

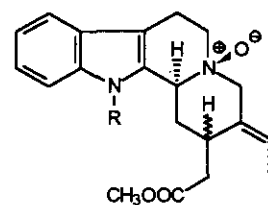
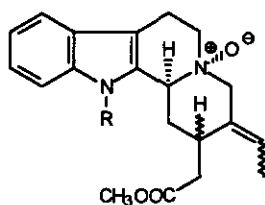
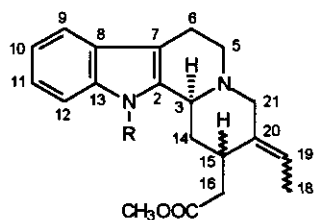
PREPARATION AND CONFORMATIONAL STUDY OF DEFORMYL-Z- AND DEFORMYL-E-GEISSOSCHIZINE EPIMERS AND N_a -BOC DERIVATIVES, AND THEIR N_b -OXIDES

Mauri Lounasmaa*, Reija Jokela*, Pirjo Hanhinen, Christiane Laine, and Ulla Anttila

Laboratory for Organic and Bioorganic Chemistry,
Technical University of Helsinki, FIN-02150 Espoo, Finland

Abstract - Syntheses are reported for deformylgeissoschizine isomers (**1** - **4**) and their N_a -Boc derivatives (**5** - **8**), as well as for their N_b -oxides (*cis* and *trans*) (**9** - **13**) and (**16** - **20**). Predominant conformations of the compounds were determined by nmr measurements.

The (\pm)-deformylgeissoschizine skeleton allows the existence of four stereoisomers [**1** - **4** (**5** - **8**)], and eight stereoisomers, [**9** - **16** (**17** - **24**)], can be predicted for the corresponding N_b -oxides (*cis* and *trans*) (biogenetic numbering¹).



1 R=H; H-15 α ; C-19 Z
2 R=H; H-15 β ; C-19 Z
3 R=H; H-15 α ; C-19 E
4 R=H; H-15 β ; C-19 E
5 R=Boc; H-15 α ; C-19 Z
6 R=Boc; H-15 β ; C-19 Z
7 R=Boc; H-15 α ; C-19 E
8 R=Boc; H-15 β ; C-19 E

9 R=H; H-15 α ; C-19 Z
10 R=H; H-15 β ; C-19 Z
11 R=H; H-15 α ; C-19 E
12 R=H; H-15 β ; C-19 E
17 R=Boc; H-15 α ; C-19 Z
18 R=Boc; H-15 β ; C-19 Z
19 R=Boc; H-15 α ; C-19 E
20 R=Boc; H-15 β ; C-19 E

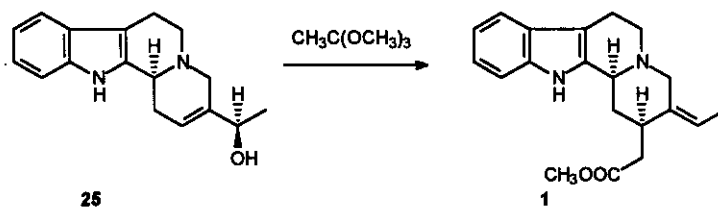
13 R=H; H-15 α ; C-19 Z
14 R=H; H-15 β ; C-19 Z
15 R=H; H-15 α ; C-19 E
16 R=H; H-15 β ; C-19 E
21 R=Boc; H-15 α ; C-19 Z
22 R=Boc; H-15 β ; C-19 Z
23 R=Boc; H-15 α ; C-19 E
24 R=Boc; H-15 β ; C-19 E

The correct determination of the different geissoschizine derivatives and their N_b -oxides is a problem of general interest.²⁻⁴ Model compounds and their N_b -oxides containing the characteristic elements of geissoschizine analogues can be expected to assist in direct

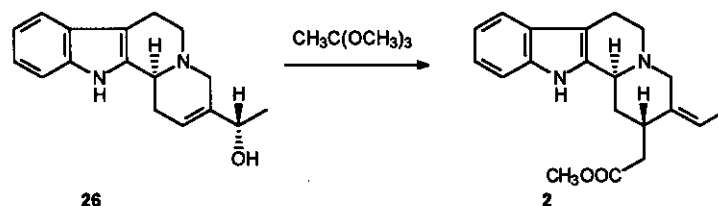
stereochemical determinations by nuclear magnetic resonance spectroscopy of the various geissoschizine isomers and their N_b -oxides. In the present paper we examine the four possible deformylgeissoschizines (**1** - **4**) (with *Z*- and *E*-ethylidene side chains) (and their Boc derivatives **5** - **8**), their *cis*- N_b -oxides (**9** - **12**) [and their Boc derivatives (**17** - **20**)], and *trans*- N_b -oxides (**13**) and (**16**). *Trans*- N_b -oxides (**14**) and (**15**) [and their Boc derivatives (**22**) and (**23**)] were not formed by the methods described.

RESULTS AND DISCUSSION

During earlier studies in our laboratory, deformyl-*Z*-geissoschizines (**1**) and (**2**) were prepared stereoselectively by using appropriate allylic alcohols (**25**) and (**26**) and trimethyl orthoacetate in the Claisen rearrangement (Schemes 1 and 2).⁵⁻⁹

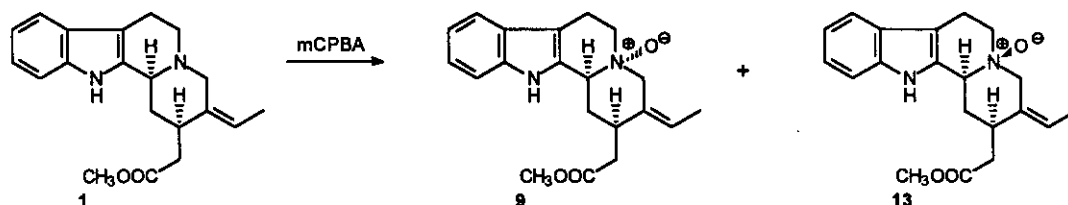


Scheme 1.

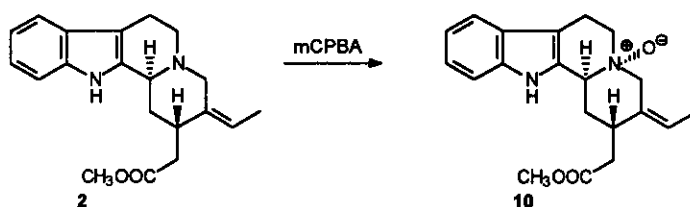


Scheme 2.

Oxidation of compounds (**1**) and (**2**) with *m*-chloroperbenzoic acid (*m*-CPBA) led to deformyl-*Z*-geissoschizine N_b -oxides (**9**) and (**13**) (*cis* and *trans*), and (**10**) (*cis*; no *trans* isomer was detected) (Schemes 3 and 4).¹⁰⁻¹⁵

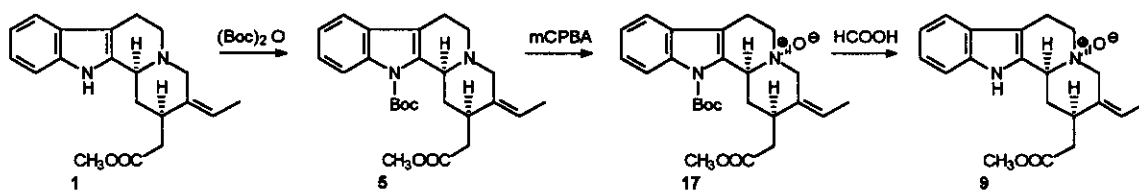


Scheme 3.

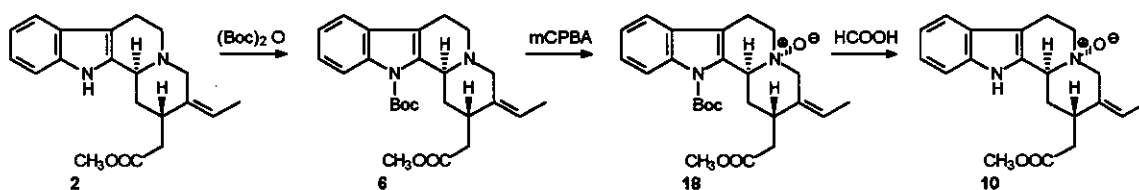


Scheme 4.

Treatment of deformed-*Z*-geissoschizines (1) and (2) with di-*t*-butyl dicarbonate [(Boc)₂O] transformed them to the corresponding *N*_a-Boc derivatives (5) and (6).^{12,14,16,17} Oxidation of compounds (5) and (6) with *m*-CPBA afforded exclusively *cis*-*N*_b-oxides (17) and (18) (no *trans*-*N*_b-oxides were detected). Cleavage of the Boc group with HCOOH led to deformed-*Z*-geissoschizine *cis*-*N*_b-oxides (9) and (10) (Schemes 5 and 6).

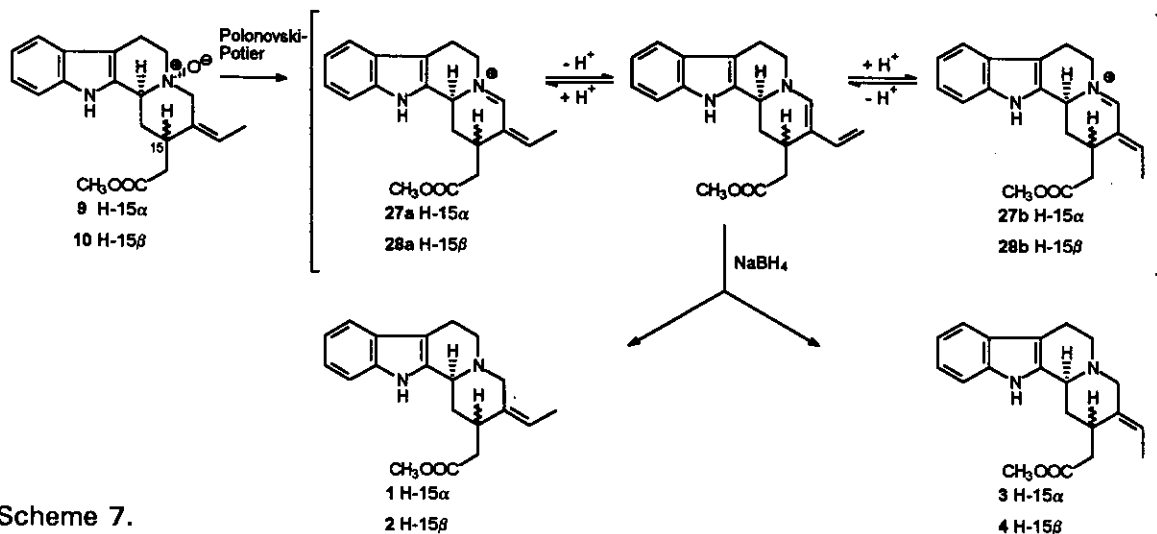


Scheme 5.



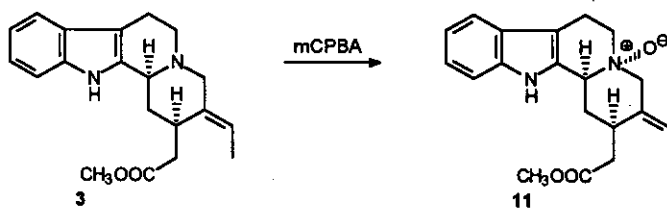
Scheme 6.

Treatment of deformed-*Z*-geissoschizine *cis*-*N*_b-oxides (9) and (10) with trifluoroacetic anhydride (TFAA) (Polonovski-Potier reaction)¹⁸⁻²⁰ led to iminium ions (27a) and (28a), respectively, which equilibrated with (27b) and (28b). Reduction of the iminium ion mixtures 27a \rightleftharpoons 27b and 28a \rightleftharpoons 28b with NaBH₄ afforded deformed-*E*-geissoschizines (3) and (4), respectively, together with deformed-*Z*-geissoschizines (1) and (2) (Scheme 7).

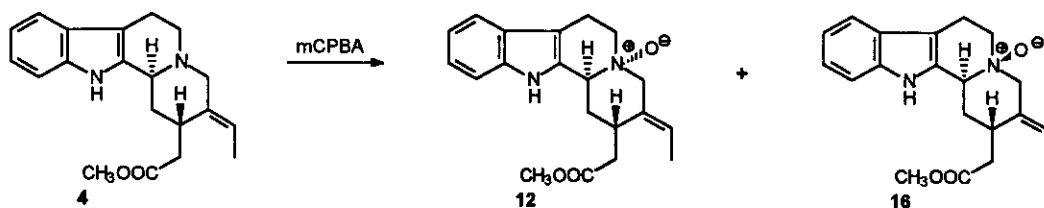


Scheme 7.

Oxidation of compounds (3) and (4) with *m*-CPBA led to deformedyl-*E*-geissoschizine *N*_b-oxide (11) (*cis*; no *trans* isomer was detected), and (12) and (16) (*cis* and *trans*) (Schemes 8 and 9).



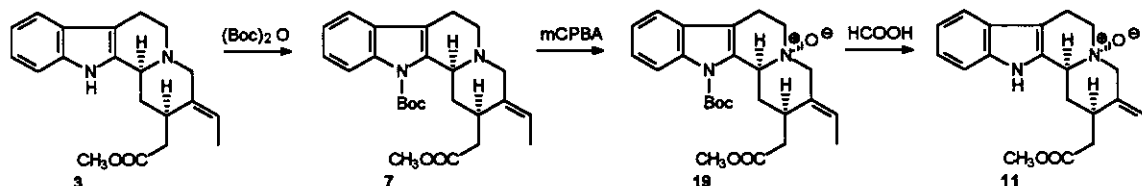
Scheme 8.



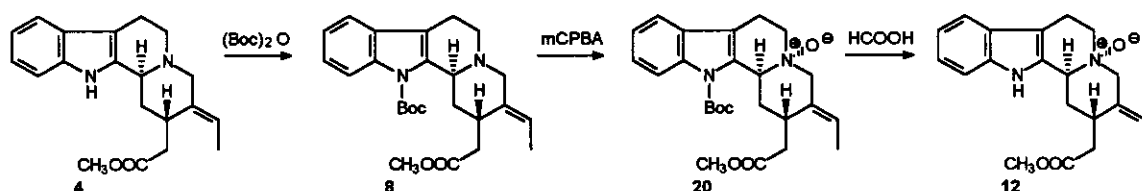
Scheme 9.

Treatment of deformedyl-*E*-geissoschizines (3) and (4) with (Boc)₂O transformed them to the corresponding *N*₉-Boc derivatives (7) and (8). Oxidation of compounds (7) and (8) with *m*-

CPBA afforded *cis*- N_b -oxides (**19**) and (**20**) (no *trans*- N_b -oxides were detected). Cleavage of the Boc group led to deformyl-*E*-geissoschizine *cis*- N_b -oxides (**11**) and (**12**) (Schemes 10 and 11).



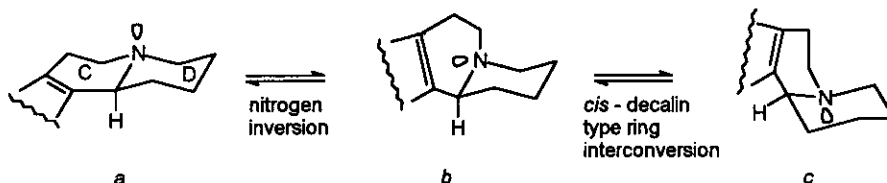
Scheme 10



Scheme 11.

CONFORMATIONAL CONSIDERATIONS

An indolo[2,3-*a*]quinolizidine system can exist in three conformations, with equilibration by nitrogen inversion and *cis*-decalin type ring interconversion (Scheme 12). In the corresponding indoloquinolizidine N_b -oxides the C/D ring juncture (*trans* or *cis*) is fixed. For a more detailed discussion, see Refs. 12, 15, 21 - 25.



Scheme 12.

The spectral data (Figure 1 and Experimental) and comparison with earlier results^{7,8,15,26-28} clearly indicate the predominance of conformation *a* for compounds (**1**, **2** and **4**) although in somewhat lesser amount for compound (**2**). The situation is completely different for compound (**3**): there the strong interaction between C-19-CH₃ and C-15-CH₂-COOCH₃ that would occur in conformations *a* and *b* is avoided in conformation *c*. Moreover, the possible

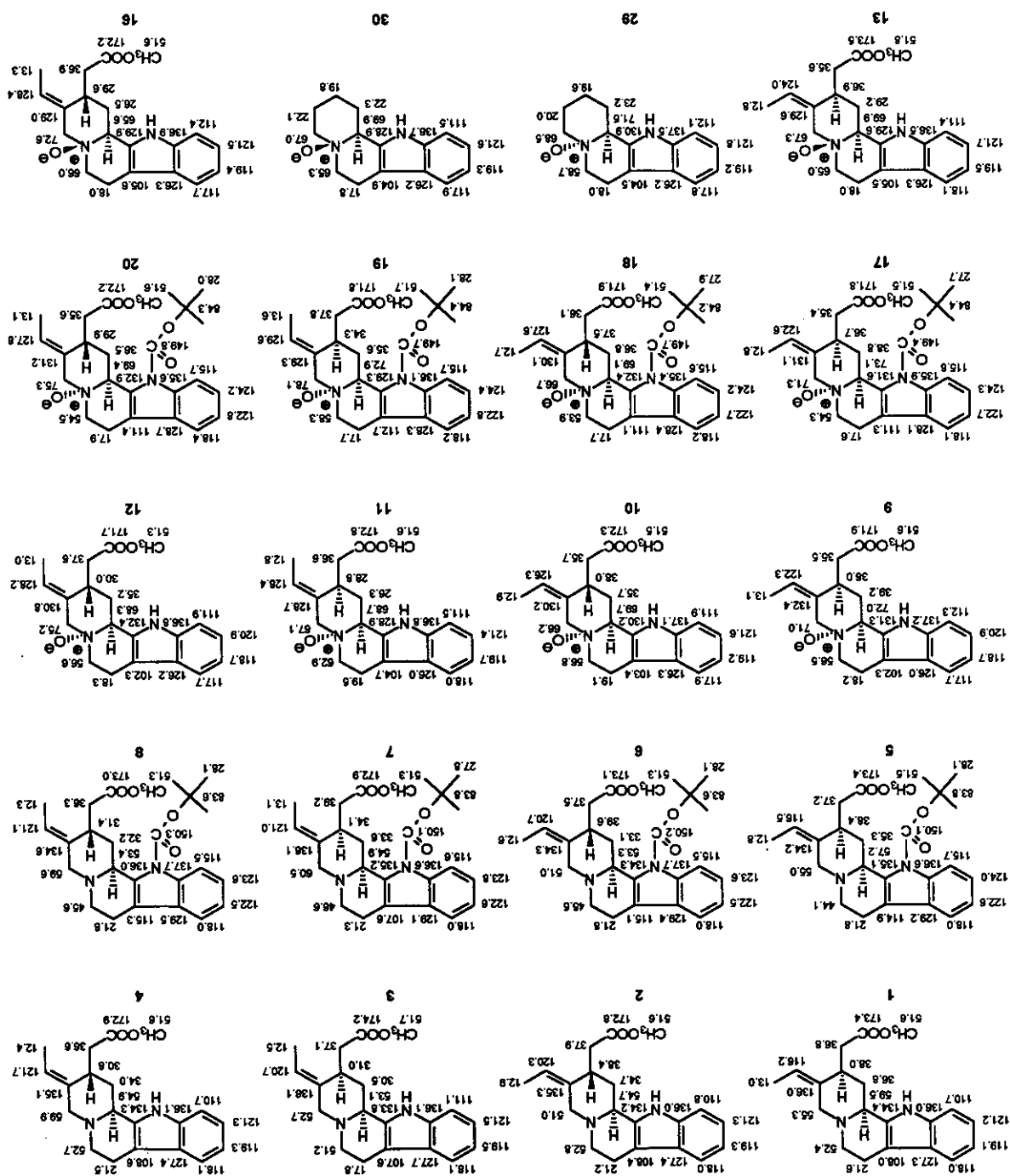


Figure 1. ¹³C-Nmr data of compounds (1 - 13), (16 - 20), (29), and (30). The ¹³C-nmr data of compounds (29) and (30) (Refs. 12 and 29) are added to the figure for purposes of comparison. Peak sharpness was reduced for several signals in the spectrum of compound (10).

existence of ring D in a boat and/or a twisted boat conformation, in addition to the normal chair conformation, has to be taken into consideration.

The earlier finding¹² that conformation *b* (and/or *c*) is generally favoured over conformation *a* in the Boc-protected series is supported by the exclusive transformation of Boc-protected compounds to *cis-N_b*-oxides (*vide supra*).

CONCLUSIONS

Syntheses are reported for the four deformylgeissoschizines (1 - 4) and their Boc derivatives (5 - 8), as well as for their *N_b*-oxides (*cis* and *trans*) (9 - 13) and (16 - 20). ¹H- and ¹³C-nmr spectra of the compounds were run and the predominant conformations are discussed. It is hoped that the nmr data presented will prove useful in the future for determinations of stereostructures of *Z*- and *E*-geissoschizine derivatives and similar compounds.

EXPERIMENTAL

Ir spectra were recorded with a Perkin-Elmer 700 IR spectrophotometer using CHCl₃ as solvent. Ir absorption bands are expressed in reciprocal centimetres (cm⁻¹). ¹H- and ¹³C-nmr spectra were measured in CDCl₃ with a Varian Gemini-200 spectrometer working at 199.975 MHz (¹H-nmr) and 50.289 MHz (¹³C-nmr). Chemical shifts are given in ppm by reference to TMS (¹H-nmr; δ_H = 0.0 ppm) and CDCl₃ (¹³C-nmr; δ_C = 77.0 ppm). Signal assignments were confirmed by APT, COSY, and HETCOR experiments. Abbreviations s, d, t, q, m, and br are used to designate singlet, doublet, triplet, quartet, multiplet, and broad, respectively. Mass spectrometry (Elms and HRms) was done on a Jeol DX 303/DA 5000 instrument.

Preparation of deformyl-*Z*-geissoschizine (1).

For the preparation and analytical data of compound (1), see Ref. 5 [compound (3a) in Ref. 5] and Figure 1.

Preparation of deformyl-15-*epi-Z*-geissoschizine (2).

For the preparation and analytical data of compound (2), see Ref. 5 [compound (3b) in Ref. 5] and Figure 1.

Preparation of deformyl-*E*-geissoschizine (3).

For the preparation and analytical data of compound (3), see Ref. 6 [compound (6) in Ref. 6] and Figure 1.

Preparation of deformyl-15-*epi-E*-geissoschizine (4).

The deformyl-15-*epi-Z*-geissoschizine *cis-N₆*-oxide (10) (*vide infra*) (88 mg, 0.26 mmol) was dissolved in dry CH₂Cl₂ (10 ml) and the mixture cooled to -17°C with an ice/salt bath. TFAA (92 μl, 0.65 mmol, 2.5 equiv.) was added with a syringe during 5 min and stirring was continued at room temperature for 2 h (Ar atm). The solution was evaporated to dryness, redissolved in MeOH (5 ml) and stirred at room temperature for 2 h. NaBH₄ (59 mg, 1.56 mmol, 6 equiv.) was added at 0°C in small portions to the stirred solution during 15 min and stirring was continued at room temperature for 2 h. H₂O was added, MeOH evaporated in vacuo and the mixture extracted with CH₂Cl₂. The organic fractions were washed with H₂O, dried with Na₂SO₄ and evaporated. The crude product was purified by flash chromatography (silica gel, CH₂Cl₂/MeOH; 99.5/0.5; 99/1) to yield compounds (1), (2) and (4).

Compound(1). Traces. For analytical data, see Ref. 5 [compound (3a) in Ref. 5] and Figure 1.

Compound(2). Traces. For analytical data, see Ref. 5 [compound (3b) in Ref. 5] and Figure 1.

Compound(4). Y. 72 mg (85%). Amorphous material. Ir: 1730 (C=O). ¹H Nmr: 1.63 (3H, d, J = 7 Hz, H-18), 3.55 (1H, br d, J = 12 Hz, H-3), 3.72 (3H, s, -OCH₃), 5.48 (1H, q, J = 7 Hz, H-19), 7.0-7.2 (2H, m, H-10, H-11), 7.27 (1H, d, J = 7 Hz, H-12), 7.46 (1H, d, J = 7 Hz, H-9), 7.85 (1H, br s, NH). For the ¹³C-nmr data, see Figure 1. Ms: 324 (M⁺, 100%), 323, 309, 293, 265, 251, 249, 237, 223, 170, 169, 156. HRms: Calcd for C₂₀H₂₄N₂O₂: 324.1838. Found: 324.1851. Anal. Calcd for C₂₀H₂₄N₂O₂: C, 74.05; H, 7.46; N, 8.63. Found C, 74.07; H 7.55; N 8.60.

Preparation of *N₆*-Boc-deformyl-*Z*-geissoschizine (5).

For the preparation and analytical data of compound (5), see Ref. 27 [compound (2) in Ref. 27] and Figure 1 (N.B. corrected ¹³C-nmr values).

Preparation of *N₆*-Boc-deformyl-15-*epi-Z*-geissoschizine (6).

A solution of deformyl-15-*epi-Z*-geissoschizine (2) (358 mg, 1.11 mmol), dry CH₂Cl₂ (10 ml), DMAP (41.3 mg, 0.34 mmol, 0.3 equiv.) and (Boc)₂O (348 mg, 1.59 mmol, 1.4 equiv.) was stirred at room temperature for 3 h (Ar atm). The mixture was evaporated and purified by flash chromatography (silica gel, CH₂Cl₂/MeOH; 99.5/0.5) to yield compound (6). Y. 455 mg

(97%). Amorphous material. Ir: 1720 (2 x C=O). ^1H Nmr: 1.65 (3H, d, $J=7$ Hz, H-18), 1.67 [9H, s, $-\text{C}(\text{CH}_3)_3$], 3.50 and 3.72 (1H and 1H, d and d, $J=14$ Hz and $J=14$ Hz, 2 x H-21), 3.68 (3H, s, $-\text{OCH}_3$), 4.62 (1H, br d, $J=11$ Hz, H-3), 5.46 (1H, q, $J=7$ Hz, H-19), 7.2-7.3 (2H, m, H-10, H-11), 7.40 (1H, d, $J=7$ Hz, H-9), 7.95 (1H, d, $J=7$ Hz, H-12). For the ^{13}C -nmr data, see Figure 1. Ms: 424 (M^+), 368, 367 (100%), 323, 295, 251, 169. HRms: Calcd for $\text{C}_{25}\text{H}_{32}\text{N}_2\text{O}_4$: 424.2362. Found: 424.2350. Anal. Calcd for $\text{C}_{25}\text{H}_{32}\text{N}_2\text{O}_4$: C, 70.73; H, 7.60; N, 6.60. Found C, 70.46; H 7.52; N 6.61.

Preparation of N_8 -Boc-deformyl-*E*-geissoschizine (7).

For the preparation and analytical data of compound (7), see Ref. 17 [compound (2) in Ref. 17] and Figure 1.

Preparation of N_8 -Boc-deformyl-15-*epi-E*-geissoschizine (8).

A solution of deformyl-*E*-geissoschizine (3) (198 mg, 0.61 mmol), dry CH_2Cl_2 (6 ml), DMAP (14.5 mg, 0.12 mmol, 0.2 equiv.) and $(\text{Boc})_2\text{O}$ (330 mg, 1.51 mmol, 2.5 equiv.) was stirred at room temperature for 4 h (Ar atm). The mixture was evaporated and purified by flash chromatography (silica gel, $\text{CH}_2\text{Cl}_2/\text{MeOH}$; 99.5/0.5) to yield compound (8). Y. 232 mg (90%). Amorphous material. Ir: 1730 (2 x C=O). ^1H Nmr: 1.63 (3H, d, $J=7$ Hz, H-18), 1.67 [9H, s, $-\text{C}(\text{CH}_3)_3$], 3.16 and 3.80 (1H and 1H, d and d, $J=14$ Hz and $J=14$ Hz, 2 x H-21), 3.69 (3H, s, $-\text{OCH}_3$), 4.59 (1H, br d, $J=12$ Hz, H-3), 5.40 (1H, q, $J=7$ Hz, H-19), 7.2-7.3 (2H, m, H-10, H-11), 7.39 (1H, d, $J=8$ Hz, H-9), 7.93 (1H, d, $J=8$ Hz, H-12). For the ^{13}C -nmr data, see Figure 1. Ms: 424 (M^+), 368, 367 (100%), 323, 295, 251, 249, 170, 169. HRms: Calcd for $\text{C}_{25}\text{H}_{32}\text{N}_2\text{O}_4$: 424.2362. Found: 424.2348. Anal. Calcd for $\text{C}_{25}\text{H}_{32}\text{N}_2\text{O}_4$: C, 70.73; H, 7.60; N, 6.60. Found C, 70.42; H 7.72; N 6.57.

Preparation of deformyl-*Z*-geissoschizine *cis-N_6*-oxide (9).

For the preparation and analytical data of compound (9), see Ref. 6 [compound (4a) in Ref. 6] and Figure 1.

Preparation of deformyl-*Z*-geissoschizine *cis-N_6*-oxide (9) and *trans-N_6*-oxide (13).

For the preparation and analytical data of compounds (9) and (13), see Ref. 6 [compounds (4a) and (4b), respectively, in Ref. 6] and Figure 1.

Preparation of deformyl-15-epi-Z-geissoschizine *cis-N_b*-oxide (10).

A solution of deformyl-15-epi-Z-geissoschizine (**2**) (70 mg, 0.22 mmol) and *m*-CPBA (75 mg, 0.43 mmol, 2.0 equiv.) in dry CH₂Cl₂ (10 ml) was stirred at room temperature for 4 h (Ar atm). The mixture was evaporated and purified by column chromatography (alumina, CH₂Cl₂/MeOH; 99/1) to yield compound (**10**). Y. 46 mg (62%). White crystals. mp 199-200°C (EtOH). Ir: 1735 (C=O). ¹H Nmr: 1.72 (3H, d, J=7 Hz, H-18), 3.58 (3H, s, -OCH₃), 4.58 (1H, br s, H-3), 5.55 (1H, q, J=7 Hz, H-19), 6.9-7.1 (2H, m, H-10, H-11), 7.3-7.5 (2H, m, H-9, H-12), 9.12 (1H, br s, NH). For the ¹³C-nmr data, see Figure 1. Ms: 340 (M⁺), 323, 296, 295, 267, 249, 184, 170, 169, 156 (100%). HRms: Calcd for C₂₀H₂₄N₂O₃: 340.1786. Found: 340.1768. Anal. Calcd for C₂₀H₂₄N₂O₃: C, 70.57; H, 7.11; N, 8.23. Found C, 70.52; H 7.16; N 8.12.

Preparation of deformyl-E-geissoschizine *cis-N_b*-oxide (11).

For the preparation and analytical data of compound (**11**), see Ref. 16 [compound (**15**) in Ref. 16] and Figure 1 (N.B. corrected ¹³C-nmr values).

Preparation of deformyl-15-epi-E-geissoschizine *cis-N_b*-oxide (12).

N_b-Boc-deformyl-15-epi-E-geissoschizine *cis-N_b*-oxide (**20**) (32 mg, 0.07 mmol) was dissolved in HCOOH (5 ml). The reaction mixture was stirred at room temperature for 20 h (Ar atm). The reaction mixture was evaporated, dissolved in CH₂Cl₂, neutralized with 10% Na₂CO₃ and extracted with CH₂Cl₂. The organic fractions were washed with H₂O and dried with Na₂SO₄. Purification by plc (silica gel, CH₂Cl₂/MeOH; 90/10) yielded compound (**12**). Y. 21 mg (88%). White crystals. mp 186-188°C (EtOH). Ir: 1735 (C=O). ¹H Nmr: 1.62 (3H, d, J=7 Hz, H-18), 3.46 (3H, s, -OCH₃), 3.85 and 4.37 (1H and 1H, d and d, J=14 Hz and J=14 Hz, 2 x H-21), 4.71 (1H, br d, J=12 Hz, H-3), 5.66 (1H, q, J=7 Hz, H-19), 6.8-7.0 (3H, m, H-10, H-11, H-12), 7.44 (1H, d, J=8 Hz, H-9), 12.2 (1H, br s, NH). For the ¹³C-nmr data, see Figure 1. Ms: 340 (M⁺), 323, 296, 295, 267, 249, 184, 170, 169, 156 (100%). HRms: Calcd for C₂₀H₂₄N₂O₃: 340.1787. Found: 340.1766. Anal. Calcd for C₂₀H₂₄N₂O₃: C, 70.57; H, 7.11; N, 8.23. Found C, 70.34; H 7.02; N 8.04.

Preparation of deformyl-15-epi-E-geissoschizine *cis-N_b*-oxide (12) and *trans-N_b*-oxide (16).

A solution of deformyl-15-epi-E-geissoschizine (**4**) (57 mg, 0.18 mmol) and *m*-CPBA (66 mg, 0.38 mmol, 2.2 equiv.) in dry CH₂Cl₂ (8 ml) was stirred at room temperature for 4 h (Ar atm). The reaction mixture was neutralized with 10% Na₂CO₃ and extracted with CH₂Cl₂. The

organic fractions were washed with H₂O and dried with Na₂SO₄, yielding a mixture of compounds (12) and (16) (46 mg, 77%). Purification by flash chromatography (silica gel, CH₂Cl₂/MeOH; 95/5), followed by repeated plc (CH₂Cl₂/MeOH; 92/8), yielded pure compounds (12) and (16).

Compound(12).Y. 12 mg (20%). For the analytical data, see above.

Compound(16).Y. 7 mg (12%). Amorphous material. Ir: 1740 (C=O). ¹H Nmr: 1.55 (3H, d, J=7 Hz, H-18), 3.65 (3H, s, -OCH₃), 4.06 (1H, br d, J=13 Hz, H-21), 4.56 (1H, br d, J=11 Hz, H-3), 5.61 (1H, q, J=7 Hz, H-19), 6.83 (1H, t, J=8 Hz, H-10), 7.02 (1H, t, J=8 Hz, H-11), 7.12 (1H, d, J=8 Hz, H-12), 7.45 (1H, d, J=8 Hz, H-9), 12.1 (1H, br s, NH). For the ¹³C-nmr data, see Figure 1. Ms: 340 (M⁺), 323, 296, 295, 267, 249, 184, 170, 169, 156 (100%). HRms: Calcd for C₂₀H₂₄N₂O₃: 340.1786. Found: 340.1802. Anal. Calcd for C₂₀H₂₄N₂O₃: C, 70.57; H, 7.11; N, 8.23. Found C, 70.37; H 7.01; N 8.06.

Preparation of N_a-Boc-deformyl-Z-geissoschizine *cis*-N_b-oxide (17).

For the preparation and analytical data of compound (17), see Ref. 27 [compound (3) in Ref. 27] and Figure 1 (N.B. corrected ¹³C-nmr values).

Preparation of N_a-Boc-deformyl-15-epi-Z-geissoschizine *cis*-N_b-oxide (18).

A solution of N_a-Boc-deformyl-15-epi-Z-geissoschizine (6) (99 mg, 0.23 mmol) and *m*-CPBA (78 mg, 0.45 mmol, 2.0 equiv.) in dry CH₂Cl₂ (10 ml) was stirred at room temperature for 2.5 h (Ar atm). The mixture was evaporated and purified by column chromatography (alumina, CH₂Cl₂/MeOH; 99/1) to yield compound (18). Y. 96 mg (93%). Amorphous material. Ir: 1720 (2 x C=O). ¹H Nmr: 1.66 [9H, s, -C(CH₃)₃], 1.75 (3H, d, J=7 Hz, H-18), 3.69 (3H, s, -OCH₃), 4.22 and 4.55 (1H and 1H, d and d, J=14 Hz and J=14 Hz, 2 x H-21), 5.32 (1H, br d, J=12 Hz, H-3), 5.80 (1H, q, J=7 Hz, H-19), 7.2-7.3 (2H, m, H-10, H-11), 7.43 (1H, br d, J=7 Hz, H-9), 7.93 (1H, d, J=7 Hz, H-12). For the ¹³C-nmr data, see Figure 1. Ms: 440 (M⁺, <2%), 424, 367, 340, 323, 295, 267, 249, 184, 170, 169, 156 (100%). HRms: Calcd for C₂₅H₃₂N₂O₅: 440.2311. Found: 440.2283. Anal. Calcd for C₂₅H₃₂N₂O₅: C, 68.16; H, 7.32; N, 6.36. Found C, 68.37; H 7.11; N 6.19.

Preparation of N_a-Boc-deformyl-E-geissoschizine *cis*-N_b-oxide (19).

For the preparation and analytical data of compound (19), see Ref. 30 [compound (11) in Ref. 30] and Figure 1.

Preparation of N_a -Boc-deformyl-15-epi-*E*-geissoschizine *cis*- N_b -oxide (20).

A solution of N_a -Boc-deformyl-15-epi-*E*-geissoschizine (8) (105 mg, 0.25 mmol) and *m*-CPBA (86 mg, 0.50 mmol, 2.0 equiv.) in dry CH_2Cl_2 (5 ml) was stirred at room temperature for 2 h (Ar atm). The mixture was evaporated and purified by column chromatography (alumina, $\text{CH}_2\text{Cl}_2/\text{MeOH}$; 99/1) to yield compound (20). Y. 65 mg (60%). Amorphous material. Ir: 1730 (2 x C=O). ^1H Nmr: 1.66 [9H, s, $-\text{C}(\text{CH}_3)_3$], 1.74 (3H, d, $J=7$ Hz, H-18), 3.70 (3H, s, $-\text{OCH}_3$), 3.92 and 4.46 (1H and 1H, d and d, $J=14$ Hz and $J=14$ Hz, 2 x H-21), 5.24 (1H, br d, $J=12$ Hz, H-3), 5.71 (1H, q, $J=7$ Hz, H-19), 7.2-7.3 (2H, m, H-10, H-11), 7.43 (1H, d, $J=7$ Hz, H-9), 7.93 (1H, d, $J=7$ Hz, H-12). For the ^{13}C -nmr data, see Figure 1. Ms: 440 (M^+ , <2%), 424, 367, 340, 323, 295, 267, 249, 184, 170, 169, 156 (100%). HRms: Calcd for $\text{C}_{25}\text{H}_{32}\text{N}_2\text{O}_5$: 440.2311. Found: 440.2340. Anal. Calcd for $\text{C}_{25}\text{H}_{32}\text{N}_2\text{O}_5$: C, 68.16; H, 7.32; N, 6.36. Found C, 67.92; H 7.25; N 6.27.

Preparation of 1,2,3,4,6,7,12,12b-octahydroindolo[2,3-*a*]quinolizine *cis*- N_a -oxide (29).³¹

For the preparation and analytical data of compound (29), see Ref. 12 [compound (1b) in Ref. 12] and Figure 1.

Preparation of 1,2,3,4,6,7,12,12b-octahydroindolo[2,3-*a*]quinolizine *trans*- N_a -oxide (30).³¹

For the preparation and analytical data of compound (30), see Ref. 12 [compound (1a) in Ref. 12] and Figure 1.

REFERENCES AND NOTES

1. J. Le Men and W. I. Taylor, *Experientia*, 1965, 21, 508.
2. R. T. Brown, "The Monoterpenoid Indole Alkaloids", ed. by J. E. Saxton, Wiley, New York, 1983, pp. 63-146 and references cited therein.
3. C. Szántay, C. Blaskó, K. Honty, and G. Dörnyei, "The Alkaloids", ed. by A. Brossi, Vol. 27, Academic Press, Orlando, 1986, pp. 131-268 and 407-410 and references cited therein.
4. M. Lounasmaa and A. Tolvanen, "Monoterpenoid Indole Alkaloids", ed. by J. E. Saxton, 2nd Edition, Wiley, New York, 1994, pp. 57-159 and references cited therein.
5. M. Lounasmaa, R. Jokela, B. Tirkkonen, J. Miettinen, and M. Halonen, *Heterocycles*, 1992, 34, 321.

6. M. Lounasmaa, R. Jokela, J. Miettinen, and M. Halonen, *Heterocycles*, 1992, **34**, 1497.
7. B. Tirkkonen, J. Miettinen, J. Salo, R. Jokela, and M. Lounasmaa, *Tetrahedron*, 1994, **50**, 3537.
8. P. Hanhinen, T. Nurminen, R. Jokela, and M. Lounasmaa, *Heterocycles*, 1994, **38**, 2027.
9. M. Lounasmaa, P. Hanhinen, and R. Jokela, *Tetrahedron*, 1995, **51**, 8623.
10. N. Aimi, E. Yamanaka, M. Ogawa, T. Kohmoto, K. Mogi, and S. Sakai, *Heterocycles*, 1978, **10**, 73.
11. M. Nakagawa, Y. Ogawa, Y. Miyake, K. Yamaguchi, T. Hina, C. C. Chiang, J. L. Flippen, and B. Witkop, *Heterocycles*, 1982, **19**, 663.
12. M. Lounasmaa and T. Tamminen, *Tetrahedron*, 1991, **47**, 2879.
13. I. Moldvai, C. Szántay Jr, G. Toth, A. Vedres, A. Kálaman, and C. Szántay, *Recl. Trav. Chim. Pays-Bas*, 1988, **107**, 335.
14. R. Jokela and M. Lounasmaa, *Heterocycles*, 1993, **36**, 2373.
15. M. Lounasmaa, P. Hanhinen, and R. Jokela, *Heterocycles*, 1995, **41**, 995.
16. M. Lounasmaa, R. Jokela, M. Halonen, and J. Miettinen, *Heterocycles*, 1993, **36**, 2523.
17. R. Jokela, M. Halonen, and M. Lounasmaa, *Tetrahedron*, 1993, **49**, 2567.
18. P. Potier, *Rev. Latinoamer. Quim.*, 1978, **9**, 47.
19. M. Lounasmaa and A. Koskinen, *Heterocycles*, 1984, **22**, 1591.
20. D. Grierson, *Organic Reactions*, 1990, **39**, 85.
21. M. Lounasmaa and C.-J. Johansson, *Acta Chem. Scand.*, 1975, **B29**, 655.
22. M. Lounasmaa and C.-J. Johansson, *Tetrahedron*, 1977, **33**, 113.
23. M. Lounasmaa, R. Jokela, P. Hanhinen, J. Miettinen, and J. Salo, *Tetrahedron*, 1994, **50**, 9207.
24. M. Lounasmaa, "Studies in Natural Products Chemistry", Vol. 1, ed. by Atta-ur-Rahman, Stereoselective Synthesis (Part A), Elsevier, Amsterdam, 1988, pp.89-122.
25. M. Lounasmaa, "Studies in Natural Products Chemistry", Vol. 14, ed. by Atta-ur-Rahman, Stereoselective Synthesis (Part I), Elsevier, Amsterdam, 1994, pp. 703-730.
26. M. Lounasmaa, R. Jokela, M. Bäck, P. Hanhinen, and C. Laine, *Tetrahedron*, 1995, **51**, 11891.
27. R. Jokela, M. Halonen, and M. Lounasmaa, *Heterocycles*, 1993, **36**, 1115.
28. M. Lounasmaa and R. Jokela, *Tetrahedron*, 1989, **45**, 3975.

29. The presented, corrected ^{13}C -nmr values for compounds (29) and (30) (See Ref. 12) were measured in CDCl_3 and $\text{CDCl}_3 + \text{CD}_3\text{OD}$ (15 drops), respectively.
30. R. Jokela, M. Halonen, and M. Lounasmaa, *Heterocycles*, 1994, **38**, 189.
31. IUPAC numbering. See "*A Guide to IUPAC Nomenclature of Organic Compounds*" ed. by R. Panico, W. H. Powell, and J.-C. Richer, Blackwell, Oxford, 1993.

Received, 19th April, 1996