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SYNTHESIS OF COMPOUNDS IN THE EBURNAMONINE-HOMOEBURNAMONINE SERIES

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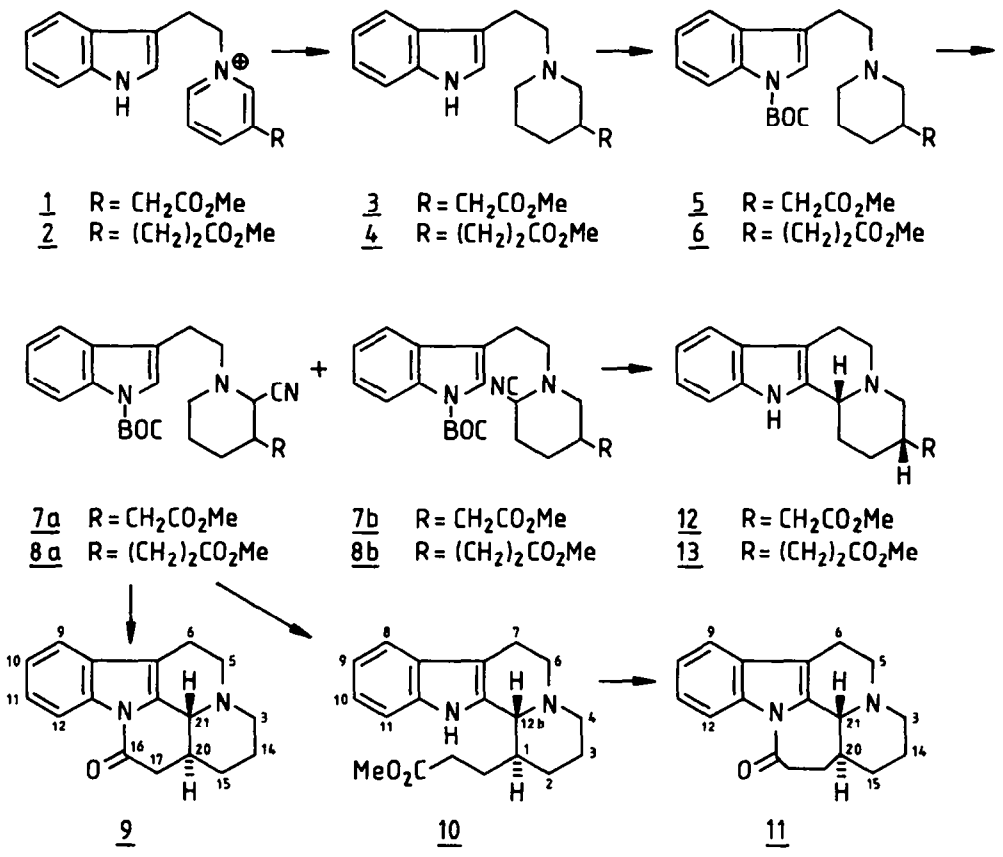
Abstract - Six different lactams of the desethyleburnamonine-homoeburnamonine series were synthesized. Complete ^{13}C NMR data are presented for these compounds, as well as for their precursors. Special attention is paid to their C(20)-C(21) stereochemistry.

The therapeutical value of several vincamine-eburnamonine derivatives is well known.[1-4] Considering their physiological properties, the stereochemical relationship of the C(20)-C(21) protons (biogenetic numbering)[5] is vitally important. In connection with a project in progress in our laboratory on compounds of vincamine-eburnamonine type,[6-7] we needed model compounds that could set the stereochemistry of these compounds on a solid basis. ^{13}C NMR spectroscopy was ideally suited for such stereochemical determinations, not least because it would permit a decision about the unambiguous determination of the identity or non-identity of compounds synthesized in different laboratories. In this paper we describe the synthesis of six compounds of the desethyleburnamonine-homo-eburnamonine series, paying special attention to their C(20)-C(21) stereo-chemistry[8] and ^{13}C NMR spectroscopy.

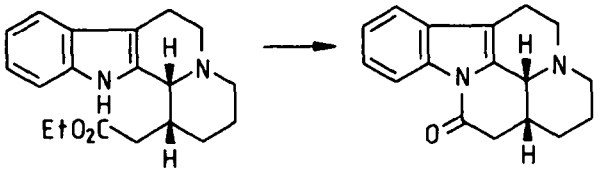
RESULTS AND DISCUSSION

The desethyl-20-epi-eburnamonine 9 and the corresponding homoderivative 11, both possessing the C(20)H-C(21)H trans-stereochemistry, were synthesized as follows (Scheme 1). Catalytic hydrogenation of salts 1 and 2, furnished the N-tryptophyl-piperidines 3 and 4, respectively. When the indole nitrogens of 3 and 4 were protected with the t-butyloxycarbonyl (BOC) group, compounds 5 and 6 were obtained. The corresponding N-oxides were subjected to the modified Polonovski reaction conditions[9], followed by cyanide trapping to furnish the α-aminonitriles 7a,7b and 8a,8b, respectively. In both cases the isomers were separated by column chromatography.



Scheme 1

The desethyl-20-epi-eburnamonine 9 formed spontaneously from the nitrile 7a under the reaction conditions used ($AgBF_4$, then MeOH/HCl). The feasible preceding indoloquinolizidine ester could not be isolated from the products. Not detected either was compound 15 [C(20)H-C(21)H cis], the C(20) isomer of compound 9. The isomer 15 was described in the literature some years ago[10,11], but without any ^{13}C NMR spectral data. To obtain the missing analytical data we synthesized this compound starting from 14[11,12] using methods described in the literature[11,13] (Scheme 2).

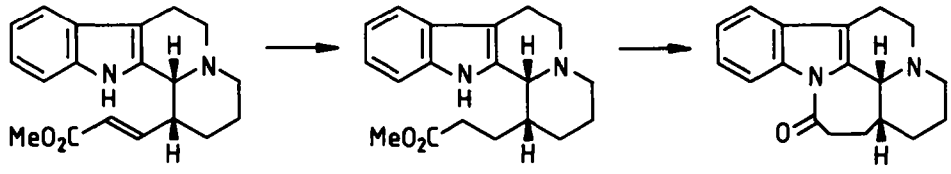


Scheme 2

In the homoseries the five-ring lactam 11 did not form spontaneously from the corresponding nitrile 8a (vide supra), and the indoloquinolizidine 10 (prepared from 8a) was first isolated instead (Scheme 1). Under basic conditions (t-BuOK), the ester 10 easily gave the lactam 11 in nearly quantitative yield. The Bohlmann bands in the IR spectrum were characteristic of a trans-fused quinolizidine system. The large coupling constant (J = 9.5 Hz) between C(20)H and C(21)H indicated a trans diaxial relationship for these protons.

Similarly, in the "outside series", nitriles 7b and 8b yielded the indoloquinolizidines 12 and 13, respectively,[14] under the reaction conditions used (Scheme 1).

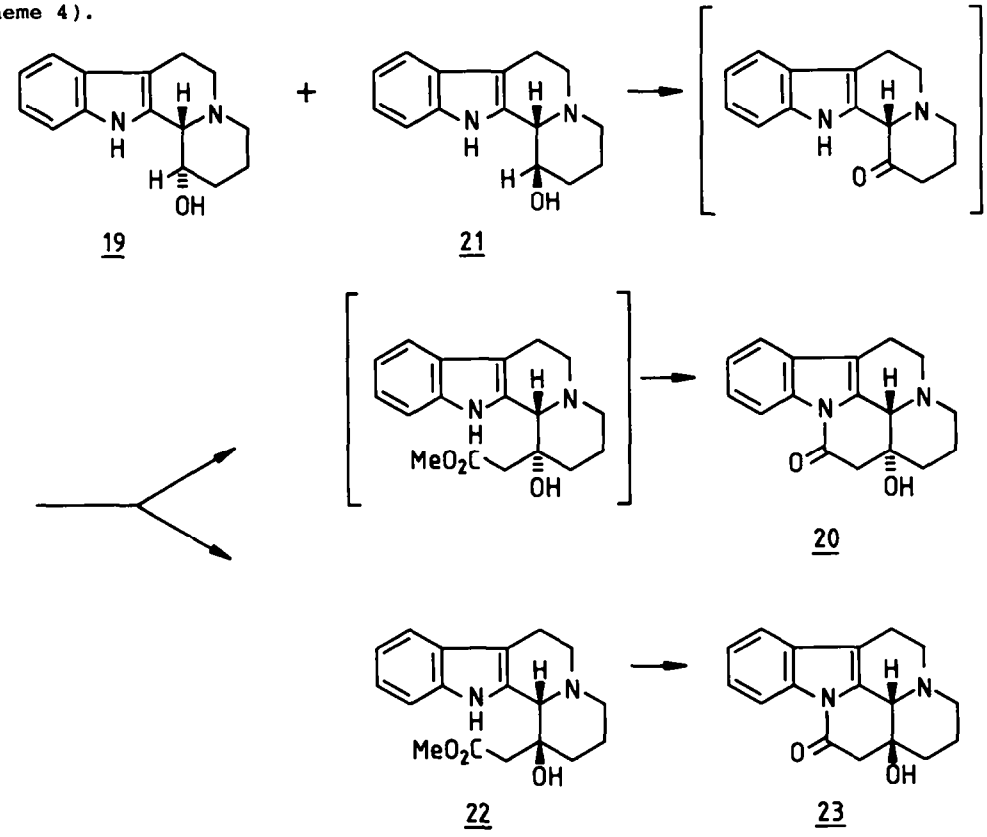
We have recently described the synthesis of the ester 16.[17] Catalytic hydrogenation of the double bond of the ester side chain led to compound 17 [C(1)H-C(12b)H cis], the C(1) isomer of compound 10. In spite of many trials, our attempts to cyclize ester 17 to the lactam 18 with potassium t-butoxide (t-BuOK) or sodium bis(trimethylsilyl)amide failed. Instead, the use of phosphorus oxychloride ($POCl_3$) led to the desired product 18 (Scheme 3).



16 17 18

Scheme 3

To take advantage of enamine indoloquinolizidines in the synthesis of eburnamonine-type alkaloids we also synthesized the C(20)OH derivatives of desethyleburnamonine (both isomers, 20 and 23). Swern oxidation of the earlier described mixture of compounds 19 and 21 (compounds 20a and 20b in ref. 18) and subsequent treatment with lithium methylacetate yielded compounds 20 and 22, which were easily separated. The C(1)OH-C(12b)H cis-indoloquinolizidine 22 was cyclized to the corresponding cis-lactam 23 under basic reaction conditions (Scheme 4).



19 21 20 22 23

Scheme 4

All the cyclization steps leading to the desired lactams either occurred spontaneously or were easily carried out under basic reaction conditions, with a single exception: the ester 17 did not cyclize to the cis-lactam 18. Possibly this was due to the interaction of the ester function with N_b. However, the use of acidic conditions ($POCl_3$) (*vide supra*), in place of basic conditions, results in salt formation at N_b. No interaction of N_b with the ester is now possible and the lactam 18 is readily formed.

The chemical shifts of C(6) [and C(3)] allowed a rapid and reliable determination of the configurations of all six lactams (9, 11, 15, 18, 20, 23) (see refs. 18-21). In general, the ^{13}C NMR values obtained (Fig. 1) are expected to be useful in future stereochemical determination of new compounds in the eburnamonine-homoeburnamonine series.

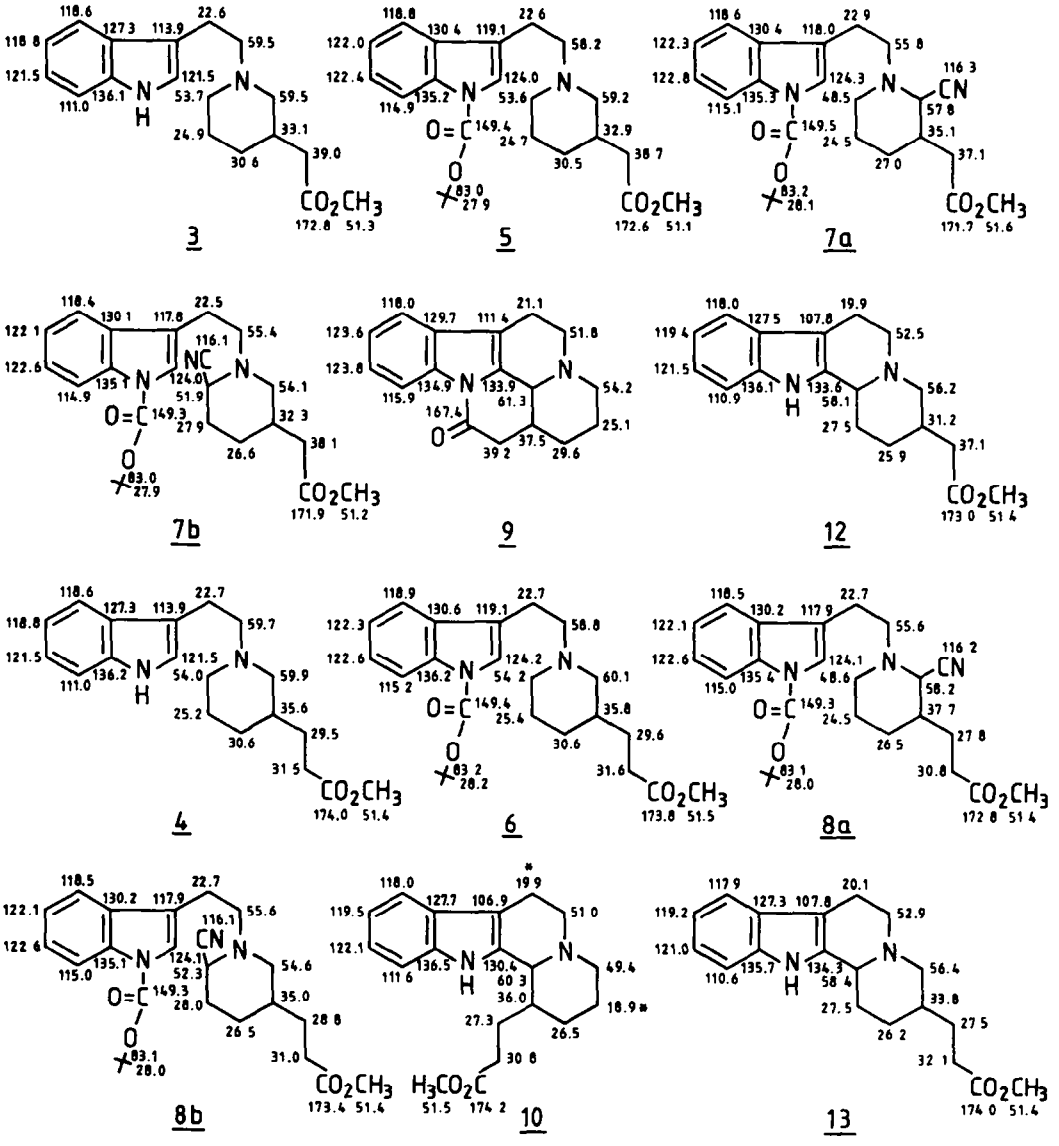


Fig. 1

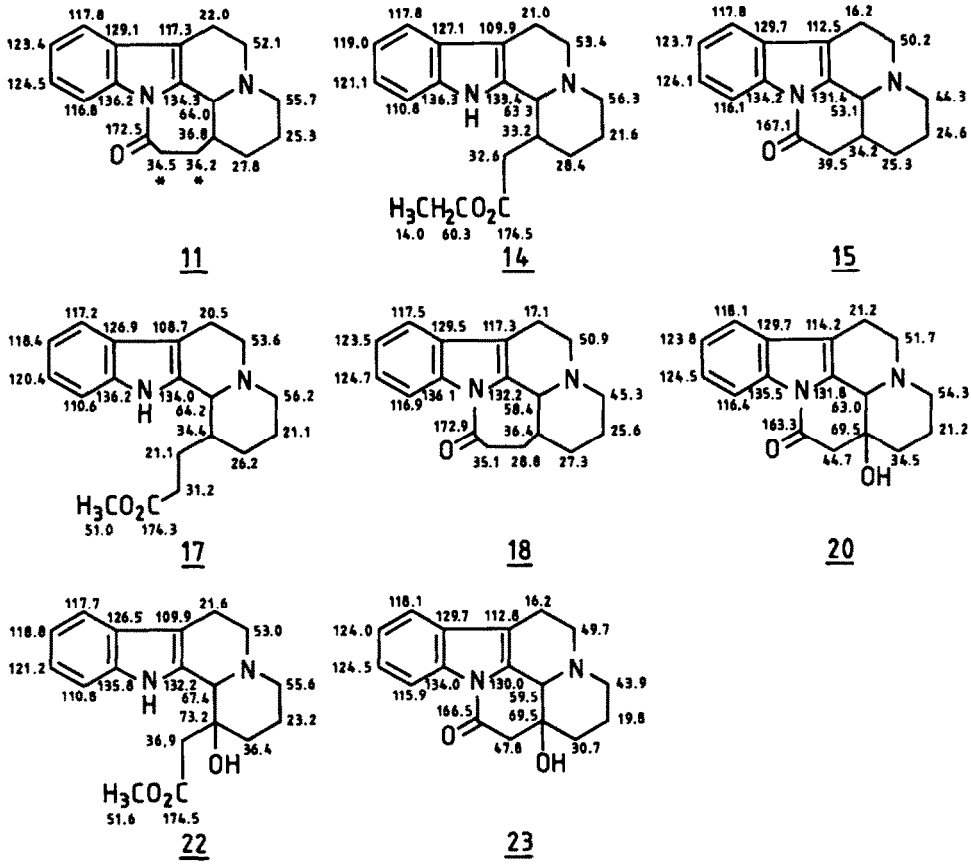


Fig. 1 (continued)

EXPERIMENTAL

IR spectra (ν_{max} in cm^{-1}) were recorded on a Perkin-Elmer 700 spectrophotometer, using liquid film between NaCl crystals. ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ on a Jeol JNM-FX 60 spectrometer working at 59.80 MHz (^1H NMR) and 15.04 MHz (^{13}C NMR). Chemical shift data are given in ppm downfield from TMS. For the ^{13}C NMR data see Fig. 1. Mass spectrometry (EIMS and HRMS) were performed on a Jeol DX 303/DA 5000 instrument.

Preparation of compounds 3 and 4

Alkylation of methyl 3-pyridylacetate and 3-(β-methoxycarbonylvinyl)pyridine[22] with tryptophyl bromide afforded the corresponding pyridinium salts 1 and 2, respectively, and subsequent catalytic hydrogenation (PtO_2) yielded compounds 3 and 4, respectively.

Compound 3: Reduction of 1 (3.61 g, 9.6 mmol) in the presence of PtO_2 (0.7 g) in methanol (100 ml) yielded 3 (2.75 g, 95%).

IR: 1730 (C=O).

^1H NMR: 3.65 (3H, s, $-CO_2CH_3$), 6.91 (1H, s, ind. α-H), 7.16-7.65 (4H, m, arom. H), 8.67 (1H, br s, NH).

MS: 300 (M^+), 269, 171 (100%), 170, 144, 130; exact mass: 300.1840 (calc. for $C_{18}H_{24}N_2O_2$: 300.1839).

Compound 4: Reduction of 2 (4.98 g, 12.8 mmol) in the presence of PtO_2 (0.88 g) in methanol (100 ml) yielded 4 (3.61 g, 90%).

IR: 1725 (C=O).

^1H NMR: 3.66 (3H, s, $-CO_2CH_3$), 6.97 (1H, s, ind. α-H), 7.00-7.69 (4H, m, arom. H), 8.23 (1H, br s, NH).

MS: 314 (M^+), 283, 256, 184 (100%), 144, 130; exact mass: 314.2015 (calc. for $C_{19}H_{26}N_2O_2$: 314.1994).

Preparation of compounds 5 and 6

To compound 3 (or compound 4) in toluene were added 50% aq NaOH and tetrabutylammonium hydrogen sulphate. The two-phase system was stirred under argon for 5 min, after which di-t-butyl dicarbonate [$(BOC)_2O$] (2 equiv.) in toluene was added during 10 min and stirring was continued for another 10 min. The organic

layer was separated and the aqueous layer was washed several times with CH_2Cl_2. The combined organic layers were washed with H_2O, dried over Na_2SO_4 and evaporated to dryness to give 5 (6).

Compound 5: Reaction between 3 [(2.75 g, 9.2 mmol) in toluene (35 ml), 50% NaOH (15 ml) and tetrabutylammonium hydrogen sulphate (0.93 g)] and di-t-butyl dicarbonate [(4.16 g, 2 equiv,) in toluene (10 ml)] yielded 5 (3.59 g, 98%).
IR: 1730 (C=O).
^{1}H NMR: 1.65 (9H, s, $-C(CH_3)_3$), 3.65 (3H, s, $-CO_2CH_3$), 7.42 (1H, s, ind. α-H).
MS: 400 (M^+), 369, 171 (100%), 170, 144, 130; exact mass: 400.2369 (calc. for $C_{23}H_{32}N_2O_4$: 400.2363).

Compound 6: Reaction between 4 [(1.58 g, 5.0 mmol) in toluene (15 ml), 50% NaOH (15 ml) and tetrabutylammonium hydrogen sulphate (0.53 g)] and di-t-butyl dicarbonate [(2.35 g, 2 equiv.) in toluene (10 ml)] yielded 6 (2.04 g, 98%).
IR: 1730 (C=O).
^{1}H NMR: 1.67 (9H, s, $-C(CH_3)_3$), 3.69 (3H, s, $-CO_2CH_3$), 7.43 (1H, s, ind. α-H).
MS: 414 (M^+), 413, 357, 325, 313, 184 (100%), 144, 130; exact mass: 414.2528 (calc. for $C_{24}H_{34}N_2O_4$: 414.2519).

Preparation of compounds 7a,7b and 8a,8b

Compound 5 (or compound 6) was reacted with H_2O_2 (30%) in $CHCl_3$-MeOH (1:1) (60°C, 2d) to afford after the usual work-up the corresponding N-oxide in 90% yield. The N-oxide in dry CH_2Cl_2 was stirred at 0°C (Ar-atm) and trifluoroacetic anhydride (TFAA) (2.5 equiv.) was added during 15 min. Stirring was continued for 1 h at 0°C and 15 min at rt. KCN (1.5 equiv.) in H_2O was added and the pH of the aqueous layer was adjusted to pH 5 by the addition of NaOAc. The mixture was stirred at rt for 0.5 h, basified to pH 10 with 10% aq Na_2CO_3 and extracted with CH_2Cl_2 several times. The organic layer was washed with H_2O, dried over Na_2SO_4 and evaporated to dryness. The isomers were separated using column chromatography (alumina, CH_2Cl_2-hexane, 4:6).

Compounds 7a and 7b: Reaction between 5 (3.8 g, 9.5 mmol) and H_2O_2 (2.5 ml) in $CHCl_3$/MeOH (1:1, 40 ml) yielded the corresponding N-oxide (3.54 g, 90%). The N-oxide (3.54 g, 8.51 mmol) in abs. CH_2Cl_2 (20 ml) was reacted with TFAA (2.98 ml, 2.5 equiv.) and then with KCN (0.83 g, 1.5 equiv.) in H_2O (10 ml) to yield a mixture of 7a and 7b (1:1) (3.09 g, 86%).

Compound 7a:
IR: 2260 (CN), 1725 (C=O).
^{1}H NMR: 1.65 (9H, s, $-C(CH_3)_3$), 3.64 (3H, s, $-CO_2CH_3$), 3.82 (1H, br s, -CHCN), 7.45 (1H, s, ind. α-H).
MS: 425 (M^+), 398, 195 (100%), 169, 168; exact mass: 425.2303 (calc. for $C_{24}H_{31}N_3O_4$: 425.2316).

Compound 7b:
IR: 2260 (CN), 1725 (C=O).
^{1}H NMR: 1.67 (9H, s, $-C(CH_3)_3$), 3.68 (3H, s, $-CO_2CH_3$), 7.43 (1H, s, ind. α-H).
MS: 425 (M^+), 398, 195 (100%), 169, 168; exact mass: 425.2308 (calc. for $C_{24}H_{31}N_3O_4$: 425.2316).

Compounds 8a and 8b: Reaction between 6 (0.43 g, 1.0 mmol) and H_2O_2 (0.32 ml) in $CHCl_3$/MeOH (1:1, 20 ml) yielded the N-oxide (0.40 g, 90%). The N-oxide (0.40 g, 0.9 mmol) in abs. CH_2Cl_2 (10 ml) was reacted with TFAA (0.4 ml, 2.5 equiv.), and then with KCN (0.11 g, 1.5 equiv.) in H_2O (3 ml) to yield a mixture of 8a and 8b (1:1) (0.42 g, 91%).

Compound 8a:
IR: 2250 (CN), 1720 (C=O).
^{1}H NMR: 1.65 (9H, s, $-C(CH_3)_3$), 3.65 (3H, s, $-CO_2CH_3$), 3.90 (1H, br s, -CHCN), 7.44 (1H, ind. α-H).
MS: 439 (M^+), 413, 412, 209 (100%), 183, 182; exact mass: 439.2467 (calc. for $C_{25}H_{33}N_3O_4$: 439.2471).

Compound 8b:
IR: 2250 (CN), 1725 (C=O).
^{1}H NMR: 1.65 (9H, s, $-C(CH_3)_3$), 3.66 (3H, s, $-CO_2CH_3$), 7.42 (1H, s, ind. α-H).
MS: 439 (M^+), 413, 412, 209 (100%), 183, 182; exact mass: 439.2464 (calc. for $C_{25}H_{33}N_3O_4$: 439.2471.

Preparation of compound 9

Compound 7a (1.14 g, 2.68 mmol) was dissolved in dry THF (40 ml). $AgBF_4$ (0.57 g, 2.92 mmol) in dry THF (8 ml) was added during 20 min and stirring was continued for 90 min (Ar-atm, dark). The mixture was evaporated to dryness. MeOH (80 ml) presaturated with dry HCl gas was added and the reaction mixture was stirred for 36 h. It was then poured into a suspension on $NaHCO_3$ in CH_2Cl_2. The inorganic salts were filtered off and the dried filtrate was evaporated under vacuum. Pure 9 was obtained after purification through a column of alumina (CH_2Cl_2). Y. 0.50 g, 70%.
IR: 2830 and 2780 (Bohlmann bands), 1705 (C=C).
^{1}H NMR: 3.56 (1H, d, J = 9.5 Hz, H-21), 7.14-7.50 (3H, m, arom. H), 8.33 (1H, m, H-12).
MS: 266 (M^+), 265 (100%), 238, 237, 222, 209, 180, 168, 167; exact mass: 266.1421 (calc. for $C_{17}H_{18}N_2O$: 266.1419).

Preparation of compound 10
Starting from compound 8a, compound 10 was obtained using the procedure described above for compound 9. Y. 60%.
IR: 3200 (NH), 2820 (vw) and 2750 (vw) (Bohlmann bands), 1720 (C=O).
^{1}H NMR: 3.67 (3H, s, $-CO_2CH_3$), 7.08-7.54 (4H, m, arom. H), 8.27 (1H, br s, NH).
MS: 312 (M^+), 311 (100%), 297, 281, 253, 239, 225, 197, 184, 170, 169; exact mass: 312.1832 (calc. for $C_{19}H_{24}N_2O_2$: 312.1838.

Preparation of compound 11
To compound 10 (0.132 g, 0.42 mmol) in dry benzene (12 ml), freshly sublimed t-BuOK (55 mg) was added. The mixture was refluxed (Ar-atm) overnight and then evaporated to dryness. The residue was redissolved in CH_2Cl_2. The organic phase was washed several times with water, dried over Na_2SO_4 and evaporated to dryness. Y. 0.114 g, 96%.
Mp.: 240-241°C (lit.[23]: 243°C).
IR: 2810 and 2750 (Bohlmann bands), 1695 (C=O).
^{1}H NMR: 3.26 (1H, d, J = 9.5 Hz, H-21), 7.13-7.40 (3H, m, arom. H), 8.47 (1H, m, H-12).
MS: 280 (M^+, 100%), 279, 252, 224; exact mass: 280.1564 (calc. for $C_{18}H_{20}N_2O$: 280.1576).

Preparation of compounds 12 and 13
The nitriles 7b and 8b were transformed to compounds 12 (Y. 45%) and 13 (Y. 65%) respectively, using the procedure described above for compound 9.
Compound 12:
IR: 3300 (NH), 2820 and 2760 (Bohlmann bands), 1720 (C=O).
^{1}H NMR: 3.65 (3H, s, $-CO_2CH_3$), 7.18-7.52 (4H, m, arom. H), 8.18 (1H, br s, NH).
MS: 298 (M^+), 297 (100%), 283, 267, 239, 225, 197, 184, 170, 169; exact mass: 298.1675 (calc. for $C_{18}H_{22}N_2O_2$: 298.1681).
Compound 13:
IR: 3250 (NH), 2820 (vw) and 2750 (vw) (Bohlmann bands), 1720 (C=O).
^{1}H NMR: 3.63 (3H, s, $-CO_2CH_3$), 7.08-7.54 (4H, m, arom. H), 8.52 (1H, br s, NH).
MS: 312 (M^+), 311 (100%), 297, 281, 253, 239, 197, 184, 170, 169; exact mass: 312.1830 (calc. for $C_{19}H_{24}N_2O_2$: 312.1838.

Preparation of compound 14
The ester 14 was prepared by the method of Husson et al.[11] and purified by flash chromatography (1-2.5% MeOH in CH_2Cl_2).[22] Y. 73%.
IR: 2825 and 2780 (Bohlmann bands), 1720 (C=O).
^{1}H NMR: 1.10 (3H, t, J = 7 Hz, $-CH_2\underline{CH_3}$), 3.39 (1H, br s, H-12b), 3.98 (2H, q, J = 7 Hz, $-\underline{CH_2}CH_3$), 8.10 (1H, br s, NH).
MS: 312 (M^+), 311 (100%), 283, 267, 239, 224, 197, 184, 170; exact mass: 312.1840 (calc. for $C_{19}H_{24}N_2O_2$: 312.1838).

Preparation of compound 15
The ester 14 (120 mg, 0.39 mmol) was stirred with NaOEt (0.1 M, 8 ml) at 55°C for 3.5 h. Aqueous work-up gave the crude product containing about 10% starting material. Flash chromatography (CH_2Cl_2-MeOH, 98:2) yielded the pure lactam 15 (63 mg, 62%).
IR: 1700 (C=O).
^{1}H NMR: 4.12 (1H, m, H-21), 8.27 (1H, m, H-12).
MS: 266 (M^+, 100%), 265, 237, 222, 209; exact mass: 266.1429 (calc. for $C_{17}H_{18}N_2O$: 266.1419).

Preparation of compound 17
The unsaturated ester 16 (65 mg, 0.21 mmol) was hydrogenated (MeOH, Pd/C, 3 h) to afford the ester 17. Y. 59 mg, 91%.
IR: 2820 and 2770 (Bohlmann bands), 1735 (C=O).
^{1}H NMR: 3.62 (3H, s, $-CO_2CH_3$), 7.10-7.40 (4H, m, arom. H), 9.19 (1H, br s, NH).
MS: 312 (M^+), 311 (100%), 239, 197, 170, 169; exact mass: 312.1835 (calc. for $C_{19}H_{24}N_2O_2$: 312.1838).

Preparation of compound 18
The ester 17 (61 mg, 0.20 mmol) was hydrolysed and the acid that formed treated with $POCl_3$ according to Szabó et al.[24]. Y. 40 mg, 70%.
IR: 1690 (C=O).
^{1}H NMR: 4.56 (1H, br s, H-21), 7.20-7.40 (3H, m, arom. H), 8.48 (1H, m, H-12).
MS: 280 (M^+, 100%), 279, 252, 251, 224, 223; exact mass: 280.1579 (calc. for $C_{18}H_{20}N_2O$: 280.1576).

Preparation of compounds 20 and 22
Dimethyl sulfoxide (72 µl, 1.01 mmol) was added dropwise to a cooled (-80°C) stirred solution of oxalyl chloride (80 µl, 0.93 mmol) in dry THF (4 ml) under argon. The solution was allowed to warm to -40°C where it was stirred for 4 min, after which it was recooled to -80°C. A mixture of alcohols 19 and 21 (0.204 g, 0.84 mmol) in THF (2 ml) was added over a period of 6 min. The yellow mixture was allowed to warm to -40°C and stirring was continued for 20 min. Triethylamine (0.59 ml, 4.2 mmol) was added dropwise and the reaction mixture was then stirred

at rt for 3 min. The ketone solution was recooled to -40°C and added via cannula in 15 min to a precooled (-80°C) stirred solution of lithium methylacetate [prepared from diisopropylamine (0.59 ml, 4.2 mmol), 1.4 M BuLi (3 ml, 4.2 mmol) and methylacetate (0.33 ml, 4.2 mmol)]. The reaction mixture was stirred at -80°C for 45 min, MeOH (3.5 ml) was then added and the mixture was allowed to warm to rt. It was then poured into sat aq NH_4Cl, the layers were separated and the aqueous layer was extracted with EtOAc and CH_2Cl_2. The combined extracts were dried (Na_2SO_4), filtered and concentrated to give the crude product, which was purified by flash chromatography [EtOAc-hexane (1:1) containing 0.25% triethylamine] to give pure 22 (87 mg, 33%). Subsequent fractions, which were obtained by adding MeOH to the eluent, were rechromatographed (CH_2Cl_2-MeOH, 93:7) to give 20 (24 mg, 10%) and the starting alcohols 19 and 21 (48.5 mg, 24%). An analytical sample of 20 was obtained by rechromatography ($CHCl_3$-hexane-diethylamine, 25:30:5).

Compound 20:
IR: 2830 and 2780 (Bohlmann bands), 1710 (C=O).
^{1}H NMR: 3.65 (1H, br s, H-21), 8.32 (1H, m, H-12).
MS: 282 (M^+, 100%), 281; exact mass: 282.1365 (calc. for $C_{17}H_{18}N_2O_2$: 282.1368).

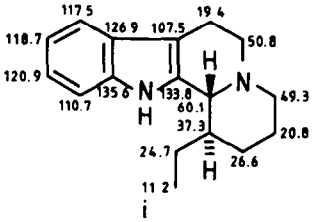
Compound 22:
IR: 2830 and 2780 (Bohlmann bands), 1720 (C=O).
^{1}H NMR: 3.32 (1H, s, H-12b), 3.61 (3H, s, $-CO_2CH_3$), 9.02 (1H, br s, NH).
MS: 314 (M^+), 313, 283, 255, 171 (100%); exact mass: 314.1636 (calc. for $C_{18}H_{22}N_2O_3$: 314.1630).

Preparation of compound 23

Hydroxyester 22 (28 mg, 0.09 mmol) was dissolved in MeOH (2.2 ml). 56 µl NaOMe (4.6 M, 9.27 mmol) was added and the solution was stirred for 20 h at 53°C under argon. The solvent was then evaporated and the residue worked up in the usual manner to give the lactam 23 (23 mg, 90%).
IR: 1710 (C=O).
^{1}H NMR: 4.11 (1H, br s, H-21), 8.20 (1H, m, H-12).
MS: 282 (M^+, 100%), 281; exact mass: 282.1374 (calc. for $C_{17}H_{18}N_2O_2$: 282.1368).

REFERENCES AND NOTES

1. Le Men, J. Chim. Thér. 1971, 137.
2. Arzneim.-Forsch. (Drug Res.) 1976, 26, 1905-1989.
3. Arzneim.-Forsch. (Drug Res.) 1977, 27(I), 1237-1298.
4. Vereczkey, L. Eur. J. Drug Metab. Pharm. 1985, 10, 89.
5. Le Men, J.; Taylor, W.I. Experientia 1965, 21, 508. For simplicity, we also use the biogenetic numbering in the homoeburnamonine series.
6. Jokela, R.; Schüller, S.; Lounasmaa, M. Heterocycles 1985, 23, 1751.
7. Lounasmaa, M.; Jokela, R. Heterocycles 1986, 24, 1663.
8. Döpke, W. The Alkaloids, Chemistry and Physiology, Ed. Rodrigo, R., Vol. 20, Academic Press, New York, 1981, pp. 297-332.
9. Lounasmaa, M.; Koskinen, A. Heterocycles 1984, 22, 1591.
10. Thal, C.; Sévenet, T.; Husson, H.-P.; Potier, P. C.R. Acad. Sc. Paris, Sér. C, 1972, 275, 1295.
11. Husson, H.-P.; Imbert, T.; Thal, C.; Potier, P., Bull. Soc. Chim. Fr. 1973, 2013.
12. Thal, C.; Imbert, T.; Husson, H-P.; Potier, P. Bull. Soc. Chim. Fr. 1973, 2010.
13. Schut, R.; Leipzig, T. J. Heterocycl. Chem. 1966, 101.
14. The ^{13}C NMR values found for compounds 10, 12 and 13 and those found for 1- and 3-ethyl-1,2,3,4,6,7,12,12b-octahydroindolo [2,3-a]quinolizines prepared by us earlier,[15] were in full agreement with the structures presented for the compound. The chemical shift of C(7) (compound 10) indicated a strong contribution of conformer c to the conformational equilibrium between a-c.[16] The very weak Bohlmann bands in the IR spectrum of compound 10 were in full agreement with the conformational conclusions.
15. Lounasmaa, M.; Jokela, R.; Tamminen, T. Heterocycles 1985, 23, 1367. [Reconsideration of the ^{13}C NMR spectra of compounds 1 and 3, has led us to interchange the assignments of two signals in both cases (see compounds i and ii)].



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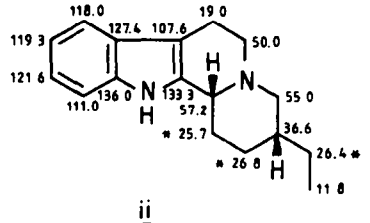

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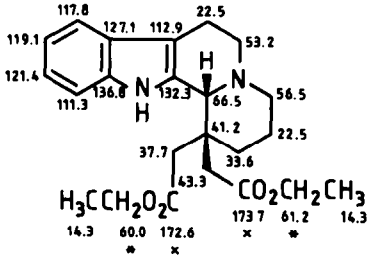
16. For definition of conformers a-c, see ref. 15.
17. Tolvanen, A.; Lounasmaa, M. Tetrahedron 1987, 43, 1123.
18. Lounasmaa, M.; Karvinen, E.; Koskinen, A.; Jokela, R. Tetrahedron 1987, 43, 2135.
19. Lounasmaa, M.; Hämeilä, M. Tetrahedron, 1978, 34, 437.
20. Lounasmaa, M.; Jokela, R. Tetrahedron 1978, 34, 1841.
21. Lounasmaa, M.; Merikallio, H.; Puhakka, M. Tetrahedron 1978, 34, 2995.
22. Wenkert, E.; Halls, T.; Kunesch, G.; Orito, K.; Stephens, R.; Temple, W.; Yadav, J. J. Am. Chem. Soc. 1979, 101, 5370.
23. Imbert, T.; Thal, C.; Husson, H.-P.; Potier, P. Bull. Soc. Chim. Fr. 1973, 2705.
24. Szabó, L.; Kalaus, G.; Szántay, C. Arch. Pharm. (Weinheim) 1983, 316, 629.
25. A small amount of diester iii (2%) was isolated too.



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