

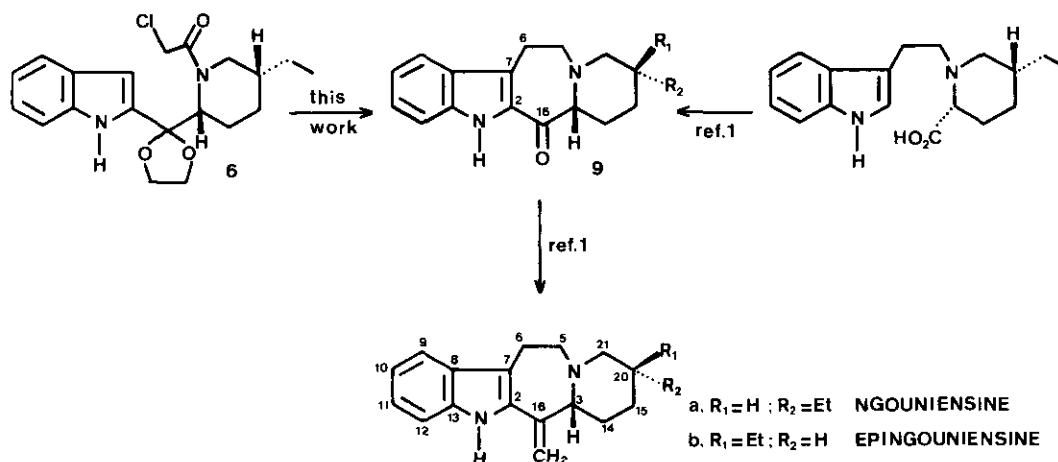
FORMAL SYNTHESIS OF THE INDOLE ALKALOIDS NGOUNIENSINE AND
EPINGOUNIENSINE

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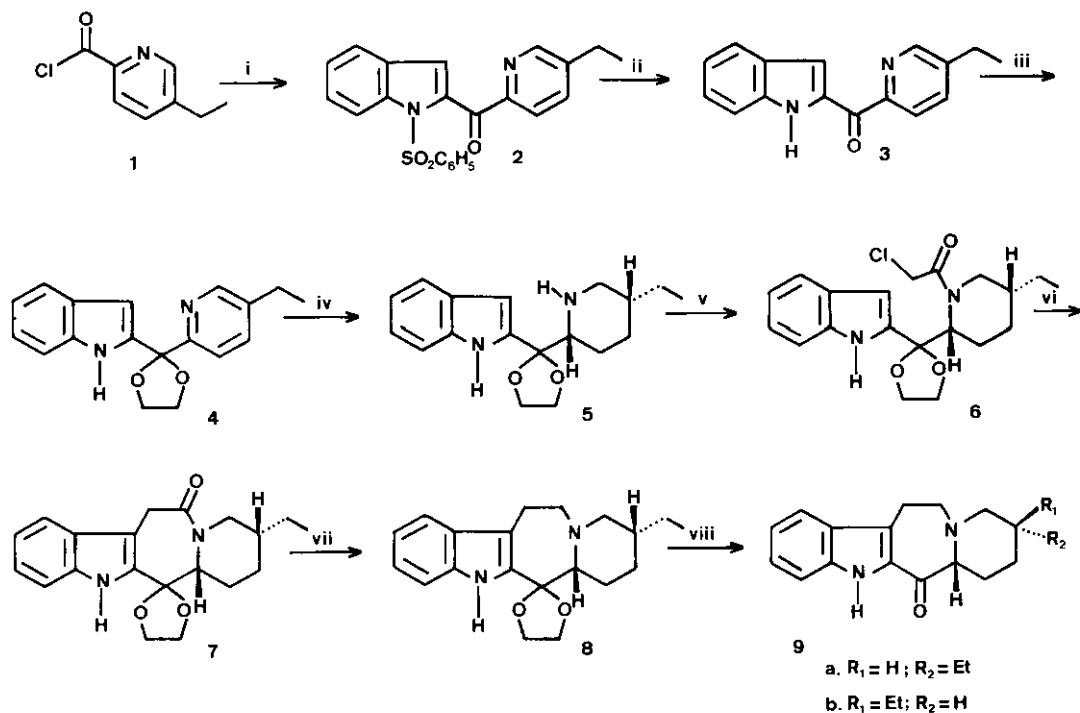
Abstract - An alternative route to the tetracyclic ketones **9**,
key intermediates in our total synthesis of (±)-ngouniensiene
and (±)-epingouniensiene, is reported.

In a previous paper¹ we reported the first total synthesis of (±)-ngouniensiene and (±)-epingouniensiene, two indole alkaloids isolated from *Strychnos ngouniensiis*² whose most characteristic structural feature is the existence of a bond connecting positions 3 and 16.³ The key intermediates in this synthesis were ketones **9**, from which the exocyclic conjugated C-16 methylene substituent present in ngouniensiensines was elaborated. Ketones **9** were prepared by formation of C₂-C₁₆ bond by means of electrophilic cyclization of *cis*-5-ethyl-1-[2-(3-indolylolethyl)]-2-piperidinecarboxylic acid (Scheme I).



SCHEME I

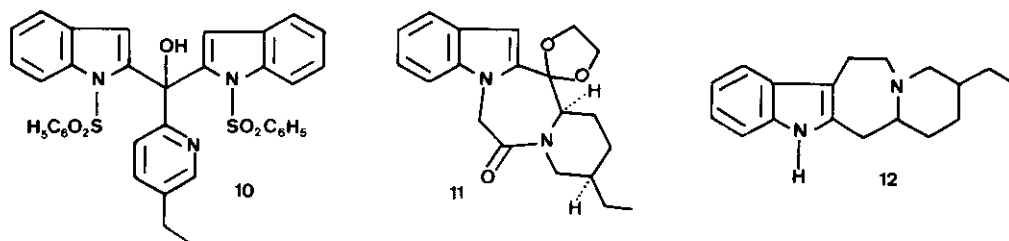
We report here an alternative synthetic route to the tetracyclic intermediates 9. The crucial step of this synthesis is the formation of C₆-C₇ bond through photocyclization of an appropriate 2-(N-chloroacetyl-2-piperidylmethyl)indole 6⁴ (see Scheme II). Thus, condensation between 2-lithio-1-(phenylsulfonyl)indole⁵ and acid chloride 1 gave ketone 2 in 48% yield. In addition, carbinol 10 was obtained as a minor by-product. Ketone 2 could be transformed into the desired *cis*-chloroacetamide 6 through a four-step sequence consisting of deprotection of the indole nucleus, protection of the 2-acylindole carbonyl group as ethylene acetal, stereoselective catalytic hydrogenation, and acylation of the resulting *cis*-piperidine 5 with chloroacetyl chloride. Photocyclization⁶ of *cis*-chloroacetamide 6 was effected in a diluted methanolic solution in the presence of potassium carbonate to prevent the hydrolysis of the acetal function. Under these conditions, the reaction took place regioselectively upon the indole 3-position giving the tetra-



Reagents and Conditions. (i) 2-Lithio-1-(phenylsulfonyl)indole, THF, -70 °C to rt, 1 h; (ii) 2 N NaOH, MeOH, reflux, 3 h; (iii) (CH₂OH)₂, TsOH, benzene, reflux, 24 h; (iv) H₂-PtO₂, AcOH, 50 psi, rt, 24 h; (v) ClCH₂COCl, CH₂Cl₂- 1 N NaOH, rt, 4 h; (vi) hν, MeOH, K₂CO₃, rt, 1 h; (vii) 1 M B₂H₆-THF, THF, reflux, 24 h; (viii) 1% HCl, MeOH, reflux, 3 h.

SCHEME II

cyclic cis-lactam **7** in 55% yield. A minor amount (5% yield) of the N-alkylation product **11** was also isolated.⁷ When the photocyclization was effected in more concentrated solutions of chloroacetamide **6**, the yield of lactam **11** rose to 18% whereas that of lactam **7** decreased to 35%. As can be observed in Table II, the structural assignment of tetracyclic lactams **7** and **11** was evident from the ¹³C-nmr chemical shift of carbon 6, which is more deshielded ($\Delta\delta = 32.1$ ppm) in the N-alkylated regioisomer **11**. In the ¹H-nmr spectrum of **11** the signal at $\delta 6.6$ due to the proton at the indole 3-position (7-H) was also of diagnostic value.

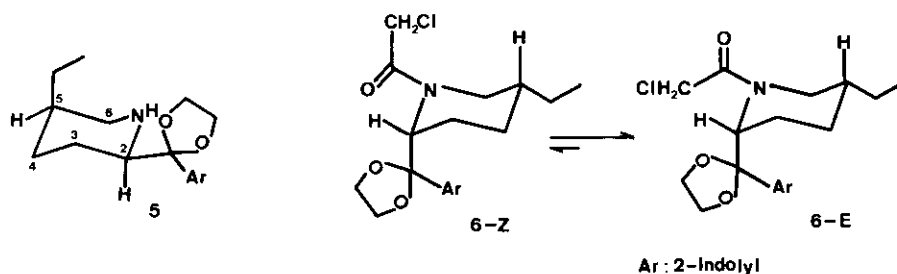


SCHEME III

Removal of the carbonyl group of lactam **7** to give **8** was accomplished in moderate yield (42%) by using diborane as reducing agent. It is worth mentioning that other procedures such as the reduction via the corresponding thiolactam or with lithium aluminium hydride were unsuccessful. In the first case no reaction was observed between lactam **7** and Lawesson's reagent whereas, in the second, demethylenengouniensine (**12**) was obtained as the only identifiable product (54% yield). Reduction of the lactam carbonyl group occurred with concomitant reductive cleavage of C-O bonds adjacent to the indole 2-position.⁸ Finally, hydrolysis of cis-acetal **8** afforded the target ketones **9** in 88% yield as a 1:1 mixture of cis-trans diastereomers, **9a** and **9b**. Clearly, under the acidic reaction conditions epimerization at the chiral center α to the carbonyl group had occurred. Ketones **9a** and **9b** were identical by spectroscopic and tlc comparison to those we had obtained by an alternative route in a previous work.¹

At this point it is worth commenting upon some stereochemical aspects of piperidines **5** and **6** and tetracyclic lactams **7** and **11**. As discussed above, only one stereoisomerically pure piperidine **5** was isolated after hydrogenation of pyridine **4**. The assignment of the cis relationship between the substituents at the piperidine 2- and 5-positions, with the smaller ethyl substituent located axially, was inferred from the chemical shift ($\delta > 2.7$) and multiplicity of 6-H in the ¹H-nmr

TABLE I. ^{13}C -Nmr Data of *cis*-Piperidine 5 and *cis*-Chloroacetamide 6^a

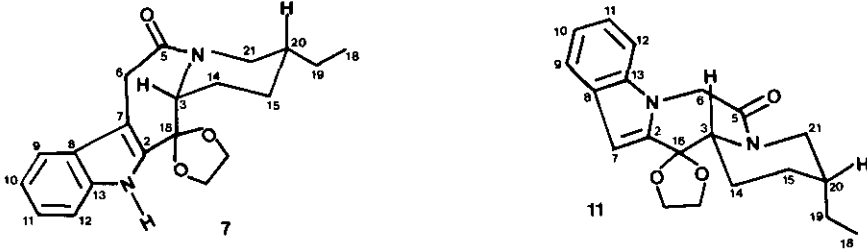


C-2	64.4	51.5	56.1
C-3	23.3	26.1	26.7
C-4	27.3	26.5	25.4
C-5	34.9	37.9	36.8
C-6	49.4	48.6	44.5
CH_3CH_2	12.0	10.8	10.8
CH_2CH_3	21.6	23.4	24.4
$\text{OCH}_2\text{CH}_2\text{O}$	64.9 and 65.3	64.5 and 64.0	64.2 and 64.9
O-C-O	107.9	109.6	109.6
In C-2	135.9	136.5	136.5
In C-3	100.6	100.3	100.6
In C-3a	127.7	127.5	127.5
In C-4	120.5 ^b	120.0 ^b	120.2 ^b
In C-5	119.5 ^b	118.9 ^b	119.2 ^b
In C-6	121.8	121.2	121.5
In C-7	111.2	111.4	111.3
In C-7a	137.6	136.8	136.8
CO	--	167.5	167.5
CH_2Cl	--	41.3	42.2

^aIn CDCl_3 solution. ^b Can be interchanged.

spectrum.

On the other hand, the ^1H - and ^{13}C -nmr spectra of *cis*-chloroacetamide 6 (see Table I) showed the presence of two rotamers, 6-E (major) and 6-Z (minor), resulting from hindered rotation of the chloroacetamide group.^{9,10} Both rotamers were easily assignable on the basis of the chemical shift of protons or carbons at positions 2 and 6 of the piperidine ring. As could be expected, equatorial 2-H and 6-H appear more strongly deshielded when they are located *syn* respect to the carbonyl group,¹¹ whereas in the same stereochemical situation C-2 and C-6 resonate at a higher magnetic field.¹² The *cis*-relationship between the piperidine 2- and 5-substituents of chloroacetamide 6 was confirmed from the multiplicity and

TABLE II. ^{13}C -Nmr Data of *cis*-Lactams **7**^a and **11**^{b,c}


	7	11		7	11
C-2	135.8	133.6	C-13	137.0	137.4
C-3	58.9	67.4	C-14	27.8 ^e	24.0
C-5	176.6	166.4	C-15	26.9 ^e	28.5
C-6	33.1	65.2	C-16	107.6	105.5
C-7	107.8	101.3	C-18	11.4	12.2
C-8	127.4	127.0	C-19	22.3	23.1
C-9	120.0 ^d	121.1 ^d	C-20	37.1	36.0
C-10	119.0 ^d	120.1 ^d	C-21	45.3	49.2
C-11	123.5	122.5	OCH ₂ CH ₂ O	67.1	65.8
C-12	112.2	109.3		and 66.9	and 65.8

^a In $\text{CDCl}_3\text{-CD}_3\text{OD}$ solution. ^b In CDCl_3 solution. ^c To allow a clearer comparison with **7**, the numbering system used for compound **11** is the biogenetic one.
^{d,e} Can be interchanged.

coupling constants of 2-H (d, \underline{J} = 5.4 Hz) and 6-Hax (t, \underline{J} = 12 Hz) in both rotamers. These data also indicated that, in this case, the bulkier substituent at C-2 adopts an axial disposition.¹³

The same conformational preference was observed in the tetracyclic lactam **7**, whose 21-Hax appeared again as a triplet (\underline{J} = 12 Hz) thus indicating the equatorial position of the ethyl substituent. On the contrary, the multiplicity of ^1H -nmr signals due to 3-H (dd, \underline{J} = 11 and 2.4 Hz) and 21-Hax (dd, \underline{J} = 13.6 and 3.2 Hz) in the regioisomeric lactam **11** revealed that, in the preferred conformation, the bulky substituent at C-3 was located equatorially whereas the C-20 ethyl group was in an axial disposition.

The ^{13}C -nmr data of lactams **7** and **11** (see Table II) are in accordance with the above configurational and conformational assignment. Thus, the axial ethyl group of **11** induces a shielding γ -effect upon C-14 (δ 24.0; compare with δ ~27 in **7**), whereas the axial C-3 substituent in **7** exerts a similar effect upon C-21 (δ 45.3; compare with δ 49.2 in **11**). Moreover, the shielding of the substituted piperidine

carbons bearing an axial substituent (C-3 in 7 and C-20 in 11) was observed.

EXPERIMENTAL

Melting points were determined in a capillary tube on a Büchi apparatus and are uncorrected. ^1H -Nmr spectra were recorded on a Perkin-Elmer R-24B (60 MHz) instrument or on a Varian XL-200 spectrometer. ^{13}C -Nmr spectra were measured with a Varian XL-200 spectrometer. Unless otherwise noted nmr spectra were recorded in CDCl_3 , and chemical shifts are expressed in ppm downfield (δ) from TMS. Ir spectra were taken with a Perkin-Elmer 1430 spectrophotometer and only noteworthy absorptions (reciprocal centimeters) are listed. Mass spectra were determined on a Hewlett-Packard 5930A mass spectrometer. Tic and column chromatography were carried out on SiO_2 (silica gel 60, Merck 0.063-0.200 mm), and the spots were located with uv light or iodoplatinate reagent. Prior concentration under reduced pressure, all organic extracts were dried over anhydrous sodium sulfate powder. Microanalyses were performed on a Carlo-Erba 1106 analyzer by Instituto de Química Biológica, Barcelona.

Condensation of 2-Lithio-1-(phenylsulfonyl)indole with 5-Ethyl-2-pyridinecarbonyl Chloride (1)

Sodium hydroxide (1.8 g, 33 mmol) in methanol (30 ml) was added to a solution of 5-ethyl-2-pyridinecarboxylic acid¹⁴ (5 g, 33 mmol) in methanol (20 ml). The solvent was removed and the resulting residue was suspended in anhydrous benzene (50 ml). The suspension was cooled at 0°C and then oxalyl chloride (2.8 ml, 33 mmol) in anhydrous benzene (10 ml) was slowly added. The reaction mixture was stirred at room temperature for 15 min and refluxed for an additional 40 min period. The solvent was eliminated and the residue was dissolved in anhydrous THF (100 ml). To the resulting solution, cooled at -70°C, was slowly added a suspension of 2-lithio-1-(phenylsulfonyl)indole, prepared⁵ from 1-phenylsulfonylindole¹⁵ (8 g, 31 mmol), *tert*-butyllithium (1.4 M, 26.6 ml, 37 mmol), and anhydrous THF (40 ml). The reaction mixture was allowed to warm slowly to room temperature (1 h) and quenched at this temperature with 0.04 N aqueous sodium hydroxide. The solvent was removed and the residue was dissolved in water and extracted with ether. The ethereal extracts were washed with 5% hydrochloric acid, dried, and evaporated to give a semisolid residue which was purified by column chromatography. Elution with 9:1 benzene-chloroform gave alcohol 10 (0.4 g, 2%): mp 234-237°C (ether); ir (KBr) 3300 (OH); ^1H -nmr (60 MHz) 1.3 (t, \underline{J} = 7 Hz, 3H, CH_3), 2.7 (q, \underline{J} = 7 Hz, 2H, CH_2), 6.1 (s, 1H, OH), 6.9-8.3 (m, 23H, ArH). Anal. Calcd for $\text{C}_{36}\text{H}_{29}\text{N}_3\text{O}_5\text{S}_2 \cdot 1\text{H}_2\text{O}$: C, 64.94; H, 4.68; N, 6.31; S, 9.63. Found: C, 65.20; H, 4.43; N, 6.27; S, 9.64. Elution with 7:3 benzene-chloroform afforded 5-ethyl-2-pyridyl 1-phenylsulfonyl-2-indolyl ketone (2, 6 g, 48%): ir (KBr) 1670 (CO); ^1H -nmr (60 MHz) 1.2 (t, \underline{J} = 7 Hz, 3H, CH_3), 2.6 (q, \underline{J} = 7 Hz, 2H, CH_2), 7.0-8.0 (m, 12H, ArH), 8.4 (s, 1H, pyridine 6-H). Anal. Calcd for $\text{C}_{22}\text{H}_{18}\text{N}_2\text{O}_3\text{S} \cdot 1/2\text{H}_2\text{O}$: C, 66.13; H, 4.79; N, 7.01; S, 8.03. Found: C, 66.28; H, 4.70; N, 6.96; S, 7.96.

5-Ethyl-2-pyridyl 2-Indolyl Ketone (3)

A solution of ketone 2 (3.9 g, 10 mmol) in methanol (100 ml) and 2 N aqueous sodium hydroxide (20 ml) was refluxed for 3 h. The solvent was removed and the resulting residue was dissolved in water and extracted with ether. The ethereal extracts were washed with water, dried, and evaporated to give ketone 3 (2.2 g, 88%). An analytical sample was obtained by recrystallization from acetone-ether: mp 137-138 °C; ir (KBr) 3320 (NH), 1625 (CO); $^1\text{H-nmr}$ (60 MHz) 1.2 (t, \underline{J} = 7 Hz, 3H, CH_3), 2.6 (q, \underline{J} = 7 Hz, 2H, CH_2), 6.9-8.1 (m, 7H, ArH), 8.4 (s, 1H, pyridine 6-H). Anal. Calcd for $\text{C}_{16}\text{H}_{14}\text{N}_2\text{O}$: C, 77.01; H, 5.63; N, 11.19. Found: C, 77.18; H, 5.52; N, 11.14.

5-Ethyl-2-pyridyl 2-Indolyl Ketone Ethylene Acetal (4)

A stirred solution of ketone 3 (2.7 g, 10.8 mmol), *p*-toluenesulfonic acid (2.8 g, 16.3 mmol), and ethylene glycol (34 ml) in anhydrous benzene (550 ml) was refluxed for 24 h with removal of water by a Dean-Stark trap. The reaction mixture was poured into aqueous sodium carbonate and extracted with ether. The organic extracts were washed several times with water, dried, and evaporated. The residue was chromatographed (3:2 benzene-chloroform) to give acetal 4 (2.4 g, 78%): mp 167-168 °C (acetone); ir (KBr) 3180 (NH); $^1\text{H-nmr}$ (60 MHz) 1.1 (t, \underline{J} = 7 Hz, 3H, CH_3), 2.5 (q, \underline{J} = 7 Hz, 2H, CH_2), 4.0 (s, 4H, OCH_2), 6.4 (s, 1H, indole 3-H), 6.8-7.5 (m, 6H, ArH), 8.3 (s, 1H, pyridine 6-H). Anal. Calcd for $\text{C}_{18}\text{H}_{18}\text{N}_2\text{O}_2$: C, 73.44; H, 6.16; N, 9.51. Found: C, 73.45; H, 6.07; N, 9.56.

cis-5-Ethyl-2-piperidyl 2-Indolyl Ketone Ethylene Acetal (5)

A solution of pyridine 4 (3.4 g, 11.5 mmol) in glacial acetic acid (50 ml) was shaken under 50 psi hydrogen pressure at room temperature over platinum dioxide (0.2 g) for 24 h. The catalyst was filtered off and the filtrate was diluted with water, neutralized by addition of 50% aqueous sodium hydroxide, and extracted with ether. Evaporation of the dried organic extracts left cis-piperidine 5 (3 g, 87%). An analytical sample was obtained by recrystallization from acetone-ether: mp 170 °C; ir (KBr) 2500-3500 (NH); $^1\text{H-nmr}$ (200 MHz, $\text{CDCl}_3\text{-CD}_3\text{OD}$) 0.88 (t, \underline{J} = 7 Hz, 3H, CH_3), 1.10-1.74 (m, 7H), 2.76 (dd, \underline{J} = 12 and 4 Hz, 1H, 6-H), 2.98 (m, 2H, 6-H and 2-Hax), 4.00 (m, 4H, CH_2O), 6.48 (d, \underline{J} = 1 Hz, 1H, indole 3-H), 7.01-7.20 (m, 2H, indole 5 and 6-H), 7.40 (m, 1H, indole 7-H), 7.60 (m, 1H, indole 4-H). Anal. Calcd for $\text{C}_{18}\text{H}_{24}\text{N}_2\text{O}_2$: C, 71.95; H, 8.05; N, 9.33. Found: C, 71.84; H, 8.27; N, 9.40.

cis-1-Chloroacetyl-5-ethyl-2-piperidyl 2-Indolyl ketone Ethylene Acetal (6)

A solution of chloroacetyl chloride (1.1 ml, 13.6 mmol) in methylene chloride (35 ml) was added dropwise to a stirred two-phase mixture of piperidine 5 (2.1 g, 6.9 mmol) in methylene chloride (100 ml) and 1 N aqueous sodium hydroxide (74 ml). The resulting mixture was stirred for 4 h at room temperature and the organic layer was separated. The aqueous layer was extracted with methy-

lene chloride and the combined organic solutions were washed with brine, dried, and evaporated. The resulting residue was crystallized from acetone to give cis-chloroacetamide **6** (2 g, 77%): mp 160–161 °C; ir (KBr) 3220 (NH) 1620 (CO); ¹H-nmr (CDCl₃-CD₃OD, 200 MHz) 0.92 (m, 3H, CH₃), 1.16–1.90 (m, 7H), 2.70 (t, \underline{J} = 12 Hz, 0.7H, 6-Hax, E-rotamer), 3.30 (t, \underline{J} = 12 Hz, 0.3H, 6-Hax, Z-rotamer), 3.60 (dd, \underline{J} = 12 and 5 Hz, 0.3H, 6-Heq, Z-rotamer), 3.79 (m, 1.2H, CH₂O, Z-rotamer), 4.02 (m, 2.8H, CH₂O, E-rotamer), 4.18 (d, \underline{J} = 14 Hz, 0.7H, CH₂Cl, E-rotamer), 4.30 (d, \underline{J} = 5.4 Hz, 0.7H, 2-Heq, E-rotamer), 4.41 (dd, \underline{J} = 12 and 5 Hz, 0.7H, 6-Heq, E-rotamer), 4.65 (d, \underline{J} = 14 Hz, 0.7H, CH₂Cl E-rotamer), 5.18 (d, \underline{J} = 5.4 Hz, 0.3H, 2-Heq, Z-rotamer), 6.45 (d, \underline{J} = 1 Hz, 0.3H, indole 3-H, Z-rotamer), 6.52 (d, \underline{J} = 1 Hz, 0.7H, indole 3-H, E-rotamer), 7.02–7.25 (m, 2H, indole 5 and 6-H), 7.50 (d, 1H, indole 7-H), 7.60 (d, 1H, indole 4-H), 10.20 (s, 0.3H, NH, Z-rotamer), 10.74 (s, 0.7H, NH, E-rotamer). Anal. Calcd for C₂₀H₂₅ClN₂O₃: C, 63.71; H, 6.76; Cl, 9.41; N, 7.43. Found: C, 63.78; H, 6.91; Cl, 9.31; N, 7.23.

Photolysis of cis-Chloroacetamide **6**

A solution of cis-chloroacetamide **6** (0.8 g, 2.1 mmol) in methanol (650 ml) containing potassium carbonate (1.28 g, 9.2 mmol) was irradiated under nitrogen at room temperature for 1 h using a 125 W medium pressure mercury lamp in a quartz immersion well reactor. The reaction mixture was evaporated to dryness and the residue was chromatographed. Elution with 4:1 benzene-chloroform gave cis-9-ethyl-6,6-ethylenedioxy-12-oxo-6,6a,7,8,9,10,12,13-octahydropyrido[1',2':1,7][1,4]-diazepino[4,5-a]-indole (**11**, 40 mg, 5%): mp 127–129 °C (acetone-methylene chloride); ir (NaCl) 1630 (CO); ¹H-nmr (200 MHz) 0.86 (t, \underline{J} = 7 Hz, 3H, H-18), 1.02–1.90 (m, 7H), 2.90 (dd, \underline{J} = 13.6 and 3.2 Hz, 1H, 21-Hax), 3.62 (dd, \underline{J} = 11 and 2.4 Hz, 1H, 3-Hax), 3.98–4.22 (m, 4H, CH₂O), 4.60 (dm, \underline{J} = 13.6 Hz, 1H, 21-Heq), 5.06 (d, \underline{J} = 17 Hz, 1H, 6-H), 5.16 (d, \underline{J} = 17 Hz, 1H, 6-H), 6.60 (d, \underline{J} = 0.7 Hz, 1H, 7-H), 7.10–7.30 (m, 2H, 10 and 11-H), 7.40 (m, 1H, 12-H), 7.60 (d, \underline{J} = 7 Hz, 1H, 9-H). Anal. Calcd for C₂₀H₂₄N₂O₃: C, 70.55; H, 7.11; N, 8.23. Found: C, 70.55; H, 7.59; N, 8.31. Elution with 3:2 benzene-chloroform afforded cis-9-ethyl-6,6-ethylenedioxy-12-oxo-6,6a,7,8,9,10,12,13-octahydropyrido[1',2';1,2]azepino[4,5-b]indole (**7**, 0.41 g, 55%): mp 247–248 °C (acetone-methanol); ir (KBr) 1625 (CO), 3210 (NH); ¹H-nmr (CDCl₃-CD₃OD, 200 MHz) 0.94 (t, \underline{J} = 7 Hz, 3H, 18-H), 1.20–2.2 (m, 7H), 2.60 (t, \underline{J} = 12 Hz, 1H, 21-Hax), 3.76 (d, \underline{J} = 16 Hz, 1H, 6-H), 3.90 (d, \underline{J} = 16 Hz, 1H, 6-H), 4.01–4.54 (m, 6H, CH₂O, 3-Heq, and 21-Heq), 6.90–7.20 (m, 2H, 10 and 11-H), 7.30 (m, 1H, 12-H), 7.48 (m, 1H, 9-H). Anal. Calcd for C₂₀H₂₄N₂O₃: C, 70.55; H, 7.11; N, 8.23. Found: C, 70.10; H, 7.19; N, 7.88.

Demethylenengouniensiine (**12**)

Lithium aluminium hydride (2.4 g, 63 mmol) was slowly added under nitrogen to a solution of lactam **7** (0.5 g, 1.47 mmol) in anhydrous THF (200 ml). After 24 h of refluxing, the reaction mix-

ture was cooled in an ice bath, the excess of lithium aluminium hydride was decomposed with 100 ml of water, and the resulting mixture was extracted with methylene chloride. Evaporation of the dried organic extracts gave a solid which was purified by column chromatography. Elution with 99:1 chloroform-methanol afforded demethylenengouniensiene (12, 215 mg, 54%): mp 172-174 °C (acetone-ether); ir (KBr) 3120 (NH); $^1\text{H-nmr}$ (60 MHz) 0.9-3.8 (m, 19H), 6.7-7.3 (m, 4H, indole), 7.6 (s, 1H, NH); ms, m/e (relative intensity) 268 (M^+ , 68), 239 (4), 156 (59), 124 (100). Anal. Calcd for $\text{C}_{18}\text{H}_{24}\text{N}_2 \cdot 1/4\text{H}_2\text{O}$: C, 79.22; H, 9.04; N, 10.26; Found: C, 79.51; H, 9.46; N, 10.23.

cis-9-Ethyl-6,6-ethylenedioxy-6,6a,7,8,9,10,12,13-octahydropyrido[1',2':1,2]azepino[4,5-b]indole (8)

To a solution of lactam 7 (0.2 g, 0.58 mmol) in anhydrous THF (15 ml) maintained at 0-5 °C was added a solution of diborane in THF (1 M, 1.7 ml). The addition of diborane (1 M, 1.7 ml) was repeated three times at two-hour intervals. The solution was refluxed during the intervals between additions and, finally, overnight. The solvent was removed and the resultant residue was dissolved in water and extracted with ether. The organic extracts were dried and evaporated to give an oil which was purified by column chromatography. Elution with 1:4 petroleum ether-ether gave compound 8 (80 mg, 42%): ir (CHCl_3) 3450 (NH); $^1\text{H-nmr}$ (200 MHz) 0.91 (t, $\underline{J} = 7$ Hz, 3H, 18-H), 1.20-1.80 (m, 7H), 2.64-3.56 (m, 7H), 3.76-4.38 (m, 4H, CH_2O), 7.10-7.40 (m, 3H, indole), 7.52 (dd, $\underline{J} = 7$ and 2 Hz, 1H, 9-H), 8.20 (s, 1H, NH). The picrate melted at 192-193 °C (acetone-ether). Anal. Calcd for $\text{C}_{26}\text{H}_{29}\text{N}_5\text{O}_9$: C, 56.21; H, 5.26; N, 12.60. Found: C, 56.18; H, 5.23; N, 12.35.

cis- and trans-9-Ethyl-6-oxo-6,6a,7,8,9,10,12,13-octahydropyrido[1',2':1,2]azepino[4,5-b]indole (9a and 9b)

A solution of acetal 8 (40 mg, 0.12 mmol) in methanol (10 ml) and 1% hydrochloric acid (5 ml) was refluxed for 4 h. The solvent was removed and the residue was diluted with water, basified with solid sodium carbonate, and extracted with ether. The organic extracts were dried and evaporated to give essentially pure 9¹ (30 mg, 88%) as a nearly equimolecular mixture of diastereomers.

ACKNOWLEDGMENT

This investigation was supported by the Comisión Asesora de Investigación Científica y Técnica, Spain, (project number 1842/82) and by the Comissió Interdepartamental de Recerca i Innovació Tecnològica, Generalitat de Catalunya (1985).

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Received, 4th October, 1988