15. Total Synthesis of (+)-Elacomine and (−)-Isoelacomine, Two Hitherto Unnamed Oxindole Alkaloids from *Elaeagnus commutata*

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(6.X.95)

Racemic elacomine ((±)-**2**), a hemiterpene spiro oxindole alkaloid from *Elaeagnus commutata*, was synthesized in five steps from 6-methoxytryptamine (**19**) in 16% overall yield (*Scheme 3*). The final oxidative rearrangement of the corresponding β-carboline precursor (±)-**21** furnished isoelacomine ((±)-**22**) as a by-product (6% overall yield). A more elaborate route that started from L-tryptophan furnished (+)-**2** and (−)-**22** with optical purities of 76% (*Scheme 4*) and established the absolute configuration of these compounds. A reinvestigation of the alkaloidal content of the roots of *E. commutata* showed that both elacomine and isoelacomine occur naturally in racemic form.

1. Introduction. – In 1968, *Slywka* reported the isolation of a novel, optically active ($[\alpha]_D = +174.8$) hemiterpene oxindole alkaloid[3]) from the roots of the shrub *Elaeagnus commutata* (Elaegnaceae) [1]. Chemical degradation studies and spectroscopic evidence led to structure proposal **1** which, however, left open the exact position of the phenolic OH group and the relative configuration at the two asymmetric centres C(3) and C(4′)[4]). These questions were addressed subsequently by *James* and *Williams* by means of an X-ray diffraction study that allowed them to established formula **2** for this compound which they had obtained from *Locock* and *Slywka* [2]. Curiously enough, the sample investigated by X-ray crystallography must have been racemic, since the crystal was composed of alternating layers of both optical antipodes of **2**, a fact that is consistent with the reported space group $P2_1/c$. Surprisingly, the evident conflict concerning the enantiomeric purity of **2** was not commented by *James* and *Williams*, and in the context of our interest in the chemo- and diastereoselective transformation of indole alkaloids into their oxindole (1,3-dihydro-2*H*-indol-2-one) or pseudoindoxyl (1,2-dihydro-3*H*-indol-3-one) derivatives [4–8], we decided to synthesize (+)-elacomine ((+)-**2**) in a way that would allow to delineate its hitherto unknown absolute configuration.

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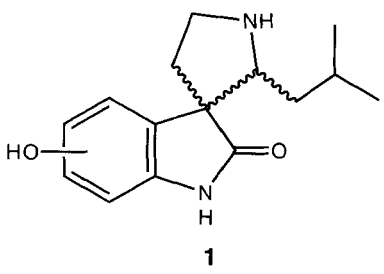
[1]) Part of the forthcoming Ph. D. thesis of *C. P.*

[2]) Taken in part from the diploma thesis of *M. W.*, ETH-Zürich, 1994.

[3]) No trivial name for this metabolite was suggested by the previous workers in this field [1] [2]. To avoid the awkward repetition of the lengthy name 'unnamed alkaloid from *Elaeagnus commutata*', we propose to call this alkaloid 'elacomine', as the more obvious label 'eleagnine' is already reserved for the alkaloid 1,2,3,4-tetrahydro-1-methyl-β-carboline [3].

[4]) The numbering system proposed by *James* and *Williams* [2] is adhered to in the present paper. For IUPAC names and numbering, see *Exper. Part*; *cis*/*trans* refer to the position with respect to the lactam carbonyl group at the pyrrolidine ring.



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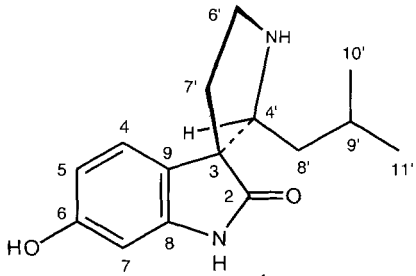
M.p. 250-252°, $[\alpha]_D$ = + 174.8 (*c* = 0.1, EtOH) [1]



(±)-**2**[4]

2. Results. – 2.1. *Model Studies in the 6-Deoxy Series.* As the required starting material 6-hydroxy-L-tryptophan was quite tedious to prepare (see below), we decided to start out with some model studies within the more readily available 6-deoxy series. The required 1,2,3,4-tetrahydro-β-carboline precursors (–)-**4** and (+)-**5** were prepared according to *Nakagawa et al.* [9] by means of a *Pictet-Spengler* condensation between L-tryptophan methyl ester (**3**) and isovaleraldehyde, catalyzed by CF_3COOH (*Scheme 1*). Under these conditions, a readily separable mixture of *cis*/*trans*-isomers was formed, the thermodynamically more stable *cis*-derivative (–)-**4** predominating [9] [10]. This outcome was not unwelcome, as – at least in principle – both antipodal series should thus become accessible starting from (*S*)-**3** as the single building block from the chiral pool[5]).

The *cis*-isomer (–)-**4** was protected as N_b-trifluoroacetyl derivative **6** which was oxidized with lead tetraacetate [12]. The presumed intermediate acetoxyindolenine hydrolyzed and rearranged *in situ* to give spiro-oxindole (–)-**9** in 41 % yield. The meanwhile superfluous chiral handle R^1 was then removed by reductive decyanation of the corresponding nitrile (–)-**11** (for a recent application and leading references, see [8]). The intermediate amide (–)-**10** was analyzed through an NOE difference spectrum (see *Exper. Part*), which clearly showed that the carboxamide group and the isobutyl side chain were located on the same side of the pyrrolidine ring as the substituted phenyl moiety. Thus, the crucial configurational relationship between the spiro center C(3) and the adjoining C(4′) of (–)-**10** is *l* (3*S*,4′*S*), and not *u* as required by structure **2** (3*R**,4′*S**). This undesired outcome notwithstanding, (–)-**10** was transformed into nitrile (–)-**11** which subsequently turned out to be accessible in higher overall yield *via* oxidation of the β-carboline-3-carbonitrile (+)-**7**. A similar result was obtained, when the *trans*-counterpart (+)-**8** was oxidized, in that the formed oxindole (+)-**14** was also endowed with the undesired *l*-configuration (3*R*,4′*R*). Surprisingly, the subsequent reductive removal of the CN group of (–)-**11** under mild conditions furnished a 2:1 mixture of two racemic diastereoisomers. The major component was shown by NOE experiments to be 6-deoxyelacomine ((±)-**12**; see *Exper. Part*), whereas the spectroscopic data (see below, *Tables 1* and *2*) of the minor isomer is consistent with the 6-deoxyisoelacomine structure (±)-**13** (for a rationalization of the observed racemization and epimerization, see *Chapt. 3*).

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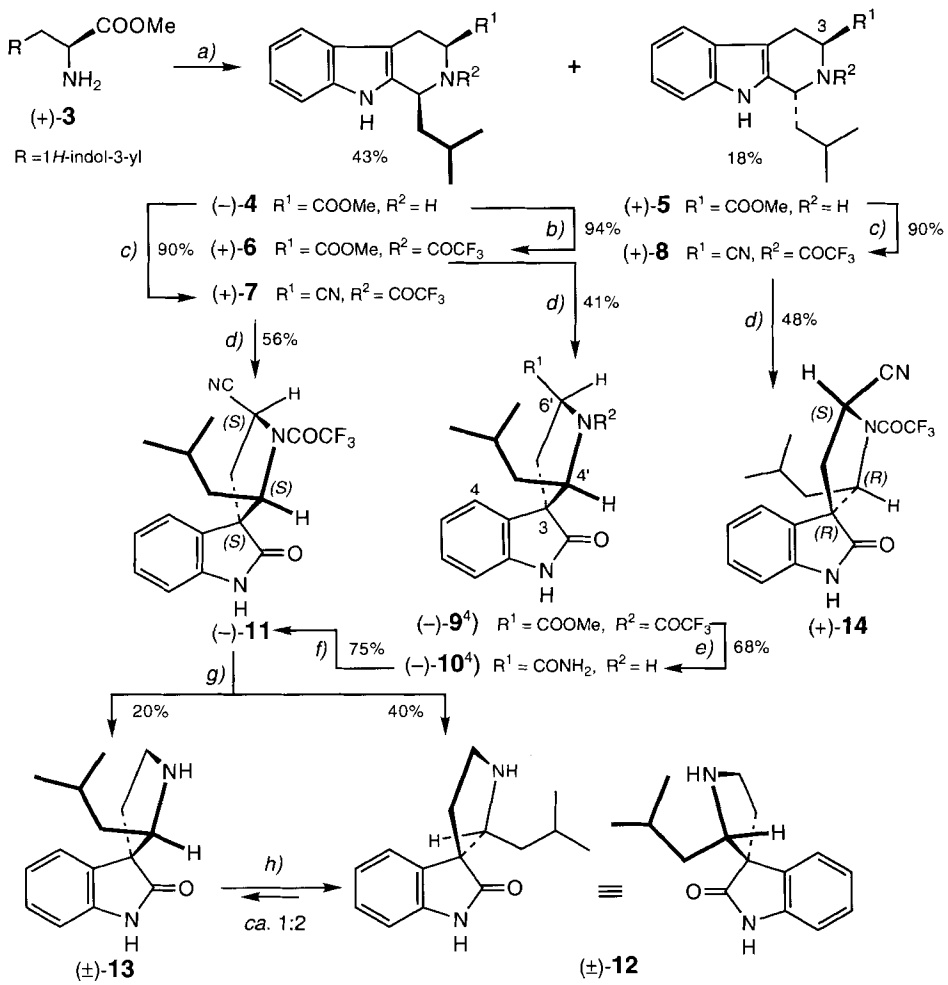
[5]) Extensive studies by *Cook* and coworkers demonstrated that the *trans*-isomers of type **5** become the exclusive products, if a sufficiently large group is temporarily added to N_b (*e.g.* R^2 = Ph_2CH instead of H). For leading references, see [11].

Scheme 1

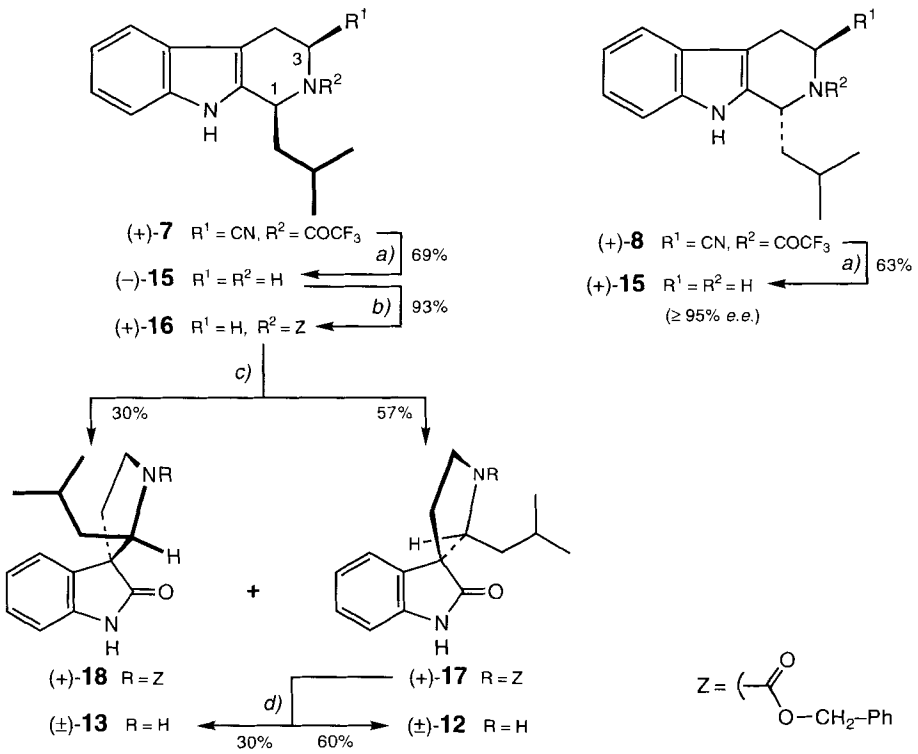


a) 3-Methylbutanal, CF_3COOH, CH_2Cl_2. *b*) $(CF_3CO)_2O$, py, 1,4-dioxane. *c*) 1. NH_3, MeOH; 2. 2.2 equiv. of $(CF_3CO)_2O$. *d*) 1. $Pb(OAc)_4$; 2. 2N HCl. *e*) NH_3, MeOH. *f*) 2.2 Equiv. of $(CF_3CO)_2O$. *g*) $NaBH_4$, EtOH. *h*) MeOH, 24 h 25°.

In a second approach, the order of events was reversed in that the chiral handle was removed reductively before the oxidative rearrangement was addressed. Treatment of (+)-**7** and (+)-**8** with $NaBH_4$ furnished (–)-(*S*)-**15** and the corresponding optical antipode, respectively (*Scheme 2*)[6]. A check [14] of their optical purity (500-MHz ^{1}H-NMR in the presence of 2.5 equiv. of (+)-(*R*)-*Mosher*'s acid) revealed that both samples had an *e.e.* of $\geq 95\%$. The (*S*)-antipode (–)-**15** was transformed into urethane (+)-**16** which was oxidized with aqueous *N*-bromosuccinimide (NBS) solution [15] to give a separable 2:1 mixture of two optically active diastereoisomeric oxindoles which

[6]) The corresponding racemate (±)-**15** was isolated from *Elaeagnus commutata* and synthesized in 1969 by *Slywka* and *Locock* [13].

Scheme 2



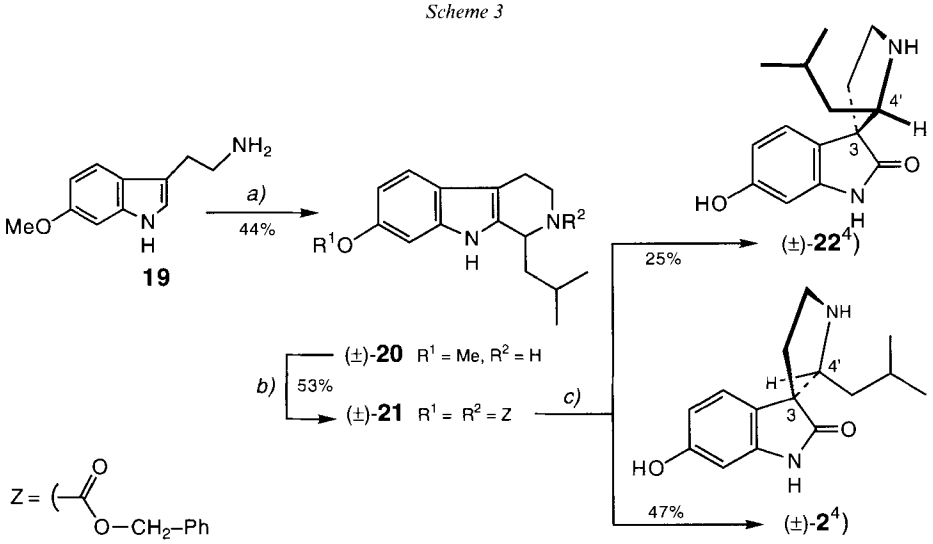
a) $NaBH_4$, EtOH. *b*) Z–Cl, Et_3N, CH_2Cl_2. *c*) NBS, THF/AcOH/H_2O. *d*) H_2, Pd/C, MeOH.

we believe to be represented by structures **17** and **18**. The benzyloxycarbonyl (Z) protecting group of the major isomer (+)-**17** was removed by hydrogenolysis under neutral conditions, but again, the same 2:1 mixture of racemic (±)-**12** and (±)-**13** was obtained as in the first approach.

2.2. *Synthesis of Racemic Elacomine and Isoelacomine.* A *Pictet-Spengler* condensation between commercially available 6-methoxytryptamine (**19**) and isovaleraldehyde in the presence of trimethylsilyl chloride (Me_3SiCl) produced the expected β-carboline (±)-**20** in 44% yield. Ether cleavage with BBr_3, followed by double protection of the crude product, led to intermediate (±)-**21** which underwent the desired oxidative rearrangement on exposure to aqueous NBS solution and furnished the targets (±)-**2** and (±)-**22** in 16 and 9% overall yield, respectively, after hydrogenolytic removal of the Z-protecting groups.

While the constitutional formulae of **2** and **22** were evident from their spectroscopic data and from their unambiguous syntheses, and whereas the relative configurations of the two compounds could readily be deduced from NOE experiments (see *Exper. Part*), a confrontation with earlier preparations met with unexpected difficulties. Natural elacomine (**2**) which was isolated in the late sixties was not available any more for a straightforward identification [16]; in addition, there are marked discrepancies between the analytical data of synthetic and natural [1] elacomine (**2**), as well as between isoelacomine (**22**) and an earlier synthetic preparation of this compound [17]. Natural **2**, which must have been racemic (see below), was recrystallized from MeOH and melted at 250–252° [1], but our material started to sublime at *ca.* 150° or decomposed at *ca.* 200°, depending on the heating rate. Whereas

Scheme 3



a) 3-Methylbutanal, Me_3SiCl, MeOH. *b*) 1. BBr_3, CH_2Cl_2; 2. Z–Cl, Et_3N, CH_2Cl_2. *c*) 1. NBS, THF/AcOH/H_2O; 2. H_2, Pd/C, MeOH.

the agreement between the IR spectra (KBr) is at best fair (see *Exper. Part*), the mass and ^{1}H-NMR spectra correspond reasonably well (see *Fig.*).

In 1978, *Mori* and *Ban* [17] synthesized a compound (m.p. 255–256.5°) whose behavior on TLC, as well as its mass and ^{1}H-NMR data, exactly matched those of natural **2**, but the IR spectra (KBr) were decidedly different, for which reason they claimed to have synthesized (±)-**22** or a mixture of (±)-**2** and (±)-**22**. In our hands, isoelacomine ((±)-**22**) failed to crystallize, and its behavior in several TLC systems was clearly different from that of (±)-**2**. It seems as if the Japanese workers had actually prepared the thermodynamically more stable elacomine (**2**), and as it is now easy to differentiate between the two diastereoisomeric series (see *Fig.* and *Tables 1* and *2*), it is unfortunate that they did not report their NMR data which would have allowed to settle the argument.

2.3. *Synthesis of Optically Active (±)-Elacomine and (−)-Isoelacomine.* The required starting material, 6-hydroxy-L-tryptophan derivative (+)-**24** (*Scheme 4*), was prepared according to the method of *Taniguchi* and *Hino* [18] from (−)-**23** and transformed *via* (+)-**25** into the 6-(2-nitrobenzyloxy) derivative [19] (+)-**26**. A *Pictet-Spengler* condensation with isovaleraldehyde furnished a 3:1 mixture of the *cis*- and *trans*-β-carbolines (−)-**28** and (+)-**27**. The chiral handle of the major product was removed by following the established protocol, passing through carboxamide (−)-**29** whose relative configuration was verified through an NOE experiment. The resulting 3-nor compound (+)-**30** was oxidized with NBS to furnish a 3:2 mixture of two doubly protected spiro-oxindoles, which were separated by chromatography. The protecting groups of both components were removed by hydrogenolysis to give elacomine ((+)-**2**) and isoelacomine ((−)-**22**), respectively.

As the optical rotation of synthetic (+)-**2** ($[\alpha]_D = +2.6$) was much smaller than the value reported for natural elacomine (**2**; $[\alpha]_D = +174.8$ [1]), we checked the enantiomeric purity of our preparation by ^{1}H-NMR spectroscopy (500 MHz, 2.5 equiv. of (+)-(*R*)-*Mosher*'s acid in (D_6)DMSO). A control experiment with (±)-**2** (*Scheme 3*) showed a sufficiently well resolved doubling of the signals of *H*–C(4) and of the two Me groups to permit a determination of the enantiomeric purity of (+)-**2** with ±3% accuracy. In the case at hand, the enantiomeric excess

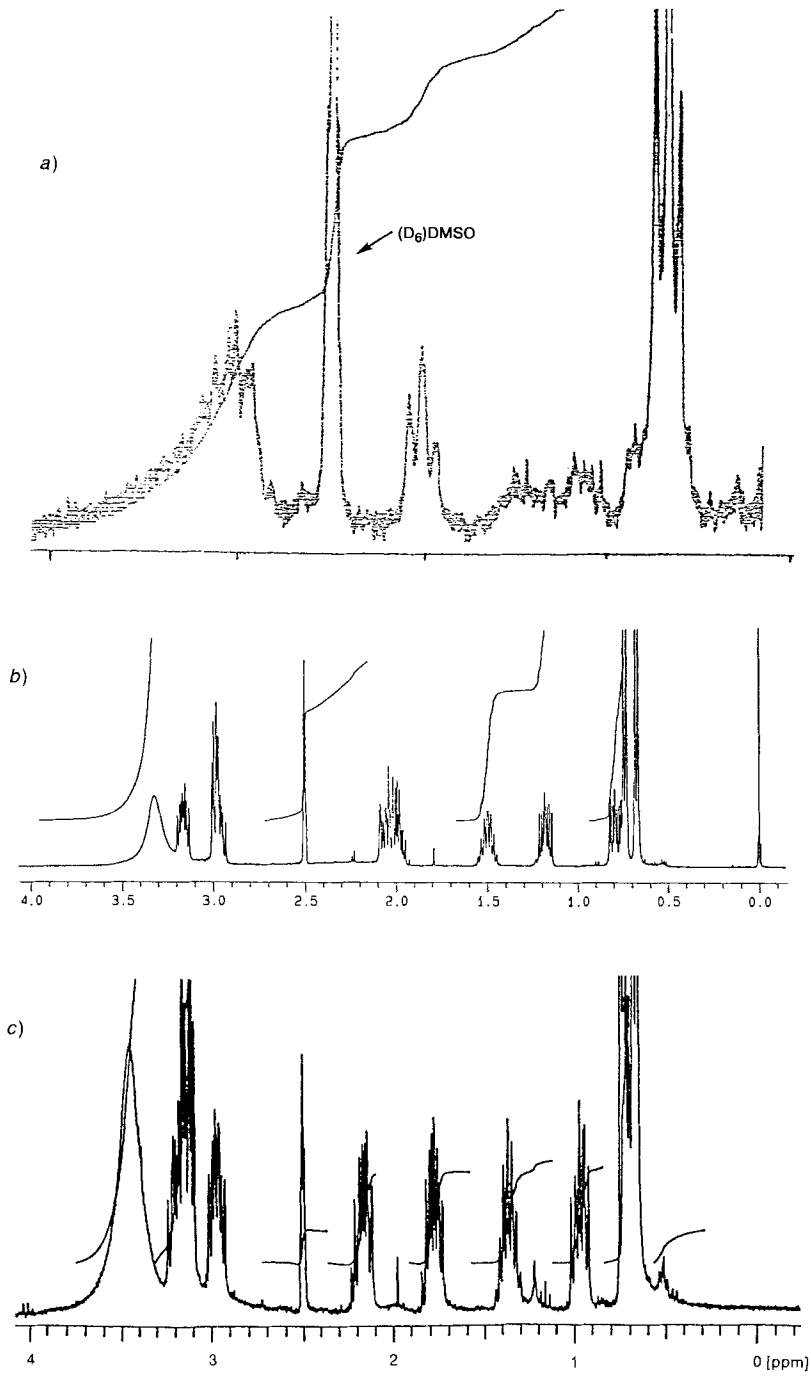
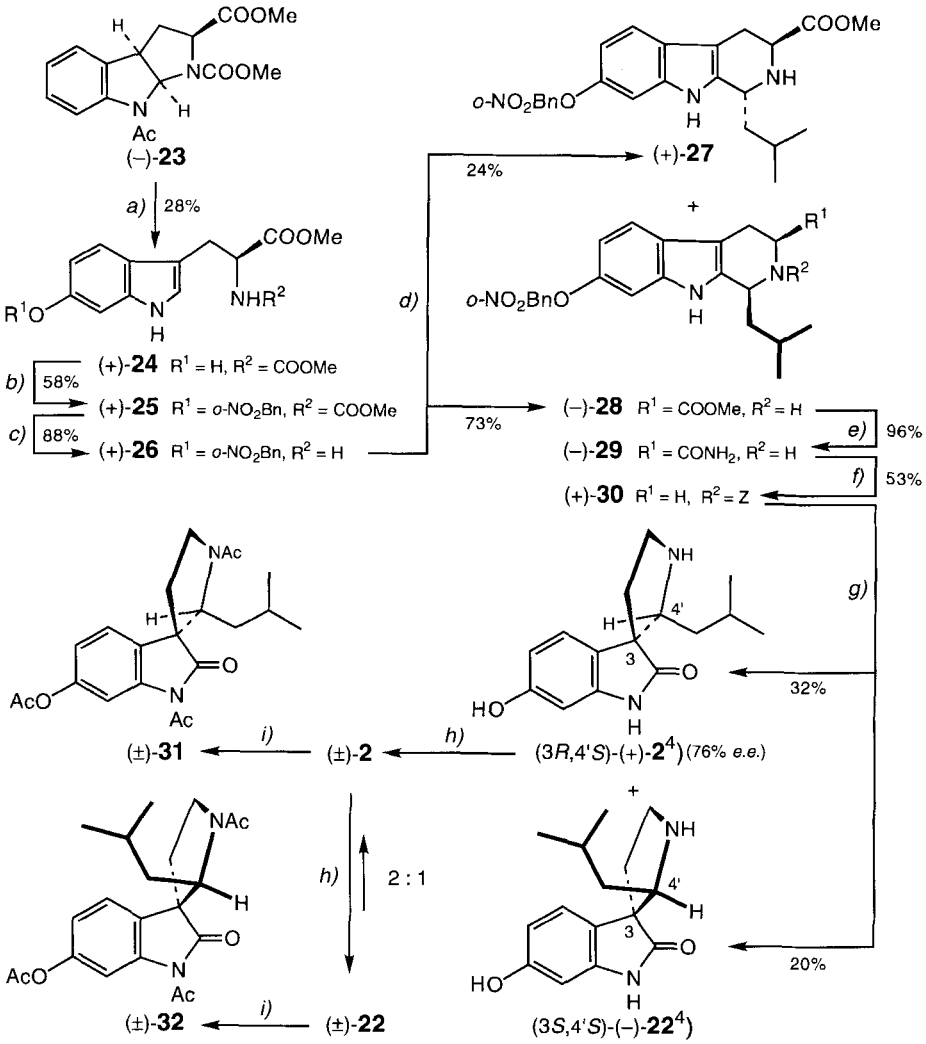


Figure. *Aliphatic sections of the* ^{1}*H-NMR spectra in* (D_6)*DMSO of* a) *natural* (±)-**2** (100 MHz), *reproduced from* [1], b) *of synthetic* (+)-**2** (400 MHz), *and* c) *of* (−)-**22** (300 MHz)

Scheme 4



a) 1. $Pb(OAc)_4$; 2. H_2SO_4, MeOH; 3. separation of isomers. *b*) 2-Nitrobenzyl chloride, K_2CO_3, Bu_4NI, DMF. *c*) Me_3SiI, CH_2Cl_2. *d*) 3-Methylbutanal, CF_3COOH, CH_2Cl_2. *e*) NH_3, MeOH. *f*) 1. 2.2 Equiv. of $(CF_3CO)_2O$; 2. $NaBH_4$, EtOH; 3. Z–Cl, Et_3N, CH_2Cl_2. *g*) 1. NBS, THF/AcOH/H_2O; 2. H_2, Pd/C, MeOH. *h*) EtOH, 2 h 80°. *i*) Ac_2O, py.

amounted to 76±3%[7]). Thus, the value reported for natural elacomine (**2**) must be ascribed either to an erroneous measurement of its optical rotation or to the presence of an unidentified, strongly dextrorotatory impurity in their specimen.

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[7]) An analogous verification of the optical purity of isoelacomine (–)-**22** ($[\alpha]_D = -15.5$) was thwarted by an insufficient splitting of the NMR signals in question, but, for mechanistic reasons, we believe it to be of the same order of magnitude as for (+)-**2** (see *Chapt. 3*).

Fortunately, **2** and **22** turned out to be more resistant to racemization and epimerization than the 6-deoxy analogues **12** and **13**. Under conditions which led to complete equilibration in the latter case (MeOH, 24 h 25°), elacomine (**2**) became contaminated with less than 10% of isoelacomine (**22**). However, even here, epimerization was complete after 2 h in refluxing EtOH[8]). As *Slywka*'s original isolation procedure involved *inter alia* a 10-h *Soxhlet* extraction with boiling EtOH, his preparation of **2** obviously must have been racemic. As a matter of fact, when we repeated the extraction of *E. commutata* following the original prescription, we isolated (±)-**2**, as well as (±)-**22** which had escaped the earlier worker's attention. When the extraction was carried out under conditions that, as had been shown, do not lead to serious racemization of (+)-**2** (MeOH, 10 h 25°), the isolated alkaloids were still racemic. Therefore, (±)-**2** and (±)-**22** can not be considered as artefacts of isolation and these alkaloids indeed seem to be produced as racemates in the plant[9]).

3. Discussion. – While epimerization at the spiro center of β-carboline oxindoles under comparatively mild conditions (usually a few hours reflux in pyridine or AcOH) is a long-standing phenomenon [20], which was rationalized by *Wenkert et al.* [21] (for reviews, see [22]), the great ease with which compounds **2**, **12**, **13**, and **22** epimerize, seems to be unprecedented. During the reductive decyanation of (+)-**33** in a recent synthesis of (−)-horsfiline ((−)-**34**), *e.g.*, less than 5% of racemization was observed [8] (*Scheme 5*), while (−)-**11** racemized and epimerized completely under the same conditions. The marked difference in stability between (+)-**2** and (−)-**34** is caused conceivably by the presence of the isobutyl side chain which probably destabilizes the spiro form and in turn renders the *retro-Mannich* intermediates **I** and **III** more stable as compared to **VII**.

The reason for the more subtle difference between the 6-deoxy model compounds **12**/**13** and the pair **2**/**22** which, however, was crucial for the successful synthesis of optically active samples of the latter, is less obvious. Though not evident in the NMR spectra of **2**, the zwitterionic form **2′** might contribute to some extent to make the *retro-Mannich* reaction more difficult than in the case of **12**. On the other hand, the π-donor properties of the phenolic OH group that confine a partial negative charge to C(9) might destabilize enolates **I** and **III** as compared to the deoxy analogues **IV** and **VI**.

The ease with which the diastereoisomeric oxindoles are interconverted called for an unambiguous assignment of their relative configuration. This problem was solved by means of difference NOE experiments, and with this information at hand, some generalizations concerning the chemical-shift differences between the two series emerged. The most significant trends are summarized in the bottom half of *Table 1* and concern mostly the methylene protons at C(8′). In the iso series both of them are shielded relative to their counterparts in the epimeric series by the aromatic π-system laying beneath, and this holds especially for the corresponding low-field branch which is arbitrarily named H_A–C(8′). The ^{13}C-NMR spectra of the epimeric pairs are very similar (*Table 2*) and the only significant difference concerns the chemical shift of C(4′). As its relative position

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[8]) An epimer mixture (±)-**2**/(±)-**22** 2:1 was acetylated and the product separated to yield the triacetyl derivatives (±)-**31** and (±)-**32**.

[9]) Interestingly, **15**, a likely biogenetic precursor of **2** and **22**, was also shown to be present in racemic form in the same species [1] [13].

Scheme 5

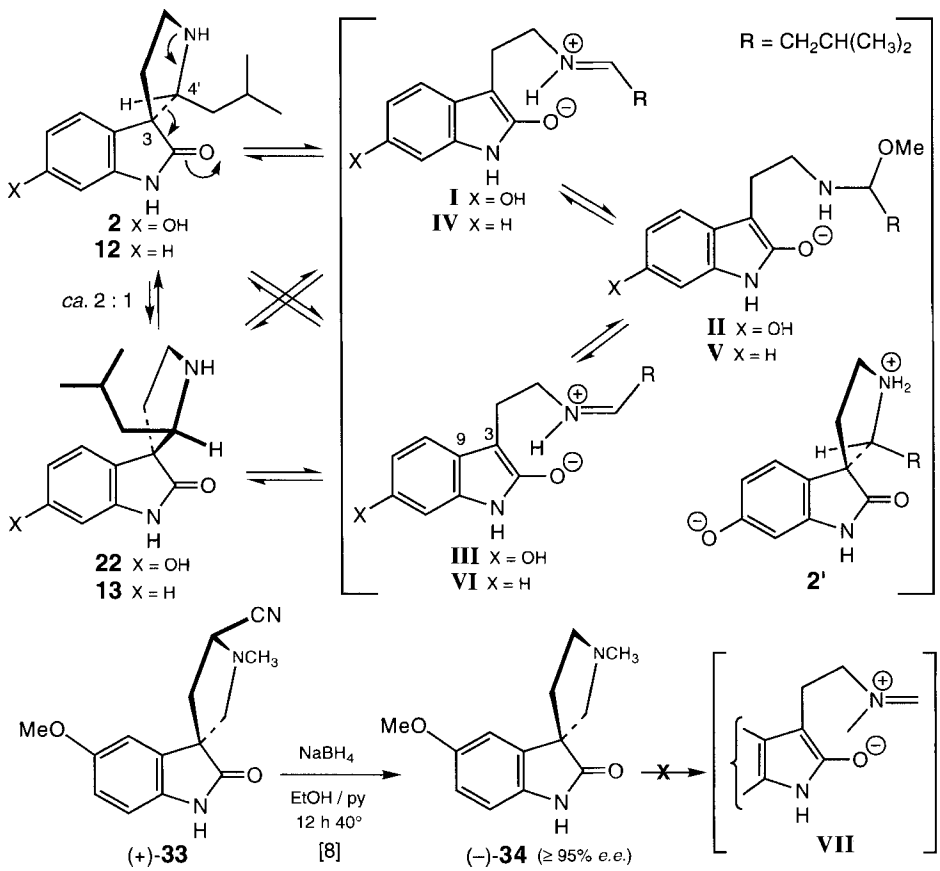


Table 1. *^{1}H-NMR Chemical-Shift Values* ($CDCl_3$) *for Some Spiro-oxindoles*[4]). δ in ppm rel. to Me_4Si.

	2[a])	**22**[b])	**35**[c])	**36**[c])	**37**[d])	**38**[d])	**12**	**13**	**10**
H–C(4)	7.00	6.77	7.07	7.06	7.10	7.18	7.21	7.15	7.30
H–C(5)	6.49	6.30	6.57	6.56	6.58	6.55	7.07	7.04	7.02
H–C(6)	–	–	–	–	–	–	7.24	7.22	7.21
H–C(7)	6.42	6.26	6.51	6.51	6.47	6.52	6.96	6.95	6.90
H–C(4′)	3.18	3.20	3.23	3.47	3.48	3.67	3.45	3.49	3.57
H_{cis}–C(6′)[e])	3.37	3.10	3.44	3.37	4.29	4.16	3.54	3.33	4.12
H_{trans}–C(6′)[e])	3.12	3.10	3.22	3.32	–	–	3.37	3.39	–
H_{cis}–C(7′)[e])	2.27	2.23	2.31	2.49	2.59	2.56	2.34	2.53	2.85
H_{trans}–C(7′)[e])	2.18	1.82	2.19	2.03	2.37	2.33	2.31	2.07	2.26
H_A–C(8′)[e])	1.35	0.90	1.38	1.07	1.32	1.06	1.47	1.04	1.18
H_B–C(8′)[e])	0.97	0.70	0.93	0.88	0.90	0.84	0.95	0.87	0.92
H–C(9′)	1.52	1.23	1.64	1.50	1.58	1.48	1.63	1.51	1.57
Me(10′)	0.77	0.60	0.78	0.80	0.78	0.79	0.78	0.79	0.83
Me(11′)	0.74	0.54	0.74	0.76	0.74	0.76	0.75	0.75	0.76

Table 1 (cont.)

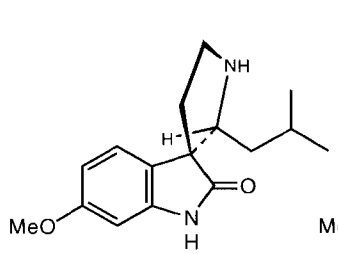
	2[a])	**22**[b])	**35**[c])	**36**[c])	**37**[d])	**38**[d])	**12**	**13**	**10**
$\Delta\delta$(6′*cis*-6′*trans*)	0.25	0.00	0.22	0.05	–	–	0.17	−0.06	–
$\Delta\delta$(7′*cis*-7′*trans*)	0.09	0.41	0.12	0.46	0.22	0.23	0.03	0.46	0.59
$\Delta\delta$(8′*A*-8′*B*)	0.38	0.20	0.45	0.19	0.42	0.22	0.52	0.17	0.26
$\Delta\delta$(8′*A*)	0.45		0.31		0.26		0.43		

[a]) In CD_3OD. [b]) In $CDCl_3/CD_3OD$ *ca.* 10:1. [c]) Prepared from 1,2,3,4-tetrahydro-1-isobutyl-7-methoxy-β-carboline (not included in *Exper. Part*). [d]) Prepared from methyl 1,2,3,4-tetrahydro-1-isobutyl-7-methoxy-β-carboline-3-carboxylate [9] (not included in *Exper. Part*). [e]) H_{cis}/H_{trans} with respect to the lactam carbonyl group at the pyrrolidine ring.

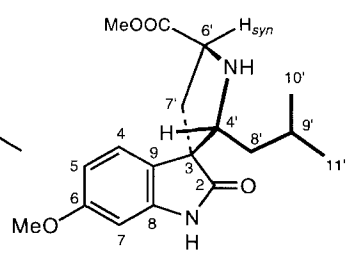
Table 2. *^{13}C-NMR Chemical-Shift Values* ($CDCl_3$) *for Some Spiro-oxindoles*[4]). δ in ppm rel. to Me_4Si.

	2[a])	**22**[b])	**35**[c])	**36**[c])	**37**[d])	**38**[d])	**12**	**13**	**10**
C(2)	184.0	182.4	182.6	181.8	181.1	180.9	181.9	182.0	181.2
C(3)	58.5	57.6	57.8	57.7	57.9	57.7	58.1	58.4	57.8
C(4)	123.6	124.2	122.9	124.7	123.1	125.2	122.5[e])	122.3[e])	122.5[e])
C(5)	109.7	108.6	107.3	107.1	107.0	107.3	122.9[e])	123.9[e])	125.2[e])
C(6)	158.3	156.9	159.9	159.8	159.7	159.9	128.2	127.7	128.0
C(7)	99.0	98.2	97.2	97.2	96.8	97.3	110.0	109.9	109.7
C(8)	143.7	141.7	142.2	141.3	141.5	141.5	141.3	140.5	140.4
C(9)	122.5	122.7	123.4	124.4	121.7	123.5	130.9	132.8	131.3
C(4′)	68.2	65.7	68.9	66.6	66.9	64.2	68.4	67.0	65.5
C(6′)	46.2	45.4	46.3	45.9	58.8	58.1	46.0	46.1	59.4
C(7′)	39.2[e])	39.7[e])	38.2[e])	39.9[e])	40.5[e])	40.9[e])	38.0[e])	38.6[e])	41.2[e])
C(8′)	38.1[e])	38.4[e])	38.0[e])	38.6[e])	38.1[e])	40.0[e])	37.4[e])	39.9[e])	40.3[e])
C(9′)	26.2	25.2	25.9	25.8	25.5	25.8	25.9	25.9	25.6
C(10′)	23.7	22.7	23.5	23.4	23.1	23.3	23.5	23.4	23.5
C(11′)	22.1	21.8	21.8	22.2	21.4	22.1	21.8	22.2	21.8
$\Delta\delta$(4′)	2.5		2.3		2.7		1.4		

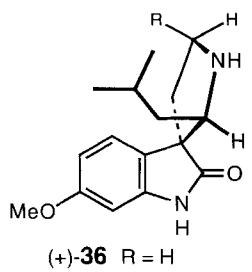
[a]) In CD_3OD. [b]) In $CDCl_3/CD_3OD$ *ca.* 10:1. [c]) Prepared from 1,2,3,4-tetrahydro-1-isobutyl-7-methoxy-β-carboline (not included in *Exper. Part*). [d]) Prepared from methyl 1,2,3,4-tetrahydro-1-isobutyl-7-methoxy-β-carboline-3-carboxylate [9] (not included in *Exper. Part*). [e]) Assignments may be interchanged.



(−)-**35**



(+)-**37**[4])



(+)-**36** R = H
(+)-**38** R = COOMe

towards the oxindole ring system is the same for both series, it seems as if different ground-state conformations of the isobutyl side chain were responsible for the observed differential shielding by 1.5–2.7 ppm.

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Experimental Part

1. *General.* Reagents and solvents: purchased from *Fluka AG* in the highest obtainable purity, unless stated otherwise. $CHCl_3$ and $CDCl_3$ were passed through basic alumina (*Woelm*, act. I) immediately before use; petroleum ether (p.e.) consisted of a fraction with a boiling range of 50–70°. Usual workup means that the mixture was evaporated at *ca.* 50 Torr, the residue taken up in CH_2Cl_2/sat. aq. Na_2CO_3 soln., the aq. phase extracted 3 times with CH_2Cl_2, and the combined org. extract dried ($MgSO_4$) and evaporated. M.p. (not corrected): *Tottoli* apparatus. Optical rotations: *Perkin-Elmer 241* at 25° and 589 nm (Na_D). IR Spectra (2–3% in $CHCl_3$, unless stated otherwise): $\tilde{\nu}_{max}$ in cm^{-1}; *Perkin-Elmer-PE-781* or *-PE-983* spectrometer. ^{1}H-NMR Spectra: δ in ppm rel. to internal Me_4Si (= 0 ppm) in $CDCl_3$, unless stated otherwise, J in Hz; 500 MHz, *Bruker AMX 500*; 400 MHz, *Bruker AMX 400*; 300 MHz, *Varian Gemini 300*; 200 MHz, *Varian Gemini 200*. Difference-NOE: *Bruker WM 300* (300 MHz); irradiated proton→affected signals. ^{13}C-NMR Spectra: multiplicities from DEPT experiments; 100 MHz, *Bruker AMX 400*; 75 MHz, *Varian Gemini 300*. Mass spectra: *m/z* [amu] (% base peak); *Hitachi-Perkin-Elmer, VG TRIBRID*; EI at 70 eV; FAB: 3-nitrobenzyl alcohol as matrix.

General Procedure A: Transformation of Methyl Esters into the Corresponding Nitriles. A soln. of the starting ester in MeOH (*ca.* 50 mmol/l) was saturated with NH_3 (g) at 0°. After stirring for 4 d at 25° under an NH_3 atmosphere, the solvent was evaporated and the residue recrystallized from AcOEt. The resulting carboxamide was suspended in 1,4-dioxane, then were added 7 equiv. of pyridine. Dropwise addition of 2.5 equiv. of $(CF_3CO)_2O$ at 25° led to a homogeneous yellow soln. which was poured onto crushed ice after 20 min. Usual workup, followed by chromatography under the specified conditions, furnished the desired nitrile.

General Procedure B: Reductive Decyanation. To a soln. of the nitrile in EtOH/pyridine 4:1 (*ca.* 30 mmol/l) were added 10 equiv. of $NaBH_4$. After stirring at 40° for 12 h, the mixture was cooled to 0° and quenched by addition of a slight excess of 2N aq. HCl soln. Usual workup, followed by chromatography under the specified conditions, furnished the desired nor compound.

General Procedure C: Determination of the Optical Purities. To a soln. of the sample in $CDCl_3$ or (D_6)DMSO were added 2.5 equiv. of (+)-(*R*)-α-methoxy-(α-trifluoromethyl)phenylacetic acid (= 3,3,3-trifluoro-2-methoxy-2-phenylpropanoic acid; *Mosher*'s acid), and the ^{1}H-NMR spectrum was recorded at 500 MHz. The required information was obtained by integrating the split signals that had been identified before by submitting the corresponding racemate to the same procedure.

2. *Syntheses. (1S,3S)-Methyl 1,2,3,4-Tetrahydro-1-(2-methylpropyl)-2-(trifluoroacetyl)-9H-pyrido[3,4-b]indole-3-carboxylate* ((+)-**6**). To a soln. of 0.80 g (2.79 mmol) of (−)-**4** [9] in 30 ml of 1,4-dioxane and 1.6 ml of pyridine were added 0.43 ml (3.07 mmol) of $(CF_3CO)_2O$ with efficient stirring at 5°. After 30 min, the mixture was worked up as usual to give 1.00 g (94%) of (+)-**6** after chromatography (20 g of silica gel, AcOEt/p.e. 1:9→1:4). Colorless crystals. M.p. 155–156°. $[\alpha]_D$ = +50.3 (*c* = 2.0, MeOH). IR ($CHCl_3$): 3460, 1744, 1687, 1462, 1448, 1440, 1434, 1180, 1144. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.82 (*s*, 1 H); 7.50 (*d*, *J* = 7.7, 1 H); 7.31 (*d*, *J* = 8.0, 1 H); 7.19 (*ddd*, *J* = 8.0, 7.1, 1.2, 1 H); 7.13 (*ddd*, *J* = 7.7, 7.1, 1.0, 1 H); 5.66 (*td*, *J* = 6.9, 1.3, 1 H); 5.08 (*dd*, *J* = 6.6, 1.3, 1 H); 3.69 (*s*, 3 H); 3.60 (*dd*, *J* = 15.9, 1.3, 1 H); 3.06 (*ddd*, *J* = 15.9, 6.6, 1.7, 1 H); 1.88 (*m*, 1 H); 1.78 (*dt*, *J* = 14.0, 6.9, 1 H); 1.64 (*dt*, *J* = 14.0, 6.9, 1 H); 1.10 (*d*, *J* = 6.4, 3 H); 1.09 (*d*, *J* = 6.6, 3 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 170.0 (*s*); 157.4 (*s* (*q*, *J* = 36)); 136.2 (*s*); 131.7 (*s*); 126.2 (*s*); 122.5 (*d*); 120.0 (*d*); 118.4 (*d*); 116.0 (*s* (*q*, *J* = 288)); 110.9 (*d*); 105.0 (*s*); 53.7 (*d*); 52.9 (*q*); 50.6 (*d*); 44.9 (*t*); 26.1 (*d*); 23.2 (*q*); 22.8 (*t*); 22.4 (*q*). MS: 382 (83, M^+), 325 (100), 293 (19), 265 (29), 169 (22), 168 (23), 156 (10).

(1S,3S)-1,2,3,4-Tetrahydro-1-(2-methylpropyl)-2-(trifluoroacetyl)-9H-pyrido[3,4-b]indole-3-carbonitrile ((+)-**7**). *General Procedure A*, starting with 3.0 g (10.5 mmol) of (−)-**4** [9], followed by chromatography (silica gel, AcOEt/p.e. 1:9→1:4) produced 3.12 g (90%) of (+)-**7**. Slightly yellow crystals. M.p. 62–64° (AcOEt). $[\alpha]_D$ = +41.9 (*c* = 0.9, MeOH). IR ($CHCl_3$): 3460, 3010, 2395, 1700, 1516, 1466, 1426, 1142, 926. ^{1}H-NMR (300 MHz, $CDCl_3$): 8.00 (br. *s*, 1 H); 7.47 (*d*, *J* = 8.0, 1 H); 7.36 (*d*, *J* = 8.0, 1 H); 7.23 (*ddd*, *J* = 8.0, 7.1, 1.3, 1 H); 7.16 (*ddd*, *J* = 8.0, 7.1, 1.1, 1 H); 5.75 (*t*, *J* = 7.0, 1 H); 5.42 (*dd*, *J* = 5.5, 1.8, 1 H); 3.33 (*dd*, *J* = 16.0, 1.8, 1 H); 3.25 (*ddd*, *J* = 16.0, 5.5, 1.5, 1 H); 2.21 (*ddd*, *J* = 14.2, 7.7, 6.5, 1 H); 2.02 (*ddd*, *J* = 14.2, 7.4, 6.7, 1 H); 1.85 (*m*, 1 H); 1.10 (*d*, *J* = 6.5, 6 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 156.0 (*s* (*q*, *J* = 37)); 136.3 (*s*); 131.4 (*s*); 126.0 (*s*); 123.1 (*d*); 120.4 (*d*); 118.2 (*d*); 117.3 (*s*); 116.4 (*s* (*q*, *J* = 288)); 111.2 (*d*); 103.1 (*s*); 50.7 (*d*); 44.1 (*t*); 41.9 (*d*); 27.0 (*t*); 25.9 (*d*); 23.0 (*q*); 22.4 (*q*). MS: 349 (29, M^+), 309 (14), 293 (18), 292 (100), 169 (19).

(1R,3S)-1,2,3,4-Tetrahydro-1-(2-methylpropyl)-2-(trifluoroacetyl)-9H-pyrido[3,4-b]indole-3-carbonitrile ((+)-**8**). As described above, starting with (+)-**5** [9]. Yield 90%. Slightly yellow crystals. M.p. 70–72° (AcOEt). $[\alpha]_D = +2.3$ ($c = 0.9$, MeOH). IR ($CHCl_3$): 3450, 3010, 2395, 1700, 1520, 1450, 1419, 1150, 926, 848. ^{1}H-NMR (200 MHz, $CDCl_3$): 7.96 (br. *s*, 1 H); 7.53 (*d*, $J = 7.5$, 1 H); 7.38 (*d*, $J = 7.5$, 1 H); 7.27 (*td*, $J = 7.5$, 1.5, 1 H); 7.19 (*td*, $J = 7.5$, 1.5, 1 H); 5.24 (br. *s*, 2 H); 3.60 (*m*, 1 H); 3.22 (*dd*, $J = 15.3$, 4.2, 1 H); 1.86 (*m*, 3 H); 1.09 (*d*, $J = 6.2$, 3 H); 0.95 (*d*, $J = 6.2$, 3 H); 0.95 (*m*, 3 H). ^{13}C-NMR (50 MHz, $CDCl_3$): 159.0 (br. *s*); 136.5 (*s*); 133.2 (*s*); 126.3 (*s*); 123.2 (*d*); 120.7 (*d*); 119.1 (*d*); 118.5 (*d*); 111.9 (*d*); 106.2 (br. *s*); 53.9 (br. *d*); 44.6 (*t*); 44.2 (*d*); 25.1 (br. *d*); 25.1 (br. *t*); 23.5 (*q*); 22.2 (*q*). MS: 349 (17, M^+), 293 (18), 292 (100), 169 (13).

(2′S,3S,5′S)-Methyl 1,2-Dihydro-2′-(2-methylpropyl)-2-oxo-1′-(trifluoroacetyl)spiro[3H-indole-3,3′-pyrrolidine]-5′-carboxylate ((−)-**9**). To a soln. of 900 mg (2.35 mmol) of (+)-**6** in 40 ml of CH_2Cl_2 were added 1.15 g (2.59 mmol) of $Pb(OAc)_4$ in small portions within 5 min under vigorous stirring at −10°. After 70 min, 25 ml of MeOH and 10 ml of 2N HCl were added and stirring was continued for 2 h at 25°. Standard workup and chromatography (40 g of silica gel, AcOEt/p.e. 1:4) furnished 384 mg (41%) of (−)-**9**. Colorless oil. $[\alpha]_D = -56.5$ ($c = 1.2$, MeOH). IR ($CHCl_3$): 3425, 1750, 1706 (br.), 1617, 1483, 1468, 1436, 1330, 1281, 1260, 1150. ^{1}H-NMR (400 MHz, $CDCl_3$): 9.21 (br. *s*, 1 H); 7.29 (*td*, $J = 7.5$, 1.0, 1 H); 7.21 (*d*, $J = 7.5$, 1 H); 7.05 (*t*, $J = 7.5$, 1 H); 6.89 (*d*, $J = 7.5$, 1 H); 5.13 (*t*, $J = 8.0$, 1 H); 4.72 (*dd*, $J = 10.5$, 4.5, 1 H); 3.84 (*s*, 3 H); 2.77 (*dd*, $J = 13.4$, 9.2, 1 H); 2.55 (*dd*, $J = 13.4$, 8.9, 1 H); 1.84 (*ddd*, $J = 13.0$, 10.5, 3.5, 1 H); 1.57 (*m*, 1 H); 1.47 (*ddd*, $J = 13.0$, 8.9, 4.5, 1 H); 0.96 (*d*, $J = 6.6$, 3 H); 0.88 (*d*, $J = 6.6$, 3 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 181.9 (*s*); 172.1 (*s*); 157.4 (*s* (*q*, $J = 37$)); 141.4 (*s*); 129.4 (*d*); 125.8 (*s*); 125.7 (*d*); 122.4 (*d*); 116.3 (*s* (*q*, $J = 288$)); 110.6 (*d*); 62.8 (*d*); 57.8 (*d*); 54.3 (*s*); 52.9 (*q*); 40.4 (*t*); 37.8 (*t*); 24.6 (*d*); 23.6 (*q*); 21.6 (*q*). MS: 398 (26, M^+), 284 (12), 185 (13), 158 (11), 146 (100), 130 (10).

(2′S,3S,5′S)-1,2-Dihydro-2′-(2-methylpropyl)-2-oxospiro[3H-indole-3,3′-pyrrolidine]-5′-carboxamide ((−)-**10**). A soln. of 350 mg (0.88 mmol) of (−)-**9** in 50 ml of MeOH was cooled to 0° and saturated with NH_3 (g). After stirring for 3 d at 25° in the dark, the solvent was evaporated and the residue chromatographed (30 g of silica gel, AcOEt containing MeOH from 0 to 17%): 182 mg (68%) of (−)-**10**. Colorless solid. M.p. 180–182°. $[\alpha]_D = -15.7$ ($c = 1.0$, MeOH). IR ($CHCl_3$): 3680, 1724, 1710, 1618, 1598, 1197. ^{1}H-NMR (400 MHz, $CDCl_3$): 8.78 (br. *s*, 1 H); 7.30 (*d*, $J = 7.7$, 1 H); 7.21 (*td*, $J = 7.7$, 1.2, 1 H); 7.05 (*s*, 1 H); 7.02 (*td*, $J = 7.7$, 1.0, 1 H); 6.90 (*d*, $J = 7.7$, 1 H); 6.17 (*s*, 1 H); 4.12 (*dd*, $J = 10.3$, 6.4, 1 H); 3.57 (*dd*, $J = 9.8$, 4.1, 1 H); 2.85 (*dd*, $J = 13.7$, 10.3, 1 H); 2.26 (*dd*, $J = 13.7$, 6.4, 1 H); 1.57 (*m*, 1 H); 1.18 (*ddd*, $J = 13.8$, 9.8, 5.2, 1 H); 0.92 (*ddd*, $J = 13.8$, 8.5, 4.1, 1 H); 0.83 (*d*, $J = 6.6$, 3 H); 0.76 (*d*, $J = 6.6$, 3 H). NOE[4]): 7.30 (H–C(4)) → 7.02 (H–C(5)), 3.55 (H–N(5′)), 2.26 (H_{trans}–C(7′)), 1.18 and 0.92 (2 H–C(8′)); 2.26 (H_{trans}–C(7′)) → 7.30 (H–C(4)), 2.85 (H_{cis}–C(7′)); 2.85 (H_{cis}–C(7′)) → 4.12 (H–C(6′)), 2.26 (H_{trans}–C(7′)); 4.12 (H–C(6′)) → 3.57 (H–C(4′)), 2.85 (H_{cis}–C(7′)). ^{13}C-NMR (100 MHz, $CDCl_3$): 181.2 (*s*); 176.8 (*s*); 140.4 (*s*); 131.3 (*s*); 128.0 (*d*); 125.2 (*d*); 122.5 (*d*); 109.7 (*d*); 65.5 (*d*); 59.4 (*d*); 57.8 (*s*); 41.2 (*t*); 40.3 (*t*); 25.6 (*d*); 23.5 (*q*); 21.8 (*q*). MS: 287 (65, M^+), 243 (49), 199 (20), 185 (11), 158 (44), 142 (100), 127 (46), 117 (21), 98 (41), 84 (40).

(2′S,3S,5′S)-1,2-Dihydro-2′-(2-methylpropyl)-2-oxo-1′-(trifluoroacetyl)spiro[3H-indole-3,3′-pyrrolidine]-5′-carbonitrile ((−)-**11**). To a soln. of 90 mg (0.30 mmol) of (−)-**10** and 0.17 ml of pyridine in 15 ml of 1,4-dioxane were added 0.1 ml (0.74 mmol) of $(CF_3CO)_2O$ with efficient stirring at 10°. After 30 min, 1 ml of H_2O was added and the mixture worked up as usual. The crude material was chromatographed (10 g of silica gel, AcOEt/p.e. 1:9 → 1:1): 82 mg (75%) of (−)-**11**. Colorless oil. $[\alpha]_D = -114.7$ ($c = 1.8$, MeOH). IR ($CHCl_3$): 3410, 2955, 1720, 1706, 1616, 1468, 1424, 1328, 1153. ^{1}H-NMR (300 MHz, $CDCl_3$): 9.06 (br. *s*, 1 H); 7.36 (*d*, $J = 7.7$, 1 H); 7.35 (*dd*, $J = 7.7$, 1.3, 1 H); 7.13 (*t*, $J = 7.7$, 1 H); 5.24 (*t*, $J = 7.5$, 1 H); 4.76 (*dd*, $J = 11.5$, 4.1, 1 H); 2.90 (*m*, 2 H); 2.00–1.20 (*m*, 3 H); 1.10–0.80 (*m*, 6 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 180.5 (*s*); 156.1 (*s* (*q*, $J = 37$)); 141.3 (*s*); 130.1 (*s*); 129.9 (*d*); 125.2 (*d*); 122.9 (*d*); 118.4 (*s*); 116.4 (*s* (*q*, $J = 288$)); 110.9 (*d*); 62.7 (*d*); 54.1 (*s*); 45.0 (*d*); 40.0 (*t*); 38.6 (*t*); 24.7 (*d*); 23.5 (*q*); 21.7 (*q*). MS: 365 (10, M^+), 242 (11), 184 (12), 146 (100).

*Reductive Decyanation of (−)-***11**. *General Procedure B*, applied to 60 mg (0.16 mmol) of (−)-**11**, produced a mixture that was chromatographed (10 g of silica gel, AcOEt containing 0 to 5% of Et_3N): 16 mg (40%) of (±)-**12** and 8 mg (20%) of the less polar (±)-**13**.

Data of 6-Deoxyelacomine (= *(2′RS,3SR)-2′-(2-Methylpropyl)spiro[3H-indole-3,3′-pyrrolidin]-2(1H)-one*; (±)-**12**): Colorless oil. $[\alpha]_D = \pm 0$ ($c = 1.8$, MeOH). IR ($CHCl_3$): 3420, 2950, 1695 (br.), 1615, 1462, 1340, 903. ^{1}H-NMR (300 MHz, $CDCl_3$): 9.10 (br. *s*, 1 H); 7.24 (*m*, 2 H); 7.07 (*td*, $J = 7.5$, 1.0, 1 H); 6.96 (*dd*, $J = 8.2$, 1.0, 1 H); 3.54 (*ddd*, $J = 11.9$, 8.2, 6.6, 1 H); 3.45 (*dd*, $J = 10.0$, 3.6, 1 H); 3.37 (*ddd*, $J = 11.9$, 9.1, 5.9, 1 H); 2.34 (*ddd*, $J = 12.5$, 8.2, 5.9, 1 H); 2.31 (*ddd*, $J = 12.5$, 9.1, 6.6, 1 H); 1.63 (*m*, 1 H); 1.47 (*ddd*, $J = 13.8$, 10.0, 4.9, 1 H); 0.95 (*ddd*, $J = 13.8$, 9.1, 3.6, 1 H); 0.78 (*d*, $J = 6.6$, 3 H); 0.75 (*d*, $J = 6.6$, 3 H). NOE[4]): 3.45 (H–C(4′)) → 7.21 (H–C(4)), 2.31 (H_{trans}–C(7′)), 1.47 and 0.95 (2 H–C(8′)), 0.75 (Me(11′)). ^{13}C-NMR (100 MHz, $CDCl_3$): 181.9 (*s*); 141.3 (*s*); 130.9 (*s*); 128.2 (*d*); 122.9 (*d*); 122.5 (*d*); 110.0 (*d*); 68.4 (*d*); 58.1 (*s*); 46.0 (*t*); 38.0 (*t*); 37.4 (*t*); 25.9 (*d*); 23.5 (*q*); 21.8 (*q*). MS: 244 (74, M^+), 229 (12), 130 (13), 117 (13), 99 (30), 84 (100).

Data of 6-Deoxyisoelacomine (= (2′RS,3RS)-2′-(2-Methylpropyl)spiro[3H-indole-3,3′-pyrrolidin]-2(1H)-one; (±)-**13**): Colorless crystals. M.p. 140–142° (CH_2Cl_2). $[\alpha]_D = \pm 0$ (c = 1.8, MeOH). IR ($CHCl_3$): 3420, 2940, 1705 (br.), 1614, 1462, 1328. ^{1}H-NMR (400 MHz, $CDCl_3$): 9.04 (br. *s*, 1 H); 7.22 (*td*, J = 7.7, 1.3, 1 H); 7.15 (*ddd*, J = 7.7, 1.1, 0.7, 1 H); 7.04 (*td*, J = 7.7, 1.0, 1 H); 6.95 (*dm*, J = 7.7, 1 H); 3.49 (*dd*, J = 9.0, 4.6, 1 H); 3.39 (*ddd*, J = 11.3, 8.3, 6.3, 1 H); 3.33 (*ddd*, J = 11.3, 9.2, 5.8, 1 H); 2.53 (*ddd*, J = 13.0, 9.2, 6.3, 1 H); 2.21 (br. *s*, 1 H); 2.07 (*ddd*, J = 13.0, 8.3, 5.8, 1 H); 1.51 (*m*, 1 H); 1.04 (*ddd*, J = 13.9, 9.0, 5.8, 1 H); 0.87 (*ddd*, J = 13.9, 8.2, 4.6, 1 H); 0.79 (*d*, J = 6.6, 3 H); 0.75 (*d*, J = 6.6, 3 H). NOE[4]): 7.15 (H–C(4)) → 7.02 (H–C(5)), 3.39 (H_{trans}–C(6′)), 2.21 (H–N(5′)), 2.07 (H_{trans}–C(7′)), 1.04 and 0.87 (2 H–C(8′)); 3.49 (H–C(4′)) → 3.33 (H_{cis}–C(6′)), 2.53 (H_{cis}–C(7′)), 1.51 (H–C(9′)), 1.04 and 0.87 (2 H–C(8′)), 0.78 and 0.75 (2 Me); 2.53 (H_{cis}–C(7′)) → 3.49 (H–C(4′)), 3.33 (H_{cis}–C(6′)), 2.07 (H_{trans}–C(7′)); 2.07 (H_{trans}–C(7′)) → 7.15 (H–C(4)), 3.39 (H_{trans}–C(6′)), 2.53 (H_{cis}–C(7′)). ^{13}C-NMR (100 MHz, $CDCl_3$): 182.0 (*s*); 140.5 (*s*); 132.8 (*s*); 127.7 (*d*); 123.9 (*d*); 122.3 (*d*); 109.9 (*d*); 67.0 (*d*); 58.4 (*s*); 46.1 (*t*); 39.9 (*t*); 38.6 (*t*); 25.9 (*d*); 23.4 (*q*); 22.2 (*q*). MS: 244 (100, M^+), 229 (16), 187 (12), 159 (14), 146 (21), 130 (17), 117 (10), 99 (22), 84 (91), 56 (39).

(2′R,3R,5′S)-1,2-Dihydro-2′-(2-methylpropyl)-2-oxo-1′-(trifluoroacetyl)spiro[3H-indole-3,3′-pyrrolidine]-5′-carbonitrile ((+)-**14**). To a soln. of 180 mg (0.516 mmol) of (+)-**8** in 20 ml of CH_2Cl_2 were added 251 mg (0.567 mmol) of $Pb(OAc)_4$ at 0° with rapid stirring. After 4 h, 10 ml of MeOH and 4 ml of 2N HCl were added, and stirring was continued for 2 h at 25°. Standard workup and chromatography (10 g of silica gel, AcOEt/p.e. 1:4 → 1:1) furnished 90 mg (48%) of (+)-**14**. Amorphous. $[\alpha]_D$ = +8.0 (c = 1.0, MeOH). IR ($CHCl_3$): 3440, 2960, 2930, 1714, 1687, 1616, 1467, 1429, 1260, 1150. ^{1}H-NMR (400 MHz, $CDCl_3$): 9.04 (br. *s*, 1 H); 7.33 (*tm*, J = 7.5, 1 H); 7.18 (br. *d*, J = 7.7, 1 H); 7.07 (*t*, J = 7.7, 1 H); 7.02 (*d*, J = 7.7, 1 H); 5.01 (br. *m*, 1 H); 4.53 (br. *m*, 1 H); 2.85 (*dd*, J = 13.8, 9.4, 1 H); 2.73 (br. *m*, 1 H); 1.90 (br. *m*, 1 H); 1.52 (br. *m*, 1 H); 1.02 (*m*, 1 H); 0.83 (br. *d*, $J \approx$ 5.3, 3 H); 0.71 (*d*, J = 6.4, 3 H). NOE[4]): 7.18 (H–C(4)) → 5.01 (H–C(6′)), 2.85 (H_{trans}–C(7′)), 1.90 (H–C(9′)), 1.52 and 1.02 (2 H–C(8′)), 0.71 (Me(11′)); 5.01 (H–C(6′)) → 7.18 (H–C(4)), 2.85 (H_{trans}–C(7′)), 2.73 (H_{cis}–C(7′)). MS: 365 (5, M^+), 242 (39), 184 (24), 146 (100).

(S)-1,2,3,4-Tetrahydro-1-(2-methylpropyl)-9H-pyrido[3,4-b]indole ((−)-**15**). *General Procedure B*, starting with 1.50 g (4.3 mmol) of (+)-7, furnished 679 mg (69%) of (−)-**15**. M.p. 125–127° (AcOEt). $[\alpha]_D$ = −76.9 (c = 1.1, MeOH); optical purity ≥ 95% (*General Procedure C*). IR ($CHCl_3$): 3460, 2945, 2920, 1458. H-NMR (300 MHz, $CDCl_3$): 7.79 (br. *s*, 1 H); 7.50 (*dd*, J = 7.4, 1.6, 1 H); 7.31 (*dd*, J = 7.3, 1.0, 1 H); 7.16 (*ddd*, J = 7.5, 7.1, 1.5, 1 H); 7.11 (*ddd*, J = 7.3, 7.1, 1.2, 1 H); 4.12 (*ddt*, J = 8.0, 5.8, 1.8, 1 H); 3.36 (*dt*, J = 12.8, 4.6, 1 H); 3.04 (*ddd*, J = 12.8, 7.6, 5.8, 1 H); 2.75 (*m*, 2 H); 2.00 (*m*, 1 H); 1.63 (*m*, 3 H); 1.05 (*d*, J = 6.6, 3 H); 1.02 (*d*, J = 6.6, 3 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 136.8 (*s*); 135.6 (*s*); 127.6 (*s*); 121.5 (*d*); 119.4 (*d*); 118.0 (*d*); 110.7 (*d*); 108.8 (*s*); 50.5 (*d*); 44.5 (*t*); 42.5 (*t*); 24.6 (*d*); 23.9 (*q*); 22.8 (*t*); 21.8 (*q*). MS: 228 (19, M^+), 172 (16), 171 (100).

(R)-1,2,3,4-Tetrahydro-1-(2-methylpropyl)-9H-pyrido[3,4-b]indole ((+)-**15**). As above, starting with (+)-**8**. Yield 63%. $[\alpha]_D$ = +83.4 (c = 1.1, MeOH).

(S)-2-(Benzyloxycarbonyl)-1,2,3,4-tetrahydro-1-(2-methylpropyl)-9H-pyrido[3,4-b]indole ((+)-**16**). To a soln. of 597 mg (2.61 mmol) of (−)-**15** and 1.09 ml of Et_3N in 25 ml of CH_2Cl_2 were added 0.54 ml (3.71 mmol) of benzyl chloroformate at −10°. After stirring for 75 min at 25°, the mixture was worked up as usual and the crude product chromatographed (30 g of silica gel, AcOEt/p.e. 1:9 → 1:4): 880 mg (93%) of (+)-**16**. $[\alpha]_D$ = +59.2 (c = 1.1, MeOH). IR ($CHCl_3$): 3450, 1681, 1460, 1442, 1418, 1245, 1089. ^{1}H-NMR (300 MHz, $CDCl_3$) and ^{13}C-NMR (75 MHz, $CDCl_3$): severe line broadening and doubling of certain signals. FAB-MS: 363 (31, $M^+ + 1$), 319 (11), 305 (33), 271 (52), 261 (14), 169 (13), 109 (11), 107 (16), 91 (100), 77 (14).

*Oxidative Rearrangement of (+)-***16**. To a soln. of 468 mg (1.29 mmol) of (+)-**16** in 30 ml of THF/AcOH/H_2O 1:1:1 were added 253 mg of *N*-bromosuccinimide (NBS). After stirring vigorously in the dark for 2 h at 25°, the mixture was worked up as usual and the crude product chromatographed (100 g of silica gel, AcOEt/p.e. 1:4 → 1:1): 280 mg (57%) of (+)-**17** and 148 mg (30%) of (+)-**18**.

Data of (2′S,3R)-1′-(Benzyloxycarbonyl)-2′-(2-methylpropyl)spiro[3H-indole-3,3′-pyrrolidin]-2(1H)-one ((+)-**17**). Colorless oil. $[\alpha]_D$ = +7.1 (c = 1.6, MeOH). IR ($CHCl_3$): 3420, 2945, 1715, 1686, 1613, 1462, 1445, 1407, 1352, 1328, 1109. ^{1}H-NMR (300 MHz, $CDCl_3$): 8.84 (br. *s*, 1 H); 7.45–7.25 (*m*, 5 H); 7.21 (*m*, 1 H); 6.98 (*m*, 2 H); 6.90 (*dm*, J = 7.7, 1 H); 5.20 (*m*, 2 H); 4.18 (*m*, 0.5 H); 4.02 (*m*, 0.5 H); 3.88 (*m*, 2 H); 2.51 (*m*, 1 H); 2.06 (*m*, 1 H); 1.86 (*m*, 2 H); 1.31 (*m*, 1 H); 0.79 (br. *s*, 3 H); 0.72 (br. *s*, 3 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 178.7 (br. *s*); 155.0 (*s*); 139.5 (*s*); 136.9 (br. *s*); 134.0 (br. *s*); 128.3 (3 br. *d*); 128.1 (*d*); 123.1 (*d*); 122.5 (*d*); 109.8 (*d*); 67.1 (br. *t*); 63.7 (*d*); 55.7 (*s*); 44.6 (*t*); 39.9 (br. *t*); 34.7 (br. *t*); 25.2 (*d*); 22.9 (br. *q*); 22.3 (*q*). MS: 378 (7, M^+), 243 (8), 160 (9), 98 (25), 91 (100).

Data of (2′S,3S)-1′-(Benzyloxycarbonyl)-2′-(2-methylpropyl)spiro[3H-indole-3,3′-pyrrolidin]-2(1H)-one ((+)-**18**). Colorless oil. $[\alpha]_D$ = +22.6 (c = 1.3, MeOH). IR ($CHCl_3$): 3420, 2945, 2980, 2860, 1715 (br.), 1682 (br.), 1613, 1462, 1445, 1400, 1350, 1326, 1306, 997. ^{1}H-NMR (300 MHz, $CDCl_3$): 9.04 (br. *s*, 1 H); 7.45–7.25 (*m*, 5 H);

7.23 (*m*, 2 H); 7.04 (*ddd*, *J* = 8.0, 7.5, 1.0, 1 H); 6.93 (*dd*, *J* = 8.5, 1.1, 1 H); 5.24 (*d*, *J* = 12.4, 1 H); 5.13 (*d*, *J* = 12.4, 1 H); 4.29 (*m*, 1 H); 4.09 (*m*, 1 H); 3.66 (*dt*, *J* = 11.2, 7.5, 1 H); 2.33 (*dt*, *J* = 12.5, 8.2, 1 H); 2.08 (*ddd*, *J* = 12.5, 7.5, 5.0, 1 H); 1.70 (*m*, 1 H); 1.35 (*ddd*, *J* = 13.5, 8.4, 5.2, 1 H); 1.05 (*m*, 1 H); 0.80 (br. *s*, 3 H); 0.60 (br. *s*, 3 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 180.9 (*s*); 155.7 (*s*); 140.8 (*s*); 136.8 (br. *s*); 129.6 (*s*); 128.5 (3 br. *d*); 128.0 (*d*); 125.1 (*d*); 122.2 (*d*); 110.3 (*d*); 67.1 (br. *t*); 61.5 (br. *d*); 56.8 (br. *s*); 45.7 (br. *t*); 40.8 (br. *t*); 35.5 (*t*); 24.7 (*d*); 23.2 (*q*); 21.9 (*q*). MS: 378 (9, M^+), 243 (6), 189 (7), 174 (8), 160 (12), 98 (23), 91 (100).

*Deprotection of (+)-***17**. To a soln. of 402 mg (1.06 mmol) of (+)-**17** in 40 ml of MeOH were added 40 mg of 10% Pd/C. The mixture was stirred vigorously under H_2 at 1 bar for 3 h and then filtered through *Celite*®. The filtrate was evaporated and the residue chromatographed (20 g of silica gel, AcOEt containing 0–50% of MeOH); 240 mg (93%) of (±)-**12**/(±)-**13** 2:1. For spectroscopic data, see above.

*(*RS*)-1,2,3,4-Tetrahydro-7-methoxy-1-(2-methylpropyl)-9*H*-pyrido[3,4-*b*]indole* ((±)-**20**). To a soln. of 200 mg (1.05 mmol) of 6-methoxytryptamine (**19**; *Aldrich*) in 20 ml of MeOH were added 0.14 ml (1.26 mmol) of 3-methylbutanal and then 0.4 ml (3.15 mmol) of Me_3SiCl at −10°. After stirring for 1 h at 25°, the mixture was evaporated and the residue worked up as usual. The crude product was chromatographed (10 g of silica gel, AcOEt/Et_3N 20:1): 120 mg (44%) of (±)-**20**. M.p. 148–150° (CH_2Cl_2). IR ($CHCl_3$): 3465, 2950, 2920, 2860, 2835, 1650, 1495, 1460, 1437, 1342, 1286, 1260, 1150, 1030. ^{1}H-NMR (400 MHz, $CDCl_3$ + 0.05 ml of CD_3OD): 8.40 (br. *s*, 1 H); 7.33 (*d*, *J* = 8.6, 1 H); 6.84 (*d*, *J* = 2.2, 1 H); 6.75 (*dd*, *J* = 8.6, 2.2, 1 H); 4.10 (*ddm*, *J* = 8.7, 5.0, 1 H); 3.83 (*s*, 3 H); 3.33 (*dt*, *J* = 12.7, 4.7, 1 H); 3.00 (*ddd*, *J* = 12.7, 8.0, 5.5, 1 H); 2.75–2.65 (*m*, 3 H); 1.94 (*m*, 1 H); 1.66 (*ddd*, *J* = 13.9, 8.5, 5.0, 1 H); 1.61 (*ddd*, *J* = 13.9, 8.7, 5.5, 1 H); 1.02 (*d*, *J* = 6.5, 3 H); 1.00 (*d*, *J* = 6.5, 3 H). ^{13}C-NMR (100 MHz, $CDCl_3$ + 0.05 ml of CD_3OD): 156.1 (*s*); 136.5 (*s*); 134.8 (*s*); 122.0 (*s*); 118.5 (*d*); 108.6 (*d*); 108.0 (*s*); 95.2 (*d*); 55.9 (*q*); 50.5 (*d*); 44.1 (*t*); 42.2 (*d*); 24.6 (*d*); 23.8 (*q*); 22.3 (*t*); 21.8 (*q*). MS: 258 (5, M^+), 212 (10), 202 (15), 201 (100), 186 (13).

*(*RS*)-2-(Benzyloxycarbonyl)-7-[(benzyloxycarbonyl)oxy]-1,2,3,4-tetrahydro-1-(2-methylpropyl)-9*H*-pyrido-[3,4-*b*]indole* ((±)-**21**). To a soln. of 170 mg (0.66 mmol) of (±)-**20** in 15 ml of CH_2Cl_2 were added dropwise 1.7 ml of 1M BBr_3 in CH_2Cl_2 at 25°. After stirring for 12 h, there were added 2 ml of MeOH, and the mixture was worked up as usual. The resulting hydrobromide salt (186 mg, 87%) was dissolved in 20 ml of CH_2Cl_2 containing 0.39 ml (2.77 mmol) of Et_3N, then 0.22 ml (1.38 mmol) of benzyl chloroformate were added, and stirring was continued for 40 min. Standard workup followed by chromatography (10 g of silica gel, AcOEt/p.e./Et_3N 10:40:1) furnished 180 mg (63%) of (±)-**21**. Colorless oil. $[\alpha]_D$ = +22.3 (*c* = 2.3, CH_2Cl_2). IR ($CHCl_3$): 3460, 3350, 2950, 2860, 1745, 1680, 1626, 1492, 1420, 1378, 1147, 1090, 1040, 1023, 940, 910. ^{1}H- and ^{13}C-NMR: very complex due to the presence of different rotamers. FAB-MS: 513 (22, $[M + 1]^+$), 512 (33), 455 (12), 377 (14), 289 (11), 123 (13), 107 (25), 91 (100).

*Oxidative Rearrangement of (±)-***21**. To a soln. of 159 mg (0.31 mmol) of (±)-**21** in 18 ml of THF/AcOH/H_2O 1:1:1 were added 61 mg (0.34 mmol) of NBS. After stirring for 150 min at 25° in the dark, the mixture was worked up as usual. Chromatography (20 g of silica gel, AcOEt/p.e. 1:4→1:1) of the crude material gave 77 mg (47%) of doubly protected (±)-**2** and 41 mg (25%) of doubly protected (±)-**22**. The protecting groups of both components were removed separately by catalytic hydrogenation as described above to give (±)-**2** and (±)-**22**, resp.

*Data of (±)-Elacomine (= (2'*RS*,3*SR*)-6-Hydroxy-2'-(2-methylpropyl)spiro[3*H*-indole-3,3'-pyrrolidin]-2(1*H*)-one*; (±)-**2**). M.p.: sublimation at *ca.* 180° in an evacuated capillary; dec. at *ca.* 200° under Ar ([1]: 250–252°). IR (KBr): 3250, 2950, 1690, 1630, 1561, 1467, 1348, 1159, 1109, 845 ([1]: 3420, 3225, 2450, 1710, 1670, 1630, 1495, 1160, 1105, 825). ^{1}H-NMR (400 MHz, (D_6)DMSO): 10.11 (*s*, 1 H); 9.60 (br. *s*, 1 H); 7.00 (*d*, *J* = 8.0, 1 H); 6.33 (*dd*, *J* = 8.0, 2.2, 1 H); 6.29 (*d*, *J* = 2.2, 1 H); 3.32 (br. *s*, 1 H); 3.17 (*ddd*, *J* = 11.5, 8.4, 5.4, 1 H); 2.99 (*dd*, *J* = 9.7, 3.8, 1 H); 2.96 (*ddd*, *J* = 11.5, 9.0, 6.2, 1 H); 2.06 (*ddd*, *J* = 12.8, 8.4, 6.2, 1 H); 1.98 (*ddd*, *J* = 12.8, 9.0, 5.4, 1 H); 1.50 (*m*, 1 H); 1.18 (*ddd*, *J* = 13.5, 9.7, 5.4, 1 H); 0.79 (*ddd*, *J* = 13.5, 8.5, 3.8, 1 H); 0.74 (*d*, *J* = 6.7, 3 H); 0.67 (*d*, *J* = 6.6, 3 H) ([1]: ^{1}H-NMR (100 MHz, (D_6)DMSO, see *Fig.*): 10.02 (*s*, 1 H); 6.99 (*d*, *J* = 8.0, 1 H); 6.31 (*d*, 2 H); 3.08 (*d*, 2 H); 3.08 (*m*, 2 H); 2.02 (*t*, 2 H); 0.73 (*t*, *J* = 7.0, 6 H)). ^{1}H-NMR (400 MHz, CD_3OD): 7.00 (*d*, *J* = 8.1, 1 H); 6.49 (*dd*, *J* = 8.1, 2.2, 1 H); 6.42 (*d*, *J* = 2.2, 1 H); 3.37 (*ddd*, *J* = 11.8, 8.7, 5.9, 1 H); 3.18 (*dd*, *J* = 9.2, 4.3, 1 H); 3.12 (*ddd*, *J* = 11.8, 9.4, 5.9, 1 H); 2.27 (*ddd*, *J* = 13.3, 8.7, 5.9, 1 H); 2.18 (*ddd*, *J* = 13.3, 9.4, 5.9, 1 H); 1.52 (*m*, 1 H); 1.35 (*ddd*, *J* = 13.8, 9.2, 5.4, 1 H); 0.97 (*ddd*, *J* = 13.8, 8.9, 4.3, 1 H); 0.77 (*d*, *J* = 6.6, 3 H); 0.74 (*d*, *J* = 6.6, 3 H). NOE (300 MHz, (D_6)DMSO[4]): 7.00 (H–C(4))→6.33 (H–C(5)), 2.99 (H–C(4')), 2.96 (H_{trans}–C(7')). ^{13}C-NMR (100 MHz, (D_6)DMSO): 181.6 (*s*); 156.9 (*s*); 143.0 (*s*); 122.7 (*d*); 121.9 (*s*); 107.9 (*d*); 97.3 (*d*); 68.3 (*d*); 56.9 (*s*); 45.9 (*t*); 38.1 (*t*); 37.7 (*t*); 25.4 (*d*); 23.3 (*q*); 21.8 (*q*). ^{13}C-NMR (100 MHz, CD_3OD): 184.0 (*s*); 158.3 (*s*); 143.7 (*s*); 123.6 (*d*); 122.5 (*s*); 109.7 (*d*); 99.0 (*d*); 68.2 (*d*); 58.5 (*s*); 46.2 (*t*); 39.2 (*t*); 38.1 (*t*); 26.2 (*d*); 23.7 (*q*); 22.1 (*q*). MS: 260 (92, M^+), 245 (14), 175 (23), 162 (17), 146 (12), 99 (21), 84 (100), 56 (57) ([1]: 260 (49, M^+), 245 (6), 175 (12), 162 (11), 99 (20), 84 (100), 56 (87)).

Data of (±)-Isoelacomine (= (2'RS,3RS)-6-Hydroxy-2'-(2-methylpropyl)spiro[3H-indole-3,3'-pyrrolidin]-2(1H)-one; (±)-**22**). Colorless oil that has to be stored at −20° to prevent decomposition ([18]: m.p. 250–252°). $[\alpha]_D = \pm 0$ (c = 1.8, MeOH). IR (KBr): 3240, 2950, 1702, 1630, 1502, 1466, 1388, 1156, 1114, 960, 840 ([18]: 1680). ^{1}H-NMR (300 MHz, (D$_6$)DMSO): 10.22 (*s*, 1 H); 9.40 (br. *s*, 1 H); 7.06 (*d*, J = 8.7, 1 H); 6.32 (*d*, J = 2.3, 1 H); 6.31 (*dd*, J = 8.7, 2.3, 1 H); 3.44 (br. *s*, 1 H); 3.20 (*ddd*, J = 10.9, 8.2, 6.5, 1 H); 3.12 (*dd*, J = 8.5, 5.0, 1 H); 2.97 (*ddd*, J = 10.9, 9.2, 5.6, 1 H); 2.17 (*ddd*, J = 12.5, 9.2, 6.5, 1 H); 1.77 (*ddd*, J = 12.5, 8.2, 5.6, 1 H); 1.37 (*m*, 1 H); 0.97 (*ddd*, J = 13.7, 8.5, 6.2, 1 H); 0.72 (*d*, J = 6.6, 3 H); 0.69 (*m*, 1 H); 0.65 (*d*, J = 6.6, 3 H). ^{1}H-NMR (300 MHz, $CDCl_3/CD_3OD$ *ca.* 10:1): 6.77 (*d*, J = 8.1, 1 H); 6.30 (*dd*, J = 8.1, 2.2, 1 H); 6.26 (*d*, J = 2.2, 1 H); 3.25–3.10 (*m*, 3 H); 2.23 (*ddd*, J = 13.0, 9.0, 6.7, 1 H); 1.82 (*ddd*, J = 13.0, 8.0, 5.6, 1 H); 1.23 (*m*, 1 H); 0.90 (*ddd*, J = 13.9, 8.2, 6.2, 1 H); 0.70 (*ddd*, J = 13.9, 7.8, 5.5, 1 H); 0.60 (*d*, J = 6.5, 3 H); 0.54 (*d*, J = 6.5, 3 H). ^{13}C-NMR (75 MHz, (D$_6$)DMSO): 180.9 (*s*); 156.9 (*s*); 142.2 (*s*); 124.6 (*d*); 122.6 (*s*); 107.6 (*d*); 97.4 (*d*); 65.9 (*d*); 56.9 (*s*); 45.3 (*t*); 39.4 (*t*); 38.8 (*t*); 25.1 (*d*); 23.0 (*q*); 22.3 (*q*). ^{13}C-NMR (75 MHz, $CDCl_3/CD_3OD$ 10:1): 182.4 (*s*); 156.9 (*s*); 141.7 (*s*); 124.2 (*d*); 122.7 (*s*); 108.6 (*d*); 98.2 (*d*); 65.7 (*d*); 57.6 (*s*); 45.4 (*t*); 39.7 (*t*); 38.4 (*t*); 25.2 (*d*); 22.7 (*q*); 21.8 (*q*). MS: 260 (34, M^+), 245 (8), 175 (18), 162 (12), 146 (9), 99 (21), 84 (100), 56 (45).

(S)-N-(Methoxycarbonyl)-6-(2-nitrobenzyloxy)tryptophan Methyl Ester ((+)-**25**). To a soln. of 2.6 g (8.9 mmol) of (+)-**24** in 70 ml of DMF were added 2.46 g of K_2CO_3, 164 mg (0.44 mmol) of Bu_4NI, and 1.68 g (9.79 mmol) of 2-nitrobenzyl chloride at 25° with rapid stirring. The mixture was stirred at 50° for 1 h and at 25° for 24 h, then 50 ml of AcOEt/petroleum ether 1:1 were added, and the formed precipitate (1.40 g (37%) of (+)-**25**) was removed by filtration. The filtrate was evaporated and the residue chromatographed (100 g of silica gel, AcOEt/p.e. 1:4→1:1): additional crop of (+)-**25** (790 mg (21%)). Yellow crystals. M.p. 155–157° (CH_2Cl_2). $[\alpha]_D$ = +21.6 (c = 0.8, THF). IR ($CHCl_3$): 3470, 3425, 3010, 2955, 2930, 1716, 1623, 1500 (br.), 1436, 1339, 1298, 1200, 1160, 1030. ^{1}H-NMR (400 MHz): 8.15 (*dd*, J = 8.2, 1.3, 1 H); 8.07 (br. *s*, 1 H); 7.94 (*dd*, J = 7.8, 1.0, 1 H); 7.66 (*ddd*, J = 7.8, 7.5, 1.3, 1 H); 7.47 (*ddd*, J = 8.2, 7.5, 1.4, 1 H); 7.42 (*d*, J = 9.0, 1 H); 6.88 (*dd*, J = 9.0, 2.3, 1 H); 6.86 (*d*, J = 2.3, 1 H); 5.49 (*s*, 2 H); 5.24 (*d*, J = 7.6, 1 H); 4.67 (*dt*, J = 7.6, 5.3, 1 H); 3.68 (*s*, 3 H); 3.66 (*s*, 3 H); 3.25 (*d*, J = 5.6, 2 H). ^{13}C-NMR (100 MHz): 172.5 (*s*); 156.5 (*s*); 155.1 (*s*); 146.9 (*s*); 136.8 (*s*); 134.4 (*s*); 134.0 (*d*); 128.7 (*d*); 128.2 (*d*); 124.9 (*d*); 122.5 (*s*); 121.9 (*d*); 119.4 (*d*); 110.4 (*d*); 110.0 (*s*); 96.1 (*d*); 67.3 (*t*); 54.4 (*d*); 52.4 (2*q*); 28.0 (*t*). MS: 427 (9, M^+), 395 (4), 291 (11), 281 (83), 259 (18), 146 (100), 136 (20), 117 (34), 89 (14), 78 (27).

(S)-6-(2-Nitrobenzyloxy)tryptophan Methyl Ester ((+)-**26**). To a suspension of 1.45 g (3.39 mmol) of (+)-**25** in 40 ml of CH_2Cl_2 were added dropwise 0.7 ml (5.09 mmol) of Me_3SiI. After refluxing for 20 min, the mixture became homogeneous and slightly green and after 2 h, additional 0.35 ml (2.55 mmol) of Me_3SiI were added. After 1 h, the mixture was cooled to 25°, and 4 ml of MeOH were added. After stirring for 20 min, the mixture was worked up normally and the crude product chromatographed (40 g of silica gel, AcOEt/MeOH 5:1): 1.205 g (88%) of (+)-**26**. Yellow oil. $[\alpha]_D$ = +19.9 (c = 0.8, MeOH). IR ($CHCl_3$): 3470, 2950, 2930, 1730, 1626, 1522, 1496, 1342, 1300, 1156. ^{1}H-NMR (300 MHz): 8.18 (br. *s*, 1 H); 8.16 (*dd*, J = 8.2, 1.3, 1 H); 7.94 (*dd*, J = 7.8, 1.0, 1 H); 7.66 (*ddd*, J = 7.8, 7.5, 1.2, 1 H); 7.50 (*d*, J = 9.2, 1 H); 7.47 (*ddd*, J = 8.2, 7.5, 1.5, 1 H); 6.95 (*d*, J = 2.2, 1 H); 6.89 (*dd*, J = 9.2, 2.3, 1 H); 6.88 (*d*, J = 2.3, 1 H); 5.50 (*s*, 2 H); 3.82 (*dd*, J = 7.6, 4.8, 1 H); 3.72 (*s*, 3 H); 3.24 (*ddd*, J = 14.4, 4.8, 0.7, 1 H); 3.02 (*dd*, J = 14.4, 7.6, 1 H). ^{13}C-NMR (75 MHz): 175.8 (*s*); 155.0 (*s*); 147.0 (*s*); 136.9 (*s*); 134.4 (*s*); 134.0 (*d*); 128.7 (*d*); 128.2 (*d*); 124.9 (*d*); 122.5 (*s*); 122.1 (*d*); 119.6 (*d*); 111.2 (*d*); 110.2 (*d*); 96.1 (*d*); 67.3 (*t*); 55.0 (*d*); 52.0 (*q*); 30.8 (*t*). MS: 369 (5, M^+), 281 (56), 174 (11), 146 (100), 136 (12), 117 (35), 78 (35).

Pictet-Spengler *Condensation between (+)-***26** *and 3-Methylbutanal.* To a soln. of 1.105 g (2.99 mmol) of (+)-**26** in 70 ml of CH_2Cl_2 were added 0.97 ml (8.98 mmol) of 3-methylbutanal and 0.69 ml (8.98 mmol) of CF_3COOH at 25°. After stirring for 4 h, the mixture was worked up as usual, and the two products were separated by chromatography (100 g of silica gel, AcOEt/p.e. 1:4→1:1): 750 mg (57%) of (−)-**28**, 210 mg (16%) of (+)-**27**, and 310 mg (24%) of (−)-**28**/(+)-**27**.

Data of (1R,3S)-Methyl 1,2,3,4-Tetrahydro-1-(2-methylpropyl)-7-(2-nitrobenzyloxy)-9H-pyrido[3,4-b]indole-3-carboxylate ((+)-**27**): Yellow oil. $[\alpha]_D$ = +28.9 (c = 1.5, MeOH). IR ($CHCl_3$): 3460, 2950, 2920, 2865, 1732 (br.), 1627, 1521, 1490, 1464, 1434, 1340, 1304, 1150. ^{1}H-NMR (300 MHz): 8.16 (*dd*, J = 8.2, 1.2, 1 H); 7.94 (*d*, J = 7.8, 1 H); 7.75 (*s*, 1 H); 7.66 (*ddd*, J = 7.8, 7.5, 1.2, 1 H); 7.47 (*ddd*, J = 8.2, 7.5, 1.4, 1 H); 7.36 (*d*, J = 9.0, 1 H); 6.87 (*d*, J = 2.2, 1 H); 6.85 (*dd*, J = 9.0, 2.2, 1 H); 5.50 (*s*, 2 H); 4.25 (*dd*, J = 9.9, 4.1, 1 H); 3.96 (*dd*, J = 7.4, 5.3, 1 H); 3.76 (*s*, 3 H); 3.07 (*dd*, J = 15.3, 5.3, 1 H); 2.94 (*ddd*, J = 15.3, 7.4, 1.3, 1 H); 2.13 (*m*, 1 H); 1.93 (*m*, 1 H); 1.69 (*ddd*, J = 13.8, 9.9, 4.8, 1 H); 1.49 (*ddd*, J = 13.8, 9.4, 4.1, 1 H); 1.02 (*d*, J = 7.4, 3 H); 0.99 (*d*, J = 6.8, 3 H). ^{13}C-NMR (75 MHz): 174.3 (*s*); 154.6 (*s*); 146.9 (*s*); 136.4 (*s*); 135.2 (*s*); 134.5 (*s*); 134.0 (*d*); 128.7 (*d*); 128.1 (*d*); 124.9 (*d*); 122.2 (*s*); 118.7 (*d*); 109.5 (*d*); 106.7 (*s*); 96.3 (*d*); 67.4 (*t*); 52.4 (*d*); 52.2 (*q*); 48.1 (*d*); 44.6 (*t*); 25.0 (*t*); 24.7 (*d*); 23.7 (*q*); 21.7 (*q*). MS: 437 (22, M^+), 380 (100), 302 (14), 245 (86), 199 (11), 185 (39), 156 (11), 121 (13), 78 (11).

*Data of (1S,3S)-Methyl 1,2,3,4-Tetrahydro-1-(2-methylpropyl)-7-(2-nitrobenzyloxy)-9*H*-pyrido[3,4-*b*]indole-3-carboxylate* ((−)-**28**): Yellow oil. $[\alpha]_D = -69.8$ ($c = 1.25$, MeOH). IR ($CHCl_3$): 3460, 2950, 2930, 1725 (br.), 1628, 1522, 1495, 1464, 1436, 1367, 1340, 1304, 1154. ^{1}H-NMR (300 MHz): 8.15 (*dd*, $J = 8.2, 1.2$, 1 H); 7.93 (*dd*, $J = 7.9, 1.0$, 1 H); 7.76 (*s*, 1 H); 7.65 (*ddd*, $J = 7.9, 7.4, 1.3$, 1 H); 7.46 (*ddd*, $J = 8.2, 7.4, 1.5$, 1 H); 7.35 (*d*, $J = 8.2$, 1 H); 6.86 (*d*, $J = 2.3$, 1 H); 6.85 (*dd*, $J = 8.2, 2.3$, 1 H); 5.49 (*s*, 2 H); 4.17 (*m*, 1 H); 3.81 (*s*, 3 H); 3.75 (*dd*, $J = 11.1, 4.2$, 1 H); 3.07 (*ddd*, $J = 15.1, 4.2, 1.9$, 1 H); 2.77 (*ddd*, $J = 15.1, 11.1, 2.7$, 1 H); 1.98 (*m*, 1 H); 1.66 (*ddd*, $J = 13.9, 9.0, 4.6$, 1 H); 1.60 (*ddd*, $J = 13.9, 8.5, 5.3$, 1 H); 1.02 (*d*, $J = 6.5$, 3 H); 0.98 (*d*, $J = 6.6$, 3 H). ^{13}C-NMR (75 MHz): 173.8 (*s*); 154.6 (*s*); 147.0 (*s*); 136.5 (*s*); 135.3 (*s*); 134.5 (*s*); 134.0 (*d*); 128.7 (*d*); 128.1 (*d*); 124.9 (*d*); 122.4 (*s*); 118.7 (*d*); 109.7 (*d*); 107.7 (*s*); 96.4 (*d*); 67.5 (*t*); 56.5 (*d*); 52.2 (*q*); 50.6 (*d*); 44.5 (*t*); 26.0 (*t*); 24.4 (*d*); 23.8 (*q*); 21.8 (*q*). MS: 437 (12, M^+), 380 (100), 245 (53), 199 (13), 185 (39), 156 (11), 78 (22).

*(1S,3S)-1,2,3,4-Tetrahydro-1-(2-methylpropyl)-7-(2-nitrobenzyloxy)-9*H*-pyrido[3,4-*b*]indole-3-carboxamide* ((−)-**29**). A soln. of 750 mg (1.71 mmol) of (−)-**28** in 100 ml of MeOH was cooled to 0° and saturated with NH_3 (g). After stirring for 4 d at 25° in the dark, the solvent was evaporated to give 700 mg (97%) of (−)-**29**. Orange powder. M.p. 176–178° (AcOEt/p.e.). $[\alpha]_D = -108.3$ ($c = 0.8$, THF). ^{1}H-NMR ((D_6)DMSO, 400 MHz): 10.55 (*s*, 1 H); 8.11 (*dd*, $J = 8.2, 1.1$, 1 H); 7.83 (*dd*, $J = 7.7, 1.1$, 1 H); 7.77 (*ddd*, $J = 7.7, 7.4, 1.1$, 1 H); 7.60 (*ddd*, $J = 8.2, 7.4, 1.4$, 1 H); 7.32 (br. *s*, 1 H); 7.26 (*d*, $J = 8.5$, 1 H); 7.08 (br. *s*, 1 H); 6.85 (*d*, $J = 2.3$, 1 H); 6.70 (*dd*, $J = 8.5, 2.3$, 1 H); 5.44 (*s*, 2 H); 4.00 (br. *d*, $J = 6.3$, 1 H); 3.34 (*m*, 1 H); 2.87 (*ddd*, $J = 15.0, 4.2, 1.7$, 1 H); 2.50 (*ddd*, $J = 15.0, 11.2, 2.5$, 1 H); 2.00 (*m*, 1 H); 1.94 (br. *s*, 1 H); 1.81 (*ddd*, $J = 13.5, 9.9, 3.0$, 1 H); 1.42 (*ddd*, $J = 13.5, 10.4, 4.0$, 1 H); 0.98 (*d*, $J = 6.5$, 3 H); 0.93 (*d*, $J = 6.7$, 3 H). NOE (300 MHz, (D_6)DMSO): irrad. 4.00 (H–C(1)) → 3.34 (H–C(3)), 2.00 (H–C(2′)), 1.81 (H_A–C(1′)), 1.42 (H_B–C(1′)), 0.98 (Me(3′)). ^{13}C-NMR ((D_6)DMSO, 100 MHz): 175.0 (*s*); 153.5 (*s*); 147.5 (*s*); 136.6 (*s*); 136.3 (*s*); 133.8 (*d*); 133.1 (*s*); 129.2 (*d*); 128.9 (*d*); 124.7 (*d*); 122.1 (*s*); 117.9 (*d*); 108.4 (*d*); 106.7 (*s*); 96.4 (*d*); 66.8 (*t*); 56.9 (*d*); 50.5 (*d*); 43.3 (*t*); 25.7 (*t*); 24.0 (*q*); 23.7 (*d*); 21.5 (*q*). MS: 422 (1, M^+), 365 (9), 241 (26), 230 (35), 198 (26), 185 (100), 172 (17), 156 (14), 92 (19), 77 (19).

*(S)-2-(Benzyloxycarbonyl)-1,2,3,4-tetrahydro-1-(2-methylpropyl)-7-(2-nitrobenzyloxy)-9*H*-pyrido[3,4-*b*]indole* ((+)-**30**). *General Procedure A*, starting with 700 mg (1.66 mmol) of (−)-**28**, furnished 760 mg (92%) of the corresponding nitrile. A portion of this material (700 mg, 1.40 mmol) was subjected to *General Procedure B* to give 300 mg (57%) of the decyano derivative which was transformed into (+)-**30** as follows: to a soln. of 250 mg (0.66 mmol) thereof in 30 ml of CH_2Cl_2 were added 0.27 ml (1.98 mmol) of Et_3N and 0.15 ml (0.99 mmol) of benzyl chloroformate. After stirring for 20 min at 25°, the yellow mixture was worked up as usual and the crude product purified by chromatography (40 g of silica gel, AcOEt/p.e. 1:4): 310 mg (92%) of (+)-**30**. Yellow oil. $[\alpha]_D = +50.1$ ($c = 1.15$, MeOH). IR ($CHCl_3$): 3460, 2950, 2920, 1685, 1630, 1577, 1521, 1492, 1468, 1420, 1341, 1152, 1090, 1020. ^{1}H-NMR (400 MHz): 8.14 (*d*, $J = 8.2$, 1 H); 7.91 (*d*, $J = 7.8$, 1 H); 7.74 (*s*, 0.5 H); 7.68 (*s*, 0.5 H); 7.64 (*dd*, $J = 7.8, 7.5$, 1 H); 7.45 (*dd*, $J = 8.2, 7.4$, 1 H); 7.35 (*m*, 5 H); 7.30 (*m*, 1 H); 6.84 (*m*, 2 H); 5.48 (*s*, 2 H); 5.41 (*m*, 0.5 H); 5.20 (*m*, 2 H); 5.12 (*m*, 0.5 H); 4.49 (*dd*, $J = 13.3, 5.3, 0.5$ H); 4.35 (*dd*, $J = 13.4, 5.1, 0.5$ H); 3.19 (*m*, 1 H); 2.82 (*m*, 1 H); 2.63 (*m*, 1 H); 1.75 (*m*, 2 H); 1.51 (*m*, 1 H); 1.07 (*d*, $J = 6.2, 1.5$ H); 0.97 (*d*, $J = 6.2, 1.5$ H); 0.90 (*d*, $J = 6.1$, 3 H). MS: 513 (6, M^+), 456 (16), 422 (10), 287 (10), 185 (20), 91 (100), 78 (12).

*Oxidative Rearrangement of (+)-***30**. To a soln. of 280 mg (0.546 mmol) of (+)-**30** in 15 ml of THF/AcOH/H_2O 1:1:1 were added 102 mg (0.573 mmol) of NBS at −10°. Stirring in the dark was continued for 1 h at −10° and for 3 h at 25°. Standard workup, followed by chromatography (40 g of silica gel, AcOEt/p.e. 1:4 → 1:1) furnished 110 mg (38%) of doubly protected elacomine as a colorless oil ($[\alpha]_D = -3.3$ ($c = 1.0$, MeOH)) and 80 mg (28%) of doubly protected isoelacomine as a colorless oil ($[\alpha]_D = +31.5$ ($c = 1.0$, MeOH)). Both samples were deprotected separately (1 bar of H_2, 10% Pd/C, MeOH, 2 h at 25°) to furnish (+)-**2** (83%) and (−)-**22** (71%), resp.

Data of (+)-Elacomine (= *(3*R*,2′*S*)-6-Hydroxy-2′-(2-methylpropyl)spiro[3*H*-indole-3,3′-pyrrolidin]-2(1*H*)-one*; (+)-**2**): $[\alpha]_D = +2.6$ ($c = 0.5$, MeOH); optical purity, determined by *General Procedure C*: *ca.* 76% e.e. NMR and MS: identical with the one obtained for (±)-**2** (see above).

Data of (−)-Isoelacomine (= *(3*S*,2′*S*)-6-Hydroxy-2′-(2-methylpropyl)spiro[3*H*-indole-3,3′-pyrrolidin]-2(1*H*)-one*; (−)-**22**): $[\alpha]_D = -15.5$ ($c = 1.4$, MeOH); optical purity estimated to be *ca.* 76% e.e. (see *Chapt. 3*). NMR and MS: identical with the one obtained for (±)-**22** (see above).

*Acetylation of (±)-***2**/*(±)-***22** *2:1*. To a soln. of 25 mg of (±)-**2**/(±)-**22** 2:1 in 1 ml of pyridine was added 1 ml of Ac_2O at 25°. After stirring at 25° for 12 h, the mixture was diluted with toluene (2 × 3 ml) and evaporated twice. The residue was worked up as usual and then chromatographed (20 g of silica gel, AcOEt/p.e. 1:4 → 1:1): 20 mg (54%) of (±)-**31** and 8 mg (22%) of (±)-**32**.

Data of (±)-Triacetylelacomine (= *(2′*RS*,3*SR*)-6-Acetoxy-1,3′-diacetyl-2′-(2-methylpropyl)spiro[3*H*-indole-3,3′-pyrrolidin]-2(1*H*)-one*; (±)-**31**): Yellow oil. ^{1}H-NMR (400 MHz): 8.01 (*d*, $J = 2.2$, 1 H); 7.12 (*d*, $J = 8.2$, 1 H); 6.95 (*dd*, $J = 8.2, 2.2$, 1 H); 4.37 (*dd*, $J = 8.6, 5.0$, 1 H); 3.97 (*dt*, $J = 10.5, 7.8$, 1 H); 3.79 (*ddd*, $J = 10.5, 8.0, 5.6$, 1 H); 2.67 (*s*, 3 H); 2.53 (*ddd*, $J = 13.0, 7.8, 5.6$, 1 H); 2.31 (*s*, 3 H); 2.17 (*s*, 3 H); 2.16 (*ddd*, $J = 13.0, 8.0, 7.8$,

1 H); 1.77 (*ddd*, J = 13.8, 8.8, 5.0, 1 H); 1.69 (*ddd*, J = 13.8, 8.6, 4.9, 1 H); 1.38 (*m*, 1 H); 0.79 (*d*, J = 6.5, 3 H); 0.77 (*d*, J = 6.5, 3 H). ^{13}C-NMR (100 MHz): 177.4 (*s*); 170.5 (*s*); 169.4 (*s*); 169.0 (*s*); 150.7 (*s*); 139.2 (*s*); 129.3 (*s*); 122.4 (*d*); 119.1 (*d*); 111.1 (*d*); 64.3 (*d*); 55.1 (*s*); 46.1 (*t*); 39.2 (*t*); 36.9 (*t*); 26.7 (*q*); 25.7 (*d*); 23.2 (2*q*); 21.8 (*q*); 21.0 (*q*).

Data of (±)-Triacetylisoelacomine (= (2'RS,3RS)-6-Acetoxy-1,3'-diacetyl-2'-(2-methylpropyl)spiro[3H-indole-3,3'-pyrrolidin]-2(1H)-one; (±)-**32**): Yellow oil. ^{1}H-NMR (300 MHz): 8.06 (*d*, J = 2.2, 1 H); 7.28 (*d*, J = 8.3, 1 H); 6.97 (*dd*, J = 8.3, 2.2, 1 H); 4.51 (*dd*, J = 8.3, 5.7, 1 H); 3.95 (*dt*, J = 10.1, 8.1, 1 H); 3.74 (*ddd*, J = 10.1, 8.7, 4.7, 1 H); 2.64 (*s*, 3 H); 2.42 (*ddd*, J = 13.0, 8.7, 8.1, 1 H); 2.41 (*ddd*, J = 13.0, 8.1, 4.7, 1 H); 2.33 (*s*, 3 H); 2.16 (*s*, 3 H); 1.64 (*ddd*, J = 13.5, 8.3, 5.7, 1 H); 1.34 (*m*, 1 H); 1.24 (*m*, 1 H); 0.88 (*d*, J = 6.4, 3 H); 0.77 (*d*, J = 6.3, 1 H). ^{13}C-NMR (75 MHz): 179.1 (*s*); 170.7 (*s*); 170.6 (*s*); 169.4 (*s*); 151.0 (*s*); 140.8 (*s*); 125.2 (*d*); 124.4 (*s*); 118.1 (*d*); 111.1 (*d*); 60.7 (*d*); 55.1 (*s*); 45.3 (*t*); 40.7 (*t*); 34.3 (*t*); 26.6 (*q*); 24.9 (*d*); 22.9 (*q*); 22.8 (*q*); 22.3 (*q*); 21.0 (*q*).

*Acetylation of Pure (±)-***2**. As described above. In the ^{1}H-NMR of the crude product, only (±)-**31** could be detected.

3. *Oxindole Equilibration Experiments*. 3.1. *6-Deoxy Series*. *a*) A soln. of 1 mg of (±)-**12** was kept in 1 ml of MeOH for 24 h at 25°. At that point, TLC (AcOEt/MeOH 1:1) showed that (±)-**12**/(±)-**23** *ca.* 2:1 was present. *b*) The same experiment, starting with (±)-**13** gave qualitatively the same result. *c*) The above experiments were repeated, but in AcOEt as the solvent. In both cases, the corresponding epimer was formed to the extent of 5–10% after 24 h at 25°, and it took 7 d at 25° to establish the 2:1 equilibrium.

3.2. *Elacomine* (**2**)/*Isoelacomine* (**22**). *a*) A soln. of 10 mg of (±)-**2** in 1.5 ml of C_2D_5OD containing 5% of D_2O was refluxed for 2 h. TLC and ^{1}H-NMR showed the presence of (±)-**2**/(±)-**22** 2:1. *b*) A soln. of 1 mg of (±)-**2** in 1 ml of MeOH was kept at 25°. After 24 h, between 5 and 10% of (±)-**22** were formed, and complete equilibration to produce (±)-**2**/(±)-**22** 2:1 took *ca.* 7 days. *c*) The same experiment, starting with (±)-**22**, gave qualitatively the same result.

4. *Isolation of (±)-***2** *and of (±)-***22** *from* Elaeagnus commutata. 4.1. *Original Procedure* [1]. Following the original procedure by extracting 90 g of finely cut roots of *E. commutata*, obtained from the horticulture *Calonder Blumen*, CH–7208 Malans, with EtOH/H_2O 95:5 at 80° for 24 h in a *Soxhlet* apparatus, 50 mg of amorphous elacomine (**2**) were isolated: $[\alpha]_D = \pm 0$ (c = 0.8, MeOH); optical purity, determined by *General Procedure C*: 0% e.e. TLC: presence of isoelacomine (**22**) in the crude extract.

4.2. *Modified Procedure*. Finely cut roots from the same source were air-dried at 25° in the dark for 4 d. This material was digested twice with 300 ml of p.e. (10 h at 25° under Ar with efficient stirring) and twice with 300 ml of MeOH under the same conditions (10 h at 25°). The combined MeOH extracts were evaporated ($T \leq 20°$) and chromatographed twice (40 g of silica gel, AcOEt/MeOH/Et_3N 10:2:1). The fractions containing TLC-pure **2** were pooled and suspended in 1 ml of acetone. After being placed in a supersonic bath for 1 min, the mixture was centrifuged and the supernatant soln. discarded. The residue consisted of 12 mg of a colorless powder, representing pure racemic elacomine ((±)-**2**). M.p. subl. at *ca.* 150° in an evacuated capillary; decomposition at *ca.* 200° in a capillary sealed under Ar. $[\alpha]_D = \pm 0$ (c = 0.5, MeOH); optical purity, determined by *General Procedure C*, 0% e.e.

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