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

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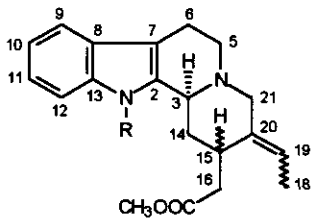
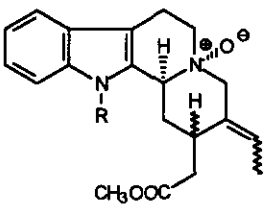
Abstract - Syntheses are reported for deformylgeissoschizine isomers (**1** - **4**) and their N_a-Boc derivatives (**5** - **8**), as well as for their N_b-oxides (*cis* and *trans*) (**9** - **13**) and (**16** - **20**). Predominant conformations of the compounds were determined by nmr measurements.

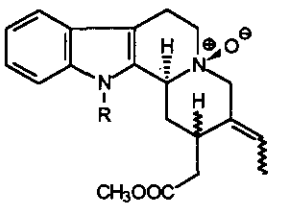
The (±)-deformylgeissoschizine skeleton allows the existence of four stereoisomers [**1** - **4** (**5** - **8**)], and eight stereoisomers, [**9** - **16** (**17** - **24**)], can be predicted for the corresponding N_b-oxides (*cis* and *trans*) (biogenetic numbering[1]).



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



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



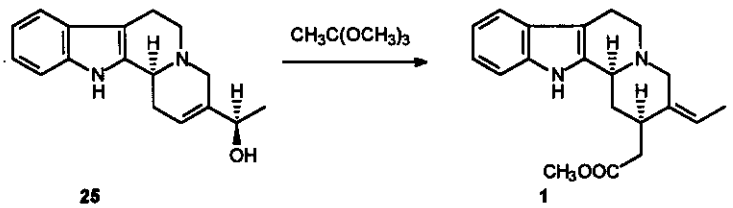
13 R=H ; H-15α ; C-19 *Z*
14 R=H ; H-15β ; C-19 *Z*
15 R=H ; H-15α ; C-19 *E*
16 R=H ; H-15β ; C-19 *E*
21 R=Boc ; H-15α ; C-19 *Z*
22 R=Boc ; H-15β ; C-19 *Z*
23 R=Boc ; H-15α ; C-19 *E*
24 R=Boc ; H-15β ; C-19 *E*

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.

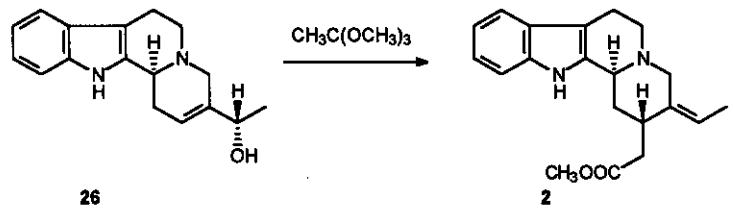
RESULTS AND DISCUSSION

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]



25 **1**

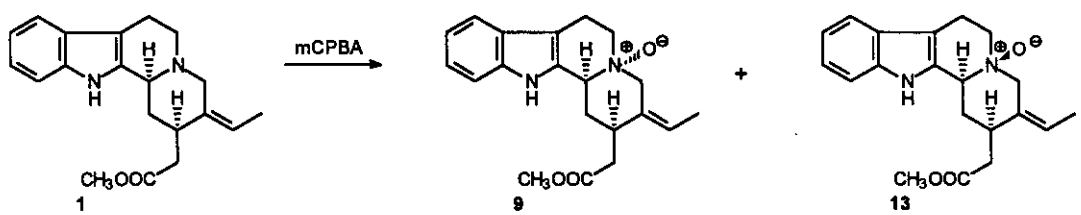
Scheme 1.



26 **2**

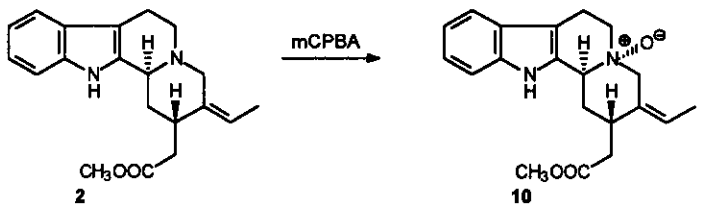
Scheme 2.

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]



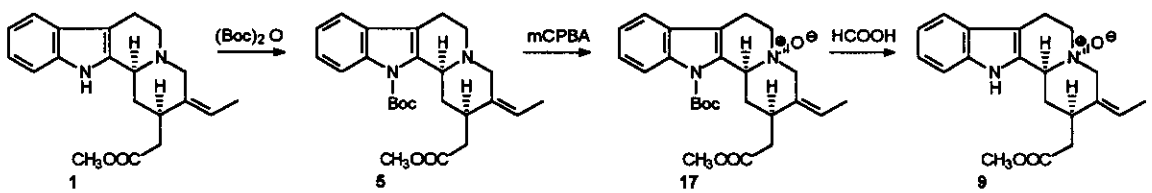
1 **9** **13**

Scheme 3.

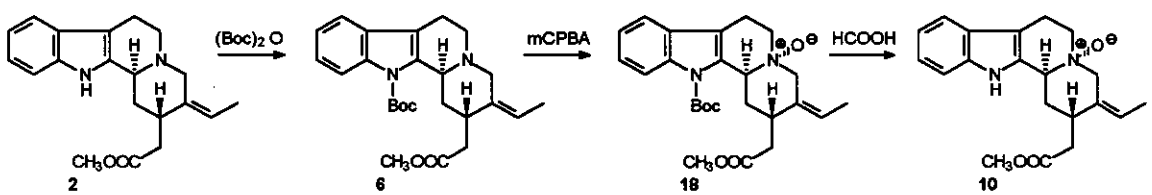


Scheme 4.

Treatment of deformyl-*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 deformyl-*Z*-geissoschizine *cis*-N_b-oxides (**9**) and (**10**) (Schemes 5 and 6).

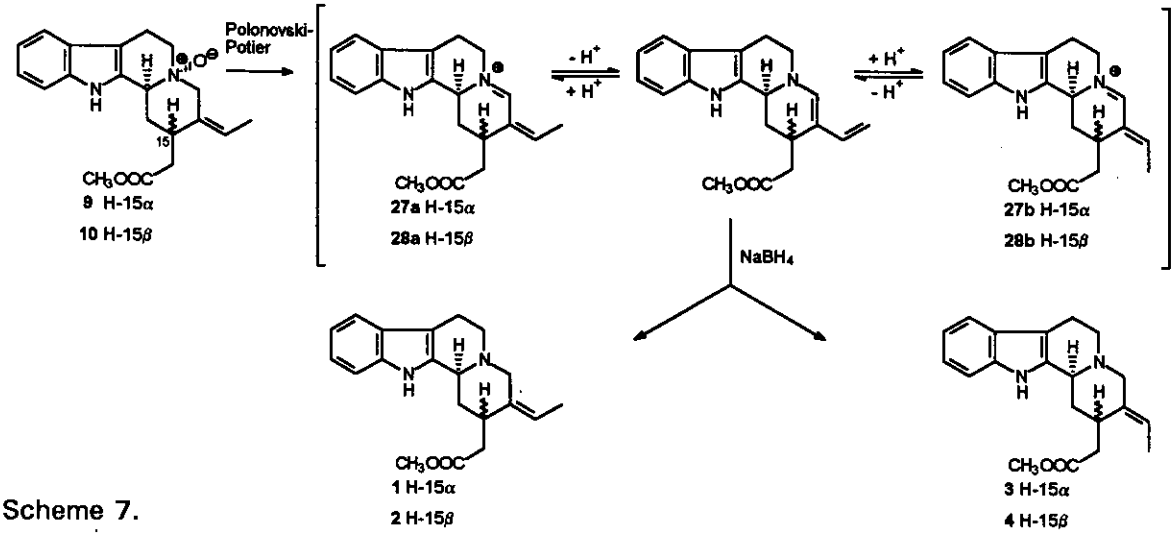


Scheme 5.



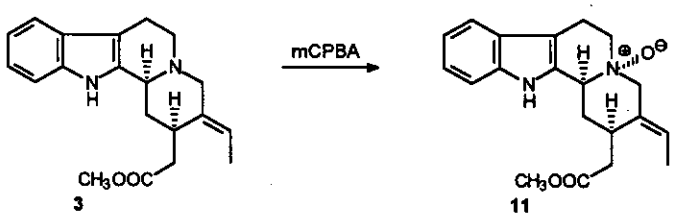
Scheme 6.

Treatment of deformyl-*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** ⇄ **27b** and **28a** ⇄ **28b** with $NaBH_4$ afforded deformyl-*E*-geissoschizines (**3**) and (**4**), respectively, together with deformyl-*Z*-geissoschizines (**1**) and (**2**) (Scheme 7).

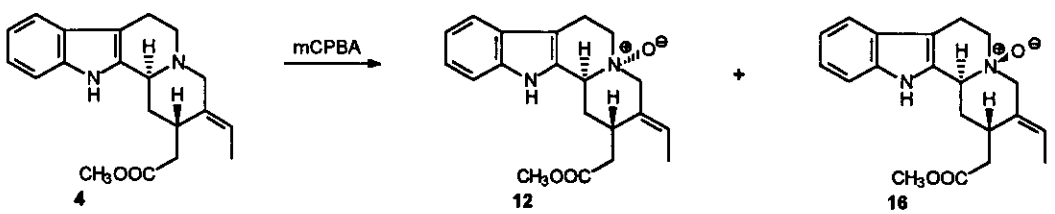


Scheme 7.

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



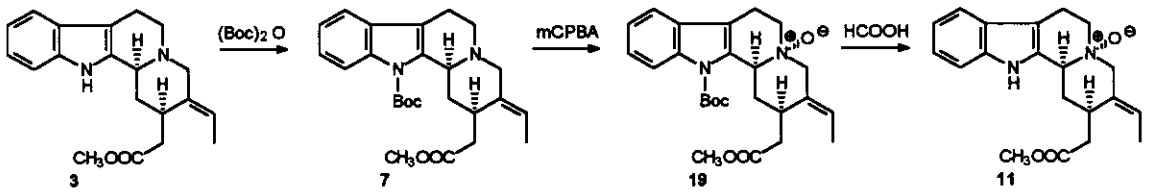
Scheme 8.



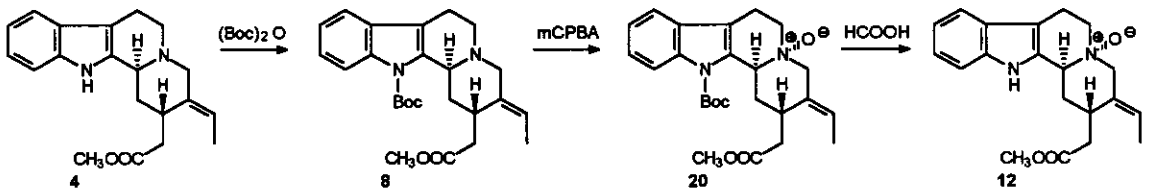
Scheme 9.

Treatment of deformyl-*E*-geissoschizines (**3**) and (**4**) with $(Boc)_2O$ transformed them to the corresponding N_a-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).



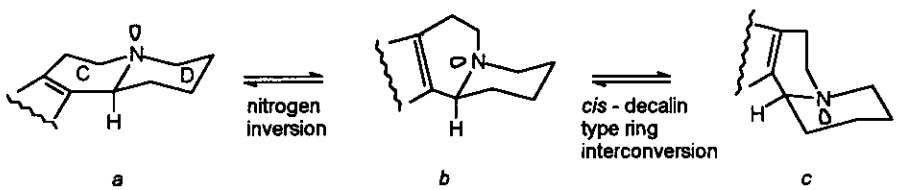
Scheme 10



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-CH_3 and C-15-CH_2-$COOCH_3$ that would occur in conformations *a* and *b* is avoided in conformation *c*. Moreover, the possible

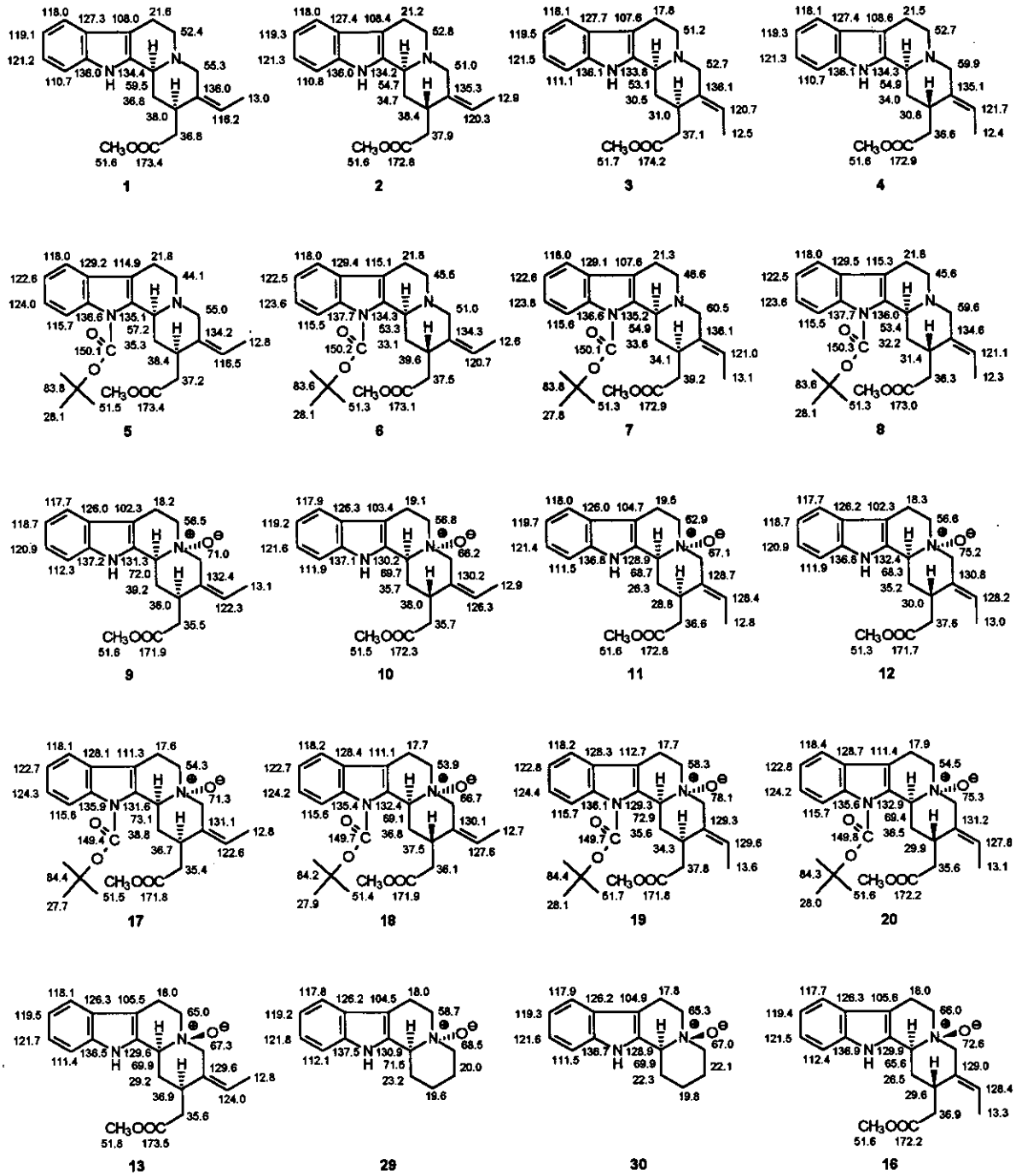


Figure 1. ^{13}C-Nmr data of compounds (**1** - **13**), (**16** - **20**), (**29**), and (**30**). The ^{13}C-nmr data of compounds (**29**) and (**30**) (Refs. 12 and 29) are added to the figure for purposes of comparison.

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 finding[12] 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**). ^{1}H- and ^{13}C-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 $CHCl_3$ as solvent. Ir absorption bands are expressed in reciprocal centimetres (cm^{-1}). ^{1}H- and ^{13}C-nmr spectra were measured in $CDCl_3$ with a Varian Gemini-200 spectrometer working at 199.975 MHz (^{1}H-nmr) and 50.289 MHz (^{13}C-nmr). Chemical shifts are given in ppm by reference to TMS (^{1}H-nmr; $\delta_H = 0.0$ ppm) and $CDCl_3$ (^{13}C-nmr; $\delta_C = 77.0$ 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*-N_b-oxide (**10**) (*vide infra*) (88 mg, 0.26 mmol) was dissolved in dry CH_2Cl_2 (10 ml) and the mixture cooled to -17^{0}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. $NaBH_4$ (59 mg, 1.56 mmol, 6 equiv.) was added at 0^{0}C in small portions to the stirred solution during 15 min and stirring was continued at room temperature for 2 h. H_2O was added, MeOH evaporated in vacuo and the mixture extracted with CH_2Cl_2. The organic fractions were washed with H_2O, dried with Na_2SO_4 and evaporated. The crude product was purified by flash chromatography (silica gel, CH_2Cl_2/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). ^{1}H Nmr: 1.63 (3H, d, J=7 Hz, H-18), 3.55 (1H, br d, J=12 Hz, H-3), 3.72 (3H, s, -OCH_3), 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 ^{13}C-nmr data, see Figure 1. Ms: 324 (M^+, 100%), 323, 309, 293, 265, 251, 249, 237, 223, 170, 169, 156. HRms: Calcd for $C_{20}H_{24}N_2O_2$: 324.1838. Found: 324.1851. Anal. Calcd for $C_{20}H_{24}N_2O_2$: C, 74.05; H, 7.46; N, 8.63. Found C, 74.07; H 7.55; N 8.60.

Preparation of N_a-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 ^{13}C-nmr values).

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

A solution of deformyl-15-epi-*Z*-geissoschizine (**2**) (358 mg, 1.11 mmol), dry CH_2Cl_2 (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, CH_2Cl_2/MeOH; 99.5/0.5) to yield compound (**6**). Y. 455 mg

(97%). Amorphous material. Ir: 1720 (2 x C=O). ^{1}H Nmr: 1.65 (3H, d, J=7 Hz, H-18), 1.67 [9H, s, -C(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, -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 $C_{25}H_{32}N_2O_4$: 424.2362. Found: 424.2350. Anal. Calcd for $C_{25}H_{32}N_2O_4$: C, 70.73; H, 7.60; N, 6.60. Found C, 70.46; H 7.52; N 6.61.

Preparation of N_a-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_a-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 $(Boc)_2O$ (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, CH_2Cl_2/MeOH; 99.5/0.5) to yield compound (**8**). Y. 232 mg (90%). Amorphous material. Ir: 1730 (2 x C=O). ^{1}H Nmr: 1.63 (3H, d, J=7 Hz, H-18), 1.67 [9H, s, -C(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, -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 $C_{25}H_{32}N_2O_4$: 424.2362. Found: 424.2348. Anal. Calcd for $C_{25}H_{32}N_2O_4$: 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_b-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_b-oxide (9) and *trans*-N_b-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 CH_2Cl_2 (10 ml) was stirred at room temperature for 4 h (Ar atm). The mixture was evaporated and purified by column chromatography (alumina, CH_2Cl_2/MeOH; 99/1) to yield compound (**10**). Y. 46 mg (62%). White crystals. mp 199-200°C (EtOH). Ir: 1735 (C=O). ^{1}H Nmr: 1.72 (3H, d, J=7 Hz, H-18), 3.58 (3H, s, -OCH_3), 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 ^{13}C-nmr data, see Figure 1. Ms: 340 (M^+), 323, 296, 295, 267, 249, 184, 170, 169, 156 (100%). HRms: Calcd for $C_{20}H_{24}N_2O_3$: 340.1786. *Found*: 340.1768. *Anal. Calcd for* $C_{20}H_{24}N_2O_3$: 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 ^{13}C-nmr values).

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

N_a-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 CH_2Cl_2, neutralized with 10% Na_2CO_3 and extracted with CH_2Cl_2. The organic fractions were washed with H_2O and dried with Na_2SO_4. Purification by plc (silica gel, CH_2Cl_2/MeOH; 90/10) yielded compound (**12**). Y. 21 mg (88%). White crystals. mp 186-188°C (EtOH). Ir: 1735 (C=O). ^{1}H Nmr: 1.62 (3H, d, J=7 Hz, H-18), 3.46 (3H, s, -OCH_3), 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 ^{13}C-nmr data, see Figure 1. Ms: 340 (M^+), 323, 296, 295, 267, 249, 184, 170, 169, 156 (100%). HRms: Calcd for $C_{20}H_{24}N_2O_3$: 340.1787. Found: 340.1766. Anal. Calcd for $C_{20}H_{24}N_2O_3$: 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 CH_2Cl_2 (8 ml) was stirred at room temperature for 4 h (Ar atm). The reaction mixture was neutralized with 10% Na_2CO_3 and extracted with CH_2Cl_2. The

organic fractions were washed with H_2O and dried with Na_2SO_4, yielding a mixture of compounds (**12**) and (**16**) (46 mg, 77%). Purification by flash chromatography (silica gel, CH_2Cl_2/MeOH; 95/5), *followed by repeated plc* (CH_2Cl_2/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). ^{1}H Nmr: 1.55 (3H, d, J=7 Hz, H-18), 3.65 (3H, s, -OCH_3), 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 ^{13}C-nmr data, see Figure 1. Ms: 340 (M^+), 323, 296, 295, 267, 249, 184, 170, 169, 156 (100%). HRms: Calcd for $C_{20}H_{24}N_2O_3$: 340.1786. Found: 340.1802. Anal. Calcd for $C_{20}H_{24}N_2O_3$: 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 ^{13}C-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 CH_2Cl_2 (10 ml) was stirred at room temperature for 2.5 h (Ar atm). The mixture was evaporated and purified by column chromatography (alumina, CH_2Cl_2/MeOH; 99/1) to yield compound (**18**). Y. 96 mg (93%). Amorphous material. Ir: 1720 (2 x C=O). ^{1}H Nmr: 1.66 [9H, s, -$C(CH_3)_3$], 1.75 (3H, d, J=7 Hz, H-18), 3.69 (3H, s, -OCH_3), 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 ^{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 $C_{25}H_{32}N_2O_5$: 440.2311. Found: 440.2283. Anal. Calcd for $C_{25}H_{32}N_2O_5$: 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, CH_2Cl_2/MeOH; 99/1) to yield compound (**20**). Y. 65 mg (60%). Amorphous material. Ir: 1730 (2 x C=O). ^{1}H Nmr: 1.66 [9H, s, -C(CH_3)$_3$], 1.74 (3H, d, J=7 Hz, H-18), 3.70 (3H, s, -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 $C_{25}H_{32}N_2O_5$: 440.2311. Found: 440.2340. Anal. Calcd for $C_{25}H_{32}N_2O_5$: 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.

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