonate and extracted 3× with dichloromethane. The combined organic extracts were dried over sodium sulfate and concentrated. Flash chromatography on silica gel, eluting with ethyl acetate:methanol:triethylamine, 8:2:0.1, gave 18.4 mg (92%) of product **8**.

(c) A solution of 19-oxotubotaiwine (**8**) (14.5 mg, 0.0428 mmol) in 15 mL of dry toluene was heated at reflux for 10 h. The solution was cooled and concentrated by rotary evaporator. Flash chromatography on silica gel, eluting with ethyl acetate/triethylamine (10:0.4), gave 12.7 mg (88%) of vinylogous amide **9**.

(d) The vinylogous amide **7** (0.0611 g, 0.180 mmol) was heated at reflux in 15 mL of toluene for 48 h. The reaction mixture was concentrated under vacuum and the residue subjected to flash chromatography as in **c** to produce 0.0438 g (72%) of vinylogous amide **9**.

(±)-Lagunamine (5) and (±)-19-*epi*-Lagunamine (10). 19-Oxotubotaiwine (**8**) (39 mg, 0.11 mmol) was dissolved in 5 mL of methanol, sodium borohydride (4 mg, 1.0 mmol) was added in two portions, and the mixture was then stirred for 2 h. One drop of 5% HCl was added to the reaction mixture, which was then made basic with concentrated NH_4OH and extracted with CH_2Cl_2 (5 × 20 mL). The organic extracts were dried with sodium sulfate, filtered, and concentrated by rotary evaporator. Flash chromatography on silica gel, eluting with ethyl acetate/ethanol/triethylamine (8:2:0.2) yielded 38 mg (97%) as a mixture of alcohols **5** and **10** in a ratio of 3:1.

For **5**: TLC (SiO_2, ethyl acetate/ethanol/triethylamine = 8:2:0.2) R_f = 0.23 (CAS, blue); 500-MHz ^1H NMR ($CDCl_3$) δ 8.87 (s, 1 H), 7.11 (d, 1 H, J = 7.2 Hz), 7.09 (t, 1 H, J = 7.8 Hz), 6.87 (t, 1 H, J = 7.6 Hz), 6.80 (d, 1 H, J = 7.7 Hz), 3.79 (s, 1 H), 3.77 (s, 3 H), 3.45 (s, 1 H), 3.03–2.89 (m, 4 H), 2.83 (dd, 1 H, J = 6.8, 10.7 Hz), 2.44 (ddd, 1 H, J = 5.1, 12.1, 12.1 Hz), 1.96 (ddd, 1 H, J = 2.4, 2.4, 9.9 Hz), 1.80 (m, 3 H), 1.03 (d, 3 H, J = 6.1 Hz); 125-MHz ^{13}C NMR ($CDCl_3$) δ 170.2, 168.7, 143.9, 136.2, 127.4, 121.1, 119.7, 109.8, 95.8, 65.6, 62.7, 55.2, 53.2, 51.2, 47.9, 45.2, 44.4, 27.98, 27.9, 21.5; IR (film) ν_{max} 3365 (m), 3352 (m), 2960 (m), 2947 (m), 2924 (m), 2872 (m), 2858 (m), 1673 (s), 1604 (s), 1474 (m), 1461 (s), 1433 (m), 1370 (m), 1345 (m), 1324 (m), 1276 (m), 1236 (s), 1202 (m), 1160 (m), 1144 (s), 1097 (s), 982 (w) cm^{-1}; UV (ethanol) λ_{max} 325, 297, 230, 201 nm; MS *m/e* (relative intensity) 340 (M^+, 23), 322 (22), 194 (12), 180 (22), 167 (13), 132 (11), 121 (14), 95 (39), 71 (100); high-resolution MS, EI ionization, calcd for $C_{20}H_{24}N_2O_3$ 340.1787, found 340.1770.

For **10**: TLC (SiO_2, ethyl acetate/ethanol/triethylamine = 8:2:0.2) R_f = 0.18 (CAS, blue); 500-MHz ^1H NMR ($CDCl_3$) δ 8.82 (s, 1 H), 7.23 (d, 1 H, J = 7.3 Hz), 7.11 (t, 1 H, J = 7.7 Hz), 6.89 (t, 1 H, J = 7.5 Hz), 6.80 (d, 1 H, J = 7.7 Hz), 4.26 (s, 1 H), 3.76 (s, 3 H), 3.07 (s, 1 H), 2.99–2.90 (m, 4 H), 2.84 (dd, 1 H, J = 6.9, 11.1 Hz), 2.43 (m, 1 H), 1.93 (ddd, 1 H, J = 2.4, 2.4, 9.6 Hz), 1.82 (m, 3 H), 1.00 (d, 3 H, J = 6.1 Hz); 125-MHz ^{13}C NMR ($CDCl_3$) δ 170.9, 168.3, 143.6, 136.6, 127.5, 121.4, 119.8, 109.8, 95.6, 66.5, 61.97, 54.9, 53.8, 51.2, 47.4, 44.9, 43.8, 29.3, 28.3, 21.9; IR (film) ν_{max} 3355 (m), 2949 (m), 2923 (s), 2872 (m), 2852 (m), 1674 (s), 1602 (s), 1474 (m), 1461 (s), 1435 (m), 1371 (m), 1329 (w), 1308 (w), 1276 (m), 1232 (s), 1202 (m), 1151 (m), 1129 (m), 1097 (m), 1026 (w) cm^{-1}; UV (ethanol) λ_{max} 326, 297, 231, 200 nm; MS *m/e* (relative intensity) 340 (M^+, 11), 322 (3), 194 (10), 180 (18), 167 (13), 95 (42), 71 (100); high-resolution MS, EI ionization, calcd for $C_{20}H_{24}N_2O_3$ 340.1787, found 340.1781.

Trifluoroacetic acid salt of **10**: 500-MHz ^1H NMR ($CDCl_3$) δ 8.91 (s, 1 H), 7.31 (d, 1 H, J = 7.4 Hz), 7.22 (t, 1 H, J = 7.6 Hz), 6.98 (t, 1 H, J = 7.5 Hz), 6.98 (t, 1 H, J = 7.5 Hz), 6.92 (d, 1 H, J = 7.8 Hz), 5.12 (s, 1 H), 3.83 (s, 3 H), 3.74 (m, 2 H), 3.35 (dd, 1 H, J = 7.5, 11.4 Hz), 3.31 (s, 1 H), 3.17 (m, 1 H), 3.06 (m, 1 H), 2.90 (ddd, 1 H, J = 7.4, 12.2, 12.2 Hz), 2.29 (m, 2 H), 2.14 (m, 1 H), 2.03 (m, 1 H), 1.11 (d, 3 H, J = 6.1 Hz).

(±)-Condylocarpine (11) and (±)-*iso*-Condylocarpine (12). Lagunamine (**5**) (13 mg, 0.0382 mmol) and triphenylphosphine (22 mg, 0.08 mmol) were dissolved in 5 mL of dry acetonitrile and heated in an oil bath at 85 °C. After 10 mincarbon tetrachloride (9.0 μL, 0.08 mmol) was added, and the reaction mixture was heated for 2 h. The reaction mixture was then cooled to room temperature, poured into 10 mL of 10% NaOH, and extracted with CH_2Cl_2 (5 × 10 mL). The organic extracts were dried with sodium sulfate, filtered, and concentrated by rotary evaporator. Flash chromatography on silica gel, eluting with chloroform/methanol (19:1), gave 10 mg (81%) of a 2:1 mixture of **11** and **12**. These products could be separated by careful rechromatography under the same conditions.

For **11**: TLC (SiO_2, chloroform/methanol = 18:2) R_f = 0.33 (CAS, blue); 500-MHz ^1H NMR ($CDCl_3$) δ 8.66 (s, 1 H), 7.21 (d, 1 H, J = 7.3 Hz), 7.11 (t, 1 H, J = 7.7 Hz), 6.89 (t, 1 H, J = 7.5 Hz), 6.77 (d, 1 H, J = 7.7 Hz), 5.35 (q, 1 H, J = 6.7 Hz), 4.22 (s, 1 H), 3.93 (dd, 1 H, J = 3.6, 5.7 Hz), 3.80 (s, 3 H), 3.17 (ddd, 1 H, J = 6.8, 9.2, 11.1 Hz), 3.06 (ddd, 1 H, J = 5.9, 7.1, 13.0 Hz), 2.99 (ddd, 1 H, J = 4.0, 7.1, 11.1 Hz), 2.75 (ddd, 1 H, J = 7.2, 9.2, 12.8 Hz), 2.71 (ddd, 1 H, J = 6.5, 6.5, 13.0 Hz), 2.02 (ddd, 1 H, J = 4.0, 6.8, 12.8 Hz), 1.92 (m, 2 H), 1.59 (d, 3 H, J = 6.7 Hz); 125-MHz ^{13}C NMR ($CDCl_3$) δ 168.1, 167.7, 144.3, 134.1, 128.0, 121.3, 120.4, 120.2, 119.6, 109.8, 101.8, 68.2, 59.5, 52.0, 51.3, 45.7, 44.2, 29.6, 28.2, 13.1; IR (film) ν_{max} 3369 (w), 2952 (s), 2921 (s), 2851 (s), 1678 (s), 1602 (s), 1474 (m), 1461 (s), 1433 (m), 1377 (m), 1358 (w), 1269 (m), 1232 (s), 1195 (s), 1160 (m), 1115 (m), 1101 (m), 1062 (m) cm^{-1}; UV (ethanol) λ_{max} 322, 298, 222, 208 nm; MS *m/e* (relative intensity) 323 ($(M + 1)^+$, 12), 322 (76), 307 (16), 279 (24), 263 (30), 253 (13), 252 (44), 249 (21), 235 (30), 221 (28), 180 (24), 120 (64); high-resolution MS, EI ionization, calcd for $C_{20}H_{22}N_2O_2$ 322.1681, found 322.1672.

For **12**: TLC (SiO_2, ethyl acetate/ethanol/triethylamine = 8:2:0.2) R_f = 0.18 (CAS, blue); 500-MHz ^1H NMR ($CDCl_3$) δ 8.65 (s, 1 H), 7.22 (d, 1 H, J = 7.2 Hz), 7.10 (t, 1 H, J = 7.7 Hz), 6.88 (t, 1 H, J = 7.5 Hz), 6.77 (d, 1 H, J = 7.8 Hz), 5.41 (q, 1 H, J = 6.7 Hz), 4.67 (s, 1 H), 3.77 (s, 3 H), 3.43 (dd, 1 H, J = 4.2, 4.2 Hz), 3.12 (ddd, 1 H, J = 7.2, 11.0, 11.0 Hz), 3.02 (m, 2 H), 2.78 (ddd, 1 H, J = 7.2, 9.2, 13.1 Hz), 2.78 (ddd, 1 H, J = 7.2, 9.2, 13.1 Hz), 2.65 (ddd, 1 H, J = 6.4, 6.4, 12.7 Hz), 1.98 (ddd, 1 H, J = 3.5, 6.8, 13.1 Hz), 1.90 (m, 2 H), 1.59 (d, 3 H, J = 6.7 Hz); 125-MHz ^{13}C NMR ($CDCl_3$) δ 168.8, 167.9, 144.5, 137.1, 135.2, 127.6, 121.0, 119.9, 117.9, 109.7, 102.1, 60.1, 59.8, 53.2, 51.1, 45.9, 44.9, 28.7, 12.8; IR (film) ν_{max} 3363 (w), 2947 (s), 2922 (s), 2855 (s), 2852 (m), 1674 (s), 1604 (s), 1475 (m), 1463 (s), 1434 (m), 1378 (m), 1356 (w), 1307 (w), 1270 (m), 1235 (s), 1198 (s), 1159 (m), 1115 (m), 1101 (m), 1064 (m) cm^{-1}; UV (ethanol) λ_{max} 324, 300, 206 nm; MS *m/e* (relative intensity) 323 ($(M + 1)^+$, 12), 322 (73), 307 (23), 294 (14), 279 (29), 263 (44), 253 (15), 252 (56), 249 (24), 235 (75), 221 (53), 180 (38), 121 (43); high-resolution MS, EI ionization, calcd for $C_{20}H_{22}N_2O_2$ 322.1681, found 322.1682.

Isomerizations of (±)-Condylocarpine (11) and (±)-Isocondylocarpine (12). (a) Solutions of 4 mg of (±)-condylocarpine or (±)-isocondylocarpine in 1.5 mL of toluene were heated at reflux for 4 h. The solvent was evaporated under reduced pressure and the product (TLC showed only spots for condylocarpine and isocondylocarpine) was directly analyzed by NMR. The ratio of (±)-condylocarpine to (±)-isocondylocarpine was 2:1.

(b) To solutions of 4 mg of (±)-condylocarpine or (±)-isocondylocarpine in 1.5 mL of chloroform was added 0.3 μL of acetic acid. The solutions were stirred at room temperature for 24 h and then basified by addition of a drop of concd ammonium hydroxide. Partitioning between dichloromethane and water, concentration of the organic extracts, and NMR analysis of the residue gave the same results as procedure **a**, above.

(c) A ^1H NMR (500 MHz) spectrum of natural condylocarpine, kindly provided by Dr. Bhupesh Das, showed a 3:1 ratio of condylocarpine to isocondylocarpine. By treating this sample by the above procedures it was also converted to a 2:1 mixture of the double bond isomers.

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Supplementary Material Available: Copies of ^{1}H NMR spectra for compounds **5** and **7–12**, ^{13}C NMR spectra for compounds **5** and **8–12**, and COSY spectra for compounds **10–12** (22 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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