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Intramolecular Alkylation of Aromatic Compounds XXXVI [1]. Stereoselective Synthesis of C/D-*cis*-Configured Ergolines

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Summary. The stereoselective synthesis of *cis*-ergoline is presented. Starting from *rac-N*-benzoyl tryptophan methyl ester, the key compound indolinylmethylpyridin-3-one was prepared *via* a seven-step reaction in good yield. Since its cyclization to the desired ergolinone failed, the key compound was reduced to yield the two diastereomeric pyridin-3-ols; only one of them cyclized in trifluoromethanesulfonic acid, affording *cis*-ergoline. Catalytic hydrogenation of the latter gave *N*,*N*′-dimethyldihydroergoline, the X-ray crystallography of which revealed both the correct structure and identical relative configurations at C-5a and C-6a (*SS* or *RR*). Hydroboration and subsequent perruthenate oxidation of the Δ^9-ergoline provided access to the regioisomeric ergolinols and ergolinones.

Keywords. Δ^4-Piperidinone; Diastereoselective cyclization; X-Ray crystal structure analysis; Determination of relative configuration; 9- and 10-Hydroxy- and -oxoergolines.

Introduction

Dihydroergolines with C/D-*trans* ring fusion, *e.g.* the so-called hydrogenated ergot alkaloids [3] or the semisynthetic dopamine agonist terguride (Mysalfon®, Teluron®) [4, 5] play an important role in therapy. Corresponding *cis*-configured active substances, particularly derivatives of C/D-*cis*-dihydrolysergic acid (dihydrolysergic acid II [6]) seem to be not available hitherto. Only the *cis*-terguride has been synthesized, but it is lacking pharmacological activity [5].

In connection with our investigations relating to the stereochemistry of the intramolecular alkylation of aromatic compounds we were interested in an efficient stereoselective approach to C/D-*cis*-configured ergolines. As recently reported, the Δ^4-piperidinone **1** has been intended to serve as a key precursor [7] (Scheme 1). Unfortunately, compound **1** could not be synthesized by a convergent route starting from conveniently available indolines with a preshaped pyridine moiety, because partial reduction of these educts yields preferably the isomeric Δ^5-piperidinones being inappropriate for our synthetic approach [1].

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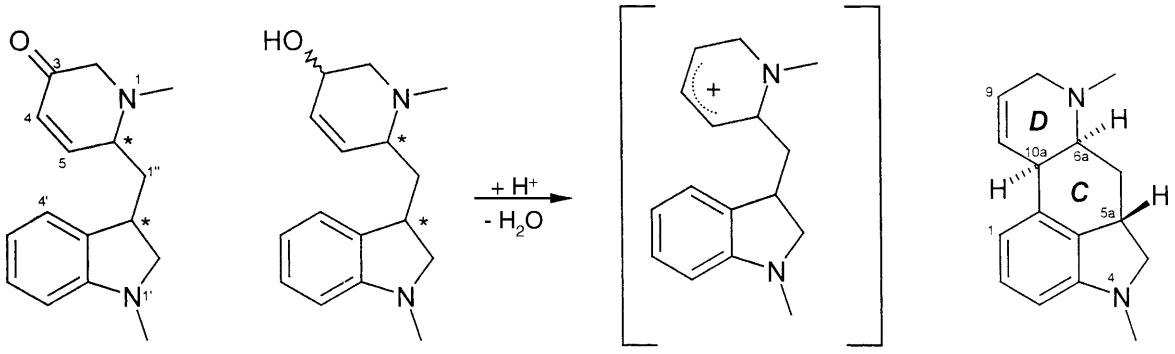


Scheme 1

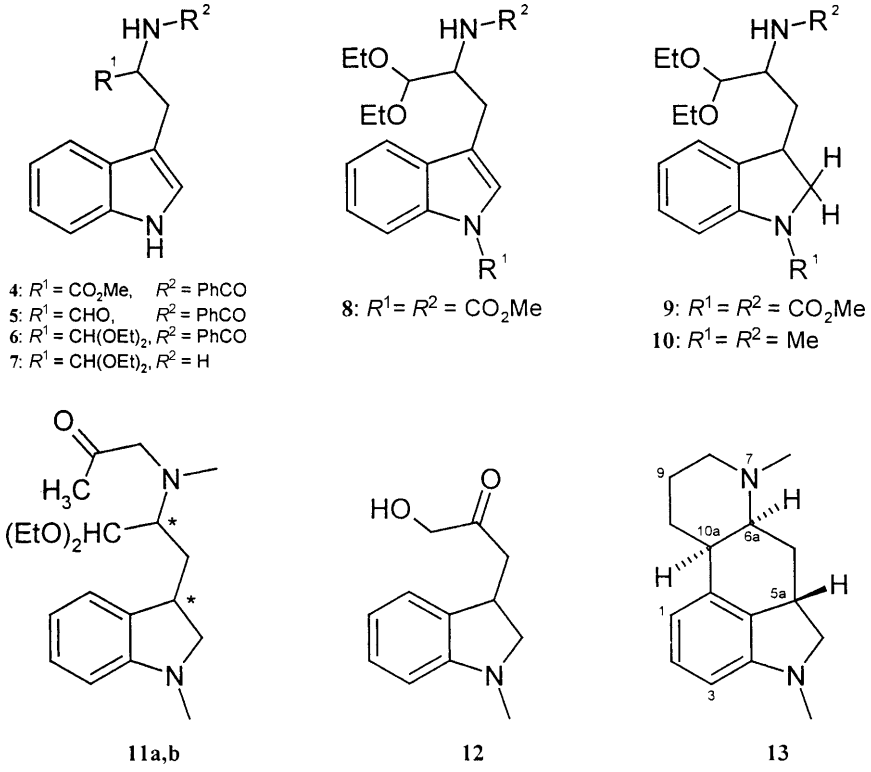
For this reason, the required educt had to be prepared by a linear sequence generating the piperidone moiety from the amino acid function of tryptophan **4** and an appropriate C-3 compound, for example iodoacetone. In this paper we present the preparation and cyclization of the precursor **1** to the ergoline **3** as well as its further functionalization.

Results and Discussion

The synthetic pathway is outlined in Schemes 1 and 2. Thus, *rac-N*-benzoyltryptophan methyl ester (**4**) was reduced by diisobutyl aluminum hydride to the corresponding labile aldehyde **5** in excellent yield. The success of the reduction depends on the size of the *N*-substituent R^2. Thus, **4** substituted by small acyl groups, *e.g.* acetyl, carboxymethyl, or carboxyethyl, provides hardly sufficient quantities of the corresponding aldehydes.

The ^{1}H NMR spectrum of **5** is remarkable concerning the number of multiple peaks with varying intensities, which presumably are caused by different rotamers and conformers fixed by H-bridges. By-products affecting the spectroscopic behaviour could be excluded because of the chromatographical purity of the compound. The aldehyde **5** could be smoothly converted to the stable diethylacetal **6**; its NMR spectrum was lacking double and multiple peaks.

After removing the benzoyl group, **7** was reacylated by methyl chloroformate, affording the diurethane **8** which in turn was catalytically hydrogenated by an approved procedure [8] giving the indoline **9**. The NMR spectrum of **9** indicated a 1:1-mixture of diastereomers which could not be separated by chromatography. Lithium aluminum hydride reduction provided the *N*,*N*′-dimethyl compound **10**. *N*-Alkylation of **10** using iodoacetone as a suitable C-3 building block afforded **11** which was cyclized with trifluoromethane sulfonic acid to the desired Δ^4-piperidinone **1** in high yield. Treatment of **11** with other acids, *e.g.* HBr in glacial acetic acid, caused degradation to the hydroxyketone **12** (Scheme 2). In contrast to **9**, compounds **1** and **11** could be separated by flash chromatography yielding the two diastereomeric racemates **1a**,**b** and **11a**,**b**. According to the concept mentioned above, the desired educt **1** for the intended cyclizations to the target compounds **3** and **17** now was easily available (overall yield 39% based on **4**).



11a,b **12** **13**

Scheme 2

First it was attempted to obtain the ergolinone **17** by immediate cyclization of **1** using an established approach with a closely related α,β-unsaturated piperidone [9]. However, upon treatment of **1** with trifluoromethane sulfonic acid no reaction occurred. Therefore, **1** was reduced by $NaBH_4$, yielding a mixture of diastereomeric piperidinols **2a** and **2b** which in turn could be cyclized to the C/D-*cis*-configured ergoline **3**. Analytical data indicating the corresponding *trans*-stereomer were not observed, signifying that the cyclization had occurred stereoselectively. The rather low yields ($<50\%$) of **3** were not unexpected; they are in line with the result of preceding investigations showing that cyclizations of the type **2** $\rightarrow$ **3** strongly depend on the configuration of the educts [10]. Thus, starting with the separated diastereomers **2a** or **2b**, only **2a** cyclized to **3** in quantitative yield, whereas **2b** was gradually decomposed under the same reaction conditions.

The structure of **3** was proven by NMR spectroscopy. Moreover, the catalytic hydrogenation of **3** led to the parent compound **13** whose X-ray data confirmed the above results and, in addition, allowed to deduce the relative configurations of the three chiral centers C-5a, C-6a, and C-10a (*R*,*R*,*S*) or (*S*,*S*,*R*) respectively (Fig. 1; crystallographic data: see Table 3).

From compound **3** the relative configurations of C-3′ and C-6 of the precursors **2** could also be deduced. Assuming that the conversion **2** $\rightarrow$ **3** occurs with retention of configuration, the diastereomer **2a** undergoing cyclization must have identical configurations at C-3′ and at C-6 (*i.e.* (3′*R*,6*R*) or (3′*S*,6*S*)), whereas the

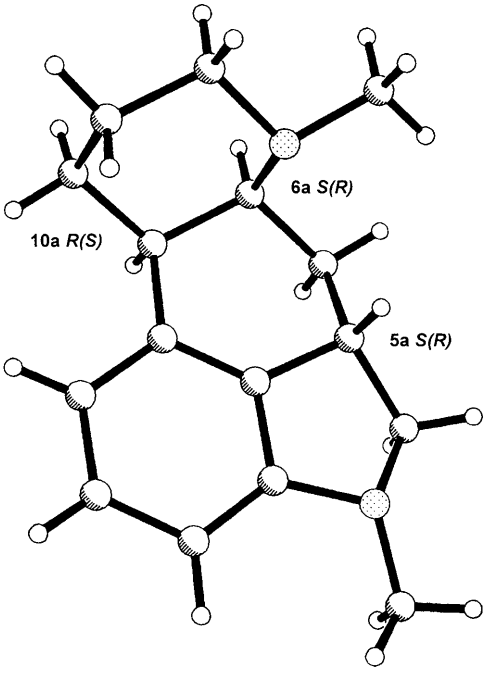


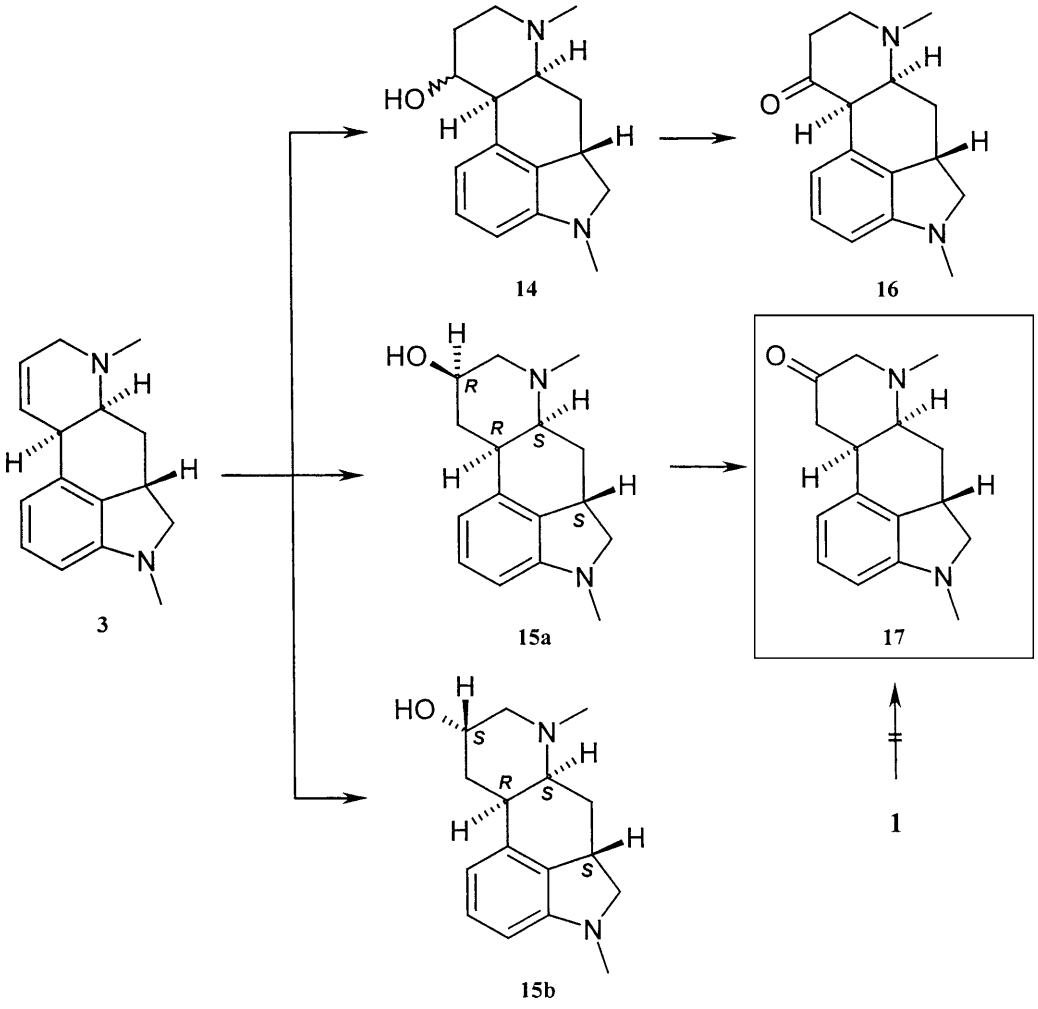
Fig. 1. Molecular structure of **13**

uncyclizeable **2b** is oppositely configured at these centers (*i.e.* (3′*R*,6*S*) or (3′*S*,6*R*)). Corresponding assignments could be achieved for compounds **1** and **11**.

The target compound **3** allowed a further functionalization of ring D for the first time. Thus, hydroboration gives a mixture of the conceivable regioisomeric 9- and 10-hydroxy derivatives **15** and **14**. The two diastereomers of **15** were successfully separated. The relative configuration of the new chiral center C-9 could be deduced from the different ^{13}C NMR shift increments caused by an axial or equatorial orientation of the hydroxy group [11]. Thus, **15a** exhibits a smaller δ-value than **15b** (64.67 *vs.* 66.26 ppm) which is characteristic for an axial OH; consequently, in **15b** the OH is equatorially orientated. In the case of **14**, an additional stereomer was not detectable; the reaction presumably occurred diastereoselectively (Scheme 3).

Finally, the hydroxy compounds **14** and **15** were oxidized with ammonium perruthenate yielding the regioisomeric ketones **16** and **17**. Compound **17** is of special interest concerning further conversions with respect to natural lead structures like lysergic acid and agroclavine. In contrast, other functionalizations of the olefinic moiety, *e.g.* addition of bromine or epoxidation, failed hitherto. The overall yield of the synthetic sequence up to the ergoline **3** amounts to about 12%, but it is to be considered that the result is limited to at most 50% due to the uncyclizable diastereomer **2b**.

In conclusion, we have developed a short stereoselective approach to C/D-*cis*-configured ergolines. This may be of special importance in so far as an obviously more efficient pathway, *i.e.* the catalytic hydrogenation of natural alkaloides, cannot be applied because it is known that the resulting hydrogenated ergot alkaloids are C/D-*trans*-configured [12–14].



Scheme 3

Experimental

Melting points were measured with a Reichert hot-stage microscope and are uncorrected. IR: Perkin Elmer FT-IR Paragon 1000; NMR: Jeol GSX 400 (^{1}H: 400 MHz, ^{13}C: 100 MHz, $CDCl_3$, *TMS* as internal reference); MS (70 eV): Hewlett Packard MS-Engine; elemental analyses: Heraeus CHN-Rapid, the results are in good agreement with the calculated values; thin layer chromatography (TLC): aluminum sheets Kieselgel 60 F_{254} (Merck), thickness of layer 0.2 mm; flash chromatography (FC): ICN-Silica 32–36 60 A; X-ray structure determination: Siemens R3m diffractometer. *rac*-3-(1*H*-Indol-3-yl)-2-(benzoylamino)-propionic acid methyl ester (*DL-N*-benzoyl-tryptophan methyl ester, **4**) was prepared according to Ref. [15].

N-(1-Formyl-2-(1H-indol-3-yl)-ethyl)-benzamide (**5**; $C_{18}H_{16}N_2O_2$)

To a solution of 40 g **4** (124.1 mmol) in 200 cm^3 anhydrous *THF* (dried over $LiAlH_4$), 60 cm^3 of a solution of *DIBAH* (45% in toluene) were added dropwise under an N_2 atmosphere and stirring at -72°C over *ca.* 100 min. After stirring the mixture for further 20 min at the same temperature it was

poured into an ice cold mixture of a saturated solution of 500 cm^3 HN_4Cl, 500 cm^3 2 *N* H_2SO_4, and 500 cm^3 diethyl ether. The addition was completed within 15 min, and stirring was continued for further 20 min. After decanting from some precipitate, the aqueous layer was extracted several times with diethyl ether. The combined organic layers were washed with saturated $NaHCO_3$ (once) and brine (twice), dried over Na_2SO_4, and filtered over silica gel (thickness of layer: 5 cm). The solvents were removed *in vacuo*. According to TLC ($CHCl_3$:CH_3OH = 19:1), the crude product (yield: 40 g; R_f = 0.44) contained some educt (R_f = 0.74) and small amounts of a by-product (R_f = 0.32); it was used for the next step without further purification. An analytical sample was obtained by FC (eluent: see TLC).

IR (film): $\tilde{\nu}$ = 1725 (CHO), 1640 (CONH) cm^{-1}; MS: a) CI: *m*/*z* (%) = 293 ($M^{+\bullet}$ + 1, 95), 275 (20), 130 (100); b) EI: *m*/*z* (%) = 292 ($M^{+\bullet}$, 5), 130 (100).

N-(2,2-Diethoxy-1-(1H-indol-3-ylmethyl)-ethyl)-benzamide (**6**; $C_{22}H_{26}N_2O_3$)

A mixture of 40 g crude aldehyde **5** (137 mmol), 400 cm^3 EtOH, 31 cm^3 triethyl orthoformate, and 1.4 g NH_4NO_3 was refluxed for 2.5 h; then, 80 g solid KOH and 40 cm^3 H_2O were added. Heating was continued for further 20 min. The solvent was removed *in vacuo*, and the residue was extracted with diethyl ether (3×330 cm^3). The combined ether extracts were washed with saturated $NaHCO_3$ and brine, dried over Na_2SO_4, and filtered over a short silica gel column ($d \times h \approx 7 \times 7$ cm). After washing the column with a few cm^3 diethyl ether, the combined eluates were concentrated *in vacuo*.

Yield: 38.2 g (84% based on **4**); TLC ($CHCl_3$:CH_3OH = 19:1): R_f = 0.78 (educt: R_f = 0.44); IR (film): $\tilde{\nu}$ = 1650 ($CONH_2$) cm^{-1}; MS: a) CI: *m*/*z* (%) = 367 ($M^{+\bullet}$ + 1, 2), 321 (100), 275 (15), 130 (20); b) EI: *m*/*z* (%) = 366 ($M^{+\bullet}$, 5), 320 (70), 274 (40), 200 (40), 130 (65), 105 (100); ^{1}H NMR ($CDCl_3$): δ = 8.26 (s, 1H), 7.73–7.67, 7.48–7.43 (m each, 3 and 1 arom. H), 7.40–7.30 (m, 3 arom. H), 7.19–7.14, 7.13–7.09 (each m, each 1 arom. H), 7.05 (d, *J* = 2.3 Hz, 1 arom. H), 6.50 (d, *J* = 9.0 Hz, CONH), 4.72–4.62 (m, 1H), 4.52 (d, *J* = 3.0 Hz, 1H), 3.84–3.76, 3.64–3.44 (each m, overall 4H, 2 OCH_2), 3.16 (d, *J* = 7.0 Hz, 2H), 1.26, 1.16 (each t, each *J* = 7.1 Hz, 2–CH_3) ppm.

2,2-Diethoxy-1-(1H-indol-3-ylmethyl)-ethylamine (**7**; $C_{15}H_{22}N_2O_2$)

Compound **6** (38.2 g, 104 mmol) and 10 g solid KOH were dissolved under N_2 in 300 cm^3 diethylene glycol at 100°C. Further 140 g KOH were added portionwise, the temperature of the heating bath was increased to 160°C, and the volatile compounds were removed under slightly reduced pressure. Heating and stirring under N_2 was continued for further 15 h. The mixture was allowed to cool to 100°C, diluted with H_2O (first 500 cm^3 and after cooling to room temperature further 2500 cm^3), and 500 cm^3 diethyl ether. After separating the organic phase, the aqueous layer was extracted twice with the same solvent. The combined organic extracts were washed consecutively with small quantities of H_2O (twice) and brine (once) and dried over Na_2SO_4. The solvent was removed *in vacuo* yielding 25.0 g (92%) of a brown oil.

TLC (EtOAc:CH_3OH:25% NH_3 = 18:2:0.15): R_f = 0.49; MS: a) CI: *m*/*z* (%) = 303 ($M^{+\bullet}$ + 49, 10), 263 ($M^{+\bullet}$ + 1, 15), 217 (65), 158 (15), 130 (100); b) EI: *m*/*z* (%) = 262 ($M^{+\bullet}$, 15), 159 (75), 131 (100), 130 (90), 103 (75); ^{1}H NMR ($CDCl_3$): δ = 8.61 (s, 1H), 7.63 (d, *J* = 7.8 Hz, 1H), 7.32 (dt, *J* = 1.0/8.2 Hz, 1H), 7.19–7.15, 7.12–7.08 (each m, each 1H), 7.00 (d, *J* = 2.3 Hz, 1H), 4.31 (d, *J* = 5.8 Hz, 1H), 3.82–3.73, 3.65–3.54 (each m, 2 OCH_2), 3.26 (ddd, *J* = 3.9/5.8/9.4 Hz, 1H), 3.16, 2.68 (each dd, *J* = 3.9/14 and 9.4/14.3 Hz, each 1H), 1.43 (s, NH_2), 1.27, 1.25 (each t, each *J* = 7.0 Hz, 2 CH_3) ppm; ^{13}C NMR ($CDCl_3$): δ = 136.45, 127.63 (2 s, each 1C), 122.77, 121.87, 119.18, 118.96 (4 d, each 1C), 112.58 (s, 1C), 111.17, 106.14 (2 d, each 1C), 63.59, 63.09 (2 t, 2 CH_2), 53.62 (d, 1C), 28.13 (t, 1C), 15.51, 15.47 (2 q, 2 CH_3) ppm.

3-(3,3′-Diethoxy-2-methoxycarbonylamino-propyl)-indol-1-carbonic acid methyl ester (**8**; $C_{19}H_{26}N_2O_6$)

To a mixture of 25 g **7** (95.3 mmol), 350 mg (*ca.* 0.01 mol%) tetrabutylammonium hydrogensulfate and 16.0 g of finely grounded NaOH (0.4 mol) in 250 cm^3 CH_2Cl_2, 18.9 g methyl chloroformate (15.4 cm^3, 0.2 mol) were added dropwise under vigorous stirring and weak refluxing (about 40°C) over 30 min, and stirring was continued for several minutes. Because residual educt was detected by TLC (EtOAc:*n*-hexane = 3:2; $R_f = 0.0$; product: $R_f = 0.55$), an additional small amount of acid chloride was added. The mixture was filtered over a silica gel column ($d \times h = 13 \times 1.5$ cm) covered with a thin layer of sand. The adsorbent was eluted with EtOAc, the combined filtrates were concentrated *in vacuo*, and the residue was recrystallized from EtOH and finally washed with *n*-hexane.

Yield: >25 g (at least 70%); some additional product was obtained from the mother liquor; m.p.: 130°C (EtOH); IR (KBr): $\tilde{\nu} = 1732, 1689$ (*het*-N–CO and NH–CO) cm^{-1}; MS: a) CI: m/z (%) = 333 ($M^{+\bullet}$ – EtOH, 5), 287 ($M^{+\bullet}$ – 2EtOH, 100), 188 (40), 103 (15); b) EI: m/z (%) = 378 ($M^{+\bullet}$, 1), 346 (10), 286 (10), 188 (25), 103 (100); ^{1}H NMR ($CDCl_3$): $\delta = 8.14$, 7.31 (each d, $J = 8.3$ and 7.9 Hz, each 1H), 7.44 (s, 1H), 7.34–7.29, 7.27–7.23 (each m, each 1H), 4.97 (br s, 1H), 4.42 (d, $J = 3.0$ Hz, 1H), 4.12 (m, 1H), 4.01 (s, OCH_3), 3.80–3.72, 3.68–3.57, 3.57–3.45 (each m, 1H, 4H, and 2H, OCH_3 and 2 OCH_2), 3.03, 2.87 (each dd, $J = 6.0/15.0$ and 7.2/15.0 Hz, each 1H), 1.23, 1.18 (each t, each $J = 7.1$ Hz, each 3H, acetal) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 156.91$, 151.50, 135.60, 130.92 (4 s, 2 CO and 2C), 124.69, 123.24, 122.90, 119.24, 118.12, 115.21, 102.56 (each d, each 1C), 63.94, 63.86 (each t, 2C, 2 OCH_2), 53.60 (q, 1C, OCH_3), 53.22 (d, 1C), 52.09 (q, 1C, OCH_3), 25.57 (t, 1C), 15.31, 15.27 (each q, 2C, 2 CH_3) ppm.

3-(3,3-Diethoxy-2-methoxycarbonylamino-propyl)-2,3-dihydroindol-1-carbonic acid methyl ester (diastereomeric mixture) (**9**; $C_{19}H_{28}N_2O_6$)

A mixture of 10.0 g (26.4 mmol) **8**, 2.0 g 5% Pd–C catalyst, and 400 cm^3 absolute EtOH was hydrogenated for 70 h at ambient temperature and 8.5×10^6 Pa initial pressure of H_2. The catalyst was filtered off, and the filtrate was concentrated *in vacuo*.

Yield: 10.0 g (100%); colorless oil; TLC (*n*-hexane/EtOAc = 3:2): $R_f = 0.36$ (educt: $R_f = 0.46$); IR (film): $\tilde{\nu} = 1713$ (C=O) cm^{-1}; MS: a) CI: m/z (%) = 335 ($M^{+\bullet} + 1 -$ EtOH, 100), 303 ($M^{+\bullet} + 1 -$ EtOH – MeOH, 20), 289 ($M^{+\bullet} + 1$ – 2EtOH, 10), 145 (30), 103 (30); b) EI: m/z (%) = 380 ($M^{+\bullet}$, 2), 334 (10), 189 (85), 145 (55), 103 (100); ^{1}H NMR ($CDCl_3$, 50°C): $\delta = 7.86$ (s, 1H), 7.37, 7.12 (each d, $J = 7.4$ and 7.5 Hz, each 0.5H), 7.22–7.14, 7.00–6.92 (each m, each 1H), 5.09, 5.04 (each d, $J = 9.5$ and 10.0 Hz, each 0.5H, NH–CO_2R), 4.38, 4.34 (each d, each $J = 3.0$ Hz, each 0.5H), 4.25–4.18, 4.15–4.07, 4.07–3.98 (each m, each 0.5H), 3.93–3.63 (m, 9.5H), 3.57–3.45 (m, 2H), 3.47–3.36 (m, 1H), 2.07–1.97, 1.95–1.86, 1.83–1.73, 1.73–1.62 (each m, each 0.5H), 1.18 (m, 6H, 2 C–CH_3) ppm; ^{13}C NMR ($CDCl_3$, 50°C): $\delta = 157.22$, 157.08 (each s, 1C, C=O), 153.67, 153.64 (each s, 1C, C=O), 142.50, 142.19 (each s, 1C), 134.75, 134.56 (each s, 1C), 127.85, 127.81 (each d, 1C), 124.67, 123.70 (each d, 1C), 122.68, 122.57 (each d, 1C), 114.68 (d, 1C), 103.58, 103.54 (each d, 1C), 64.21, 64.05 (each t, 1C, OCH_2), 63.94, 63.88 (each t, 1C, OCH_2), 54.55, 53.66 (each t, 1C), 52.47, 52.19 (each q, 2C, 2 OCH_3), 51.46, 51.32 (each t, 1C), 36.76, 36.25 (each d, 1C), 35.92, 35.41 (each t, 1C), 15.29, 15.25 (each q, 2C, 2 CH_3) ppm.

2,2-Diethoxy-1-((1-methyl-2,3-dihydro-1H-indol-3-ylmethyl)-ethyl)-methylamine (diastereomeric mixture) (**10**; $C_{17}H_{28}N_2O_2$)

To a mixture of 10.0 g **9** (26.3 mmol) in 100 cm^3 anhydrous *THF*, 5.2 g $LiAlH_4$ (137 mmol) were slowly added at 0°C under stirring and N_2 over *ca.* 20 min. After removing the ice bath the mixture started to foam; the reaction was controlled by repeated cooling. After about 40 min the mixture was heated for 1 h at 50°C with stirring, then cooled in an ice bath, diluted with 200 cm^3 diethyl ether, and

poured into a mixture of 200 cm^3 diethyl ether and 500 cm^3 2 *N* NaOH under N_2 and stirring. Stirring was continued for 10 min; then the organic phase was separated, and the aqueous layer was extracted several times with diethyl ether. The combined organic phases were consecutively washed with a small volume of H_2O and twice with brine. After drying over Na_2SO_4, the solvent was removed *in vacuo* yielding 7.53 g (98%) of a colorless oil.

TLC (EtOAc:CH_3OH:25% NH_3 = 17:3:0.3): $R_f = 0.75$; IR (film): $\tilde{\nu} = 3348$ (NH) cm^{-1}; MS: a) CI: m/z (%) = 293 ($M^{+\bullet} + 1$, 100), 247 ($M^{+\bullet} + 1$ – EtOH, 85), 231 ($M^{+\bullet}$ – EtOH – CH_3, 20), 189 (25), 127 (65); b) EI: m/z (%) = 292 ($M^{+\bullet}$, 2), 246 ($M^{+\bullet}$ – EtOH, 5), 231 ($M^{+\bullet}$ – EtOH – CH_3, 5), 189 (20), 149 (60), 132 (100); ^{1}H NMR ($CHCl_3$): $\delta = 7.12$–7.07 (m, 2H), 6.71–6.69, 6.50–6.47 (each m, each 1H), 4.42, 4.41 (each d, $J = 5.4$ and 5.6 Hz, each 0.5H), 3.78–3.67 (m, OCH_2), 3.60–3.51 (m, OCH_2 + 1H), 3.47–3.39 (m, 1H), 2.94 (t, $J = 8.2$ Hz, 1H), 2.75 (s, N–CH_3), 2.69–2.62 (m, 1H), 2.46, 2.45 (each s, each 1.5H, N–CH_3), 2.04, 1.92 (each ddd, $J = 5.6/6.8/14.0$ and $4.4/8.8/14.4$ Hz, each 0.5H), 1.78, 1.66 (each ddd, $J = 4.0/10.0/14.4$ and $5.6/9.2/14.0$ Hz, each 0.5H), 1.58 (s, NH), 1.20 (m, 2 C–CH_3) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 153.12$, 153.04 (2 s, 1C), 134.41, 134.37 (2 s, 1C), 127.48 (d, 1C), 123.38, 123.27 (2 d, 1C), 117.69 (d, 1C), 107.19, 107.16 (2 d, 1C), 105.16, 104.73 (2 d, 1C), 63.74, 63.56, 63.47, 63.34, 63.16, 62.64 (m, overall 3C), 59.81, 59.61 (2 d, 1C), 37.88 (d, 1C), 36.16, 36.13 (2 q, 1C, *het*-N–CH_3), 34.30 (q, 1C, N–CH_3), 33.97, 33.69 (2 t, 1C), 15.44, 15.41 (2 q, 2 CH_3) ppm.

1-((2,2-Diethoxy-1-(1-methyl-2,3-dihydro-1H-indol-3-ylmethyl)-ethyl)-methylamino)-propan-2-one (mixture of diastereomers) (**11a** + **11b**; $C_{20}H_{32}N_2O_3$)

To a solution of 7.53 g (25.8 mmol) **10** in 75 cm^3 *THF*, 30% K_2CO_3 (35 cm^3) and, after heating to 60°C, a solution of 5.69 g (1.2 equiv.) iodoacetone in 12 cm^3 *THF* (generated according to the *Finkelstein* reaction from chloroacetone and KI [16]) were added dropwise under stirring. Stirring was continued for further 5 min; then the cold mixture was diluted with 300 cm^3 diethyl ether, the organic phase was separated, and the aqueous layer was extracted with diethyl ether. The combined ether extracts were first extracted with 20 cm^3 2 *N* H_2SO_4 and then with 0.1 *N* H_2SO_4 (1×200 cm^3 and 2×100 cm^3). The combined acid extracts were washed with diethyl ether (twice) and, after addition of 300 cm^3 diethyl ether, rendered alkaline by K_2CO_3. After separation the organic phase was washed with brine and dried over Na_2SO_4. The solvent was evaporated *in vacuo*, and the residue (8 g) was dissolved in a few cm^3 of EtOAc. The solution was rapidly filtered over a short silica gel column covered with a layer of sand ($d \times h = 9.5 \times 3.5$ cm; sand layer: $h = 1.5$ cm). The adsorbent was eluted with EtOAc (700 cm^3), and the combined filtrates were concentrated *in vacuo*.

Yield: 7.2 g (80%); yellowish, instable oil; TLC (EtOAc): $R_f = 0.78$; IR (film): $\tilde{\nu} = 1713$ (C=O) cm^{-1}; MS: a) CI: m/z (%) = 349 ($M^{+\bullet} + 1$, 70), 303 ($M^{+\bullet} + 1$ – EtOH, 100), 245 (20), 172 (20), 132 (30); b) EI: m/z (%) = 348 ($M^{+\bullet}$, 2), 302 ($M^{+\bullet}$ – EtOH, 2), 245 (20), 132 (100); ^{1}H NMR ($CDCl_3$): $\delta = 7.11$–7.05 (m, 2H), 6.71–6.65, 6.50–6.47 (each m, each 1H), 4.47, 4.46 (each d, $J = 5.4$ and 6.1 Hz, each 0.5H), 3.75–3.62 (m, 2H), 3.56–3.39 (m, 6H), 3.00 (dd, $J = 6.7/8.4$ Hz, 0.5H), 2.96–2.89 (m, 0.5H), 2.83 (dt, $J = 5.5/8.4$ Hz, 0.5H), 2.76–2.71 (m, 0.5H), 2.75, 2.74 (each s, each 1.5H, *het*-N–CH_3), 2.39, 2.38 (each s, each 1.5H, N–CH_3), 2.17, 2.16 (each s, each 1.5H, CO–CH_3), 2.06–1.94 (m, 1H), 1.77–1.69 (m, 0.5H), 1.63 (dt, $J = 8.0/14.2$ Hz, 0.5H), 1.26–1.15 (m, 2 CH_3) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 209.95$, 209.42 (each s, 2C, 2 C=O), 153.16, 153.07, 134.31 (each s, 3C), 127.52 (d, 1C), 123.54, 123.02 (each d, 1C), 117.63, 117.59 (each d, 1C), 107.26, 107.15 (each d, 1C), 104.61, 104.44 (each d, 1C), 65.98, 65.49 (each t, 1C, CH_2–CO), 64.05, 63.50 (each d, 1C), 63.17, 63.09 (each t, 1C), 62.98, 62.20 (each t, 1C), 38.84, 38.53 (each q, 1C, N–CH_3), 38.42, 37.77 (each d, 1C), 36.12 (q, 1C, *het*-N–CH_3), 31.66, 31.49 (each t, 1C), 27.21, 27.09 (each t, 1C, CH_3–CO), 15.60, 15.56 (each t, 1C, CH_3), 15.44 (t, 1C, CH_3) ppm; separation of diastereomers (*n*-hexane:EtOAc = 3:2): $R_f = 0.51$ and 0.46 (**11a** and **11b**).

1-Methyl-6-(1-methyl-2,3-dihydro-1H-indol-3-ylmethyl)-1,6-dihydro-2H-pyridin-3-one (mixture of diastereomers) (**1a** + **1b**; $C_{16}H_{20}N_2O$)

1.59 g (4.48 mmol) **11a**/**11b** (mixture of diastereomers) were dissolved in 10 cm^3 F_3CSO_3H under N_2 and cooling (water bath, 20°C). The mixture was stirred at ambient temperature for 30 min and cautiously poured into 120 cm^3 crushed ice/H_2O. The acid solution was washed with diethyl ether, rendered alkaline with K_2CO_3, and extracted several times with diethyl ether. The combined ether extracts were washed with 10% Na_2CO_3 and brine and dried over Na_2SO_4. After evaporation of the solvent *in vacuo*, the residue was dissolved in EtOAc, and the solution was rapidly filtered over a short silica gel column ($d \times h = 2 \times 2$ cm). The solvent was removed *in vacuo* affording 1.06 g (91%) of a slightly colored oil of sufficient purity for the next step. Purification and separation of the diastereomers was accomplished by FC (silica gel, *n*-hexane:EtOAc = 3:2).

TLC (eluent: see FC): $R_f = 0.40$ (**1b**) and 0.47 (**1a**); IR (film): $\tilde{\nu} = 1682$ (C=O) cm^{-1}; MS: a) CI: m/z (%) = 257 ($M^{+\bullet} + 1$, 100), 255 (100), 132 (25), 112 (25); b) EI: m/z (%) = 256 ($M^{+\bullet}$, 10), 239 (12), 132 (40), 110 (100); ^{1}H NMR ($CDCl_3$): see Table 1; ^{13}C NMR ($CDCl_3$): see Table 2.

1-Hydroxy-3-(1-methyl-2,3-dihydro-1H-indol-3-yl)-propan-2-one (**12**; $C_{12}H_{15}NO_2$)

A solution of 70 mg (0.2 mmol) **11a** + **11b** in 0.75 cm^3 26% HBr/glacial acetic acid was stirred for 12 h at ambient temperature, the color changing from emerald green to deep blue. After diluting with a few cm^3 H_2O, the acidic solution was extracted twice with diethyl ether, rendered alkaline with solid $NaHCO_3$, and extracted with diethyl ether again. The ether extracts were washed with brine, dried over Na_2SO_4, and evaporated *in vacuo*. The residue was purified by FC (EtOAc:*n*-hexane = 3:2).

Yield: 23 mg (33%); colorless oil; TLC (eluent: see FC): $R_f = 0.44$ (educt: $R_f = 0.52$); IR (film): $\tilde{\nu} = 3047$ (OH), 1753, 1731 (C=O) cm^{-1}; ^{1}H NMR: $\delta = 7.12$ (*pseudo*-t, $J = 7.2/8.0$ Hz, 6′-H), 7.00 (d, $J = 7.2$ Hz, 4′-H), 6.68 (dt, $J = 0.8/7.2$ Hz, 5′-H), 6.50 (d, $J = 8.0$ Hz, 7′-H), 4.23 (s, 1-H),

Table 1. ^{1}H NMR data of the diastereomers of **1**

δ/ppm		Multiplicity	No. of H-Atoms	J/Hz		Assignment
1a	**1b**			**1a**	**1b**	
7.14–7.10	7.15–7.11	m	1			6′-H
7.06–7.05	7.07–7.05	m	1			4′-H
6.88	6.91	dd	1	3.2/10.4	3.2/10.4	5-H
6.70	6.71	dt	1	0.8/7.6	0.8/7.6	5′-H
6.51	6.52	d	1	8.0	7.6	7′-H
6.11	6.11	dd	1	2.0/10.4	2.0/10.4	4-H
3.52	3.53	d	1	16.8	16.39	2-H
3.53	3.50	t	1	8.4	8.4	2′-H
	3.44–3.36	m	1			3′-H
3.38–3.30		m	2			3′-H, 6-H
	3.29–3.24	m	1			6-H
3.09	3.12	dd	1	2.0/16.8	2.0/16.4	2-H
2.99	2.97	dd	1	7.2/8.4	6.8/8.4	2′-H
2.75	2.76	s	3			*ind*-N–CH_3
2.44	2.48	s	3			*pip*-N–CH_3
2.20	2.14	ddd	1	4.8/6.8/14.4	5.2/7.2/14.0	
1.91	1.94	ddd	1	5.6/9.2/14.4	6.0/8.8/14.0	C-1″

Table 2. ^{13}C NMR data of the diastereomers of **1**

δ/ppm		DEPT	Assignment
1a	**1b**		
196.34			C=O
152.92			C-7a′
151.30	151.18	CH	C-5
133.36	133.16		C-3a′
127.92	127.96	CH	C-6′
127.43	127.30	CH	C-4
123.23	123.39	CH	C-4′
117.79	117.89	CH	C-5′
107.46	107.50	CH	C-7′
62.69	62.80	CH_2	C-2′
60.46	60.35	CH_2	C-2
59.67	59.38	CH	C-6
42.45	42.17	CH_3	*pip*-N–CH_3
37.82	37.44	CH	C-3′
36.04	36.08	CH_3	*ind*-N–CH_3
34.86	35.02	CH_2	C-1″

3.75–3.67 (m, 3′-H), 3.52 (t, $J = 8.8$ Hz, 2′-H), 3.10 (s, OH), 2.98 (dd, $J = 5.6/8.8$ Hz, 2′-H), 2.84 (dd, $J = 6.0/17.2$ Hz, 3-H), 2.74 (s, N–CH_3), 2.67 (dd, $J = 8.4/17.2$ Hz, 3-H) ppm.

1-Methyl-6-(1-methyl-2,3-dihydro-1H-indol-3-yl-methyl)-1,2,3,6-tetrahydropyridin-3-ol (mixture of diastereomers) (**2a** + **2b**; $C_{16}H_{22}N_2O$)

To a solution of 960 mg (3.75 mmol) crude **1a**/**1b** in 15 cm^3 MeOH, 1.63 g $Ce(NO_3)_3 \cdot 6H_2O$ and, after stirring for 5 min, 100 mg $NaBH_4$ were added portionwise. After further 10 min, Ce^{3+} was precipitated by about 30 drops 30% K_2CO_3, and stirring was continued for 5 min. The mixture was diluted with 100 cm^3 Et_2O and filtered over a silicagel/*Kieselgur* layer (porcelain filter funnel, $d \times h = 2 \times 2$ cm). After washing the filter with Et_2O and evaporation of the combined filtrates *in vacuo*, the residue was purified by FC (EtOAc:CH_3OH:25% NH_3 = 18:2:0.2).

Yield: 670 mg (70%; if using the chromatographically purified educt, the yield was quantitative); colourless oil; TLC (eluent: see FC): $R_f = 0.43$ (educt: $R_f = 0.80$); IR (film): $\tilde{\nu} = 3374$ (OH) cm^{-1}; MS: a) CI: m/z (%) = 259 ($M^{+\bullet} + 1$, 100), 241 (20), 216 (5), 144 (5), 132 (20), 110 (10), 108 (10); b) EI: m/z (%) = 257 ($M^{+\bullet} - 1$, 2), 240 (2), 144 (30), 132 (98), 117 (45), 112 (100), 109 (70); ^1H NMR ($CDCl_3$): $\delta = 7.12–7.08$, 7.06–7.01, 6.73–6.67 (each m, each 1H, 6′-H, 4′-H, and 5′-H), 6.50 (br d, $J = 7.8$ Hz, 7′-H), 6.04–5.95, 5.87–5.73 (each m, 4-H and 5-H), 4.34–4.28, 4.01–3.97 (each m, 3-H), 3.61–3.51 (m, 2′-H), 3.45–3.30, 3.30–3.17 (each m, 3′-H), 3.10–2.80 (m, 3H), 2.74–2.73 (4 s, *ind*-N–CH_3), 2.61–2.47 (m, total 1.2H, 2-H, therein at 2.59 s, OH), 2.40–2.35 (4 s, *py*-N–CH_3), 2.34–2.24 (m, 0.8H, 2-H), 2.21–1.98, 1.94–1.74 (each m, each 1H, bridge-CH_2) ppm.

(5aS,6aS,10aR)-4,7-Dimethyl-4,5,5a,6,6a,7,8,10a-octahydroindolo[4,3-fg]quinoline (**3**; $C_{16}H_{20}N_2$)

A solution of 1.27 g (4.92 mmol) diastereomeric mixture **2a**/**2b** in 10 cm^3 F_3CSO_3H was stirred for 14 h at ambient temperature under N_2 and thereafter added dropwise to 120 cm^3 H_2O/crushed ice. The

Table 3. Crystallographic data of **13**[a]

Formula	$C_{16}H_{22}N_2$
Formula weight	242.37
Temperature/K	298
Color, shape	Colorless, transparent platelets
Crystal dimensions/mm	$0.50 \times 0.50 \times 0.1$
Crystal system	monoclinic
Space group	P2(1)/*n*
Cell dimensions:	
a/Å	7.669(2)
b/Å	13.463(3)
c/Å	13.504(4)
β/°	105.84(2)
*V*Å^3	1341.41(0)
Radiation	CuK_α ($\lambda = 1.54178$ Å)
Z	4
F(000)	528
μ/mm^{-1}	0.536
Density/g · cm^{-3}	1.200
Reflections collected	1446
Independent reflections	1376 ($R_i = 1.97\%$)
Observed reflections	1198 ($I > 4\sigma I$)
No. of parameters refined	163
R-values:	
Final *R* indices (observed data)	$R = 5.95\%$, $wR = 6.37\%$
R indices (all data)	$R = 6.68\%$, $wR = 6.62\%$
Goodness of Fit	1.15
System used	Siemens SHELXTL PLUS (PC-version)[b]

[a] Further details of the crystal structure determination are available from Cambridge Crystallographic Data Center, 12 Union Road, GB Cambridge CB21EZ quoting the deposition number CCDC 174949 and the complete literature source (e-mail: deposit@ccdc.cam.ac.uk); [b] G.M. Sheldrick: A Program for Crystal Structure Determination: SHELXTL (Release 4.2), Göttingen (1991)

mixture was washed with 50 cm^3 diethyl ether, rendered alkaline with solid K_2CO_3 after addition of further 50 cm^3 diethyl ether, and extracted three times with the same solvent. During this procedure, some dark brown resinous substance was separated. The organic extracts were washed with 10% Na_2CO_3 (twice) and brine and dried over Na_2SO_4. After evaporation of the solvent *in vacuo*, the residue was purificated by FC (EtOAc:MeOH:25% NH_3 = 18:1.5:0.2).

Yield: 500 mg (42%; caution: a too long contact with the sorbent decreased the yield; using the pure diastereomer **2a** as educt, the yield was quantitative); colourless oil; TLC (eluent: see FC): $R_f = 0.55$ (educt (diastereomeric mixture **2a**/**2b**): $R_f = 0.39$ and 0.35); MS: a) CI: m/z (%) = 241 ($M^{+\bullet} + 1$, 100); b) EI: 240 ($M^{+\bullet}$, 65), 239 ($M^{+\bullet} - 1$, 70), 182 (45); ^{1}H NMR ($CDCl_3$): $\delta = 7.05$ (dd, $J = 0.8/7.6$ Hz, 2-H), 6.64, 6.32 (each d, each $J = 7.6$ Hz, each 1H, 1-H and 3-H), 6.25–6.19 (m, 10-H), 5.78 (ddt, $J = 2.0/4.7/10.0$ Hz, 9-H), 3.62 (t, $J = 7.8$ Hz, 5-H$_{trans}$ rel. to 5a-H), 3.39–3.33 (m, 5a-H and 10a-H), 3.33–3.26 (m, 8-H), 2.84 (dddd, $J = 2.0/2.7/3.4/16.7$ Hz, 8-H), 2.78 (m, 6a-H), 2.71 (s, 4-N–CH_3), 2.62 (dd, $J = 7.8/12.3$ Hz, 5-H$_{cis}$ rel. to 5a-H), 2.50 (dt, $J = 4.0/13.5$ Hz, 6-H), 2.39 (s, 7-N–CH_3), 1.50 (ddd, $J = 2.8/9.5/13.5$ Hz, 6-H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 152.95$, 134.61, 130.60 (each s, each 1C,

C-3a, C-10c, and C-10b), 128.01, 126.71, 124.73, 115.99, 104.52 (each d, each 1C, C-2, C-10, C-9, C-1, and C-3), 64.95 (t, 1C, C-5), 58.80 (d, 1C, C-6a), 55.48 (t, 1C, C-8), 42.05 (q, 1C, 7-N–CH_3), 38.80 (d, 1C, C-10a), 37.00 (q, 1C, 4-N–CH_3), 31.88 (d, 1C, C-5a), 29.76 (t, 1C, C-6) ppm.

(5aS,6aS,10aR)-4,7-Dimethyl-4,5,5a,6,6a,7,8,9,10,10a-decahydroindolo[4,3-fg]quinoline (Dimethyldihydroergoline) (**13**; $C_{16}H_{22}N$)

A mixture of 27 mg (0.11 mmol) **3**, 3 cm^3 MeOH *p.a.*, and 12 mg 5% Pd–C catalyst was hydrogenated for 2 h at ambient temperature and 6×10^6 Pa initial pressure of H_2. The catalyst was filtered off, the solvent removed *in vacuo*, and the colorless oily residue crystallized from diethyl ether at $-20°C$.

Yield: 27 mg (100%); m.p.: 77°C; TLC (EtOAc:MeOH:25% NH_3 = 18:1.5:0.2): $R_f = 0.55$ (educt: $R_f = 0.59$); MS: a) CI: m/z (%) = 243 ($M^{+\bullet}+1$, 100); b) EI: m/z (%) = 242 ($M^{+\bullet}$, 35), 241 ($M^{+\bullet}$ – H, 35), 227 ($M^{+\bullet}$ – CH_3, 20), 149 (25); ^{1}H NMR ($CDCl_3$): $\delta = 7.06$ (dt, $J = 1.0/7.0$ Hz, 2-H), 6.64, 6.35 (each d, each $J = 7.70$ Hz, each 1H, 1-H and 3-H), 3.57 (t, $J = 7.7$ Hz, 5-H_{trans} rel. to 5a-H), 3.40–3.30, 2.92–2.87 (each m, 5a-H and 10a-H), 2.87–2.81 (dq, 8-H), 2.72 (s, 4-*N*-CH_3), 2.61 (dd, $J = 7.7/12.8$ Hz, 5-H_{cis} rel. to 5a-H), 2.50–2.47 (m, 6a-H), 2.43 (dt, $J = 4.8/12.9$ Hz, 6-H), 2.39–2.30 (m, 10-H), 2.31 (s, 7-N–CH_3), 2.17 (dt, $J = 3.1/11.0$ Hz, 8-H), 1.69–1.55, 1.55–1.41 (each m, each 2H, 9-H, 10-H or 6-H, 9-H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 153.00$, 135.40, 132.19 (each s, each 1C, C-3a, C-10c, and C-10b), 127.74, 114.87, 104.74 (each d, each 1C, C-2, C-1, and C-3), 64.96 (t, 1C, C-5), 62.23 (d, 1C, C-6a), 56.77 (t, 1C, C-8), 43.34 (q, 1C, 7-N–CH_3), 38.39 (d, 1C, C-10a), 37.09 (q, 1C, 4-N–CH_3), 32.81 (d, 1C, C-5a), 29.92, 27.19, 22.57 (each t, each 1C, C-6, C-10 and C-9) ppm.

Hydroboration of **3** *to the hydroxy compounds* **14** *and* **15** *(mixture of regio- and diastereomers)*

A mixture of 360 mg (1.50 mmol) **3** and 2.0 cm^3 Et_3N BH_3 was stirred under slightly reduced pressure and N_2 at 100°C (bath temperature) until the reaction was complete (about 4 h; TLC monitoring). After cooling to ambient temperature, the mixture was diluted with 3 cm^3 acetone, acidified with 2 *N* HCl, diluted again with 10 cm^3 of *THF*, and rendered alkaline with 2 *N* NaOH. Under vigorous stirring, 2 cm^3 30% H_2O_2 were added dropwise; stirring was continued for further 10 min, and the mixture was partitioned between Et_2O and H_2O. The organic phase was separated, and the aqueous layer was extracted several times with EtOAc. The combined organic extracts were washed with saturated $NaHCO_3$ and brine, dried over Na_2SO_4, and the solvents were removed *in vacuo*. The residue was fractionated twice by FC: a) (EtOAc:MeOH:25% NH_3 = 18:1.5:0.2): fraction I contained **13** and **15a**, fraction II contained **14** and **15b**; separation of I and II with $CHCl_3$:MeOH:25% NH_3 = 18:1.5:0.15 provided the pure compounds.

(5aS,6aS,10S/R,10aR/5aR,6aR,10R/S,10aS)-4,7-Dimethyl-4,5,5a,6,6a,7,8,9,10,10a-decahydroindolo[4,3-fg]quinolin-10-ol (**14**; $C_{16}H_{22}N_2O$)

Yield: 128 mg (33%); m.p.: 147°C (Et_2O/*n*-hexane/$CHCl_3$); IR (film): $\tilde{\nu} = 3355$ (OH) cm^{-1}; MS: a) CI: m/z (%) = 287 ($M^{+\bullet}+29$, 5), 259 ($M^{+\bullet}+1$, 100), 241 ($M^{+\bullet}+1$ – H_2O, 45); b) EI: m/z (%) = 258 ($M^{+\bullet}$, 80), 257 ($M^{+\bullet}$ – 1, 100), 241 ($M^{+\bullet}$ – OH, 20), 225 (20), 196 (10), 170 (20), 144 (20); ^{1}H NMR ($CDCl_3$): $\delta = 7.05$ (dt, $J = 1.0/7.7$ Hz, 2-H), 6.60, 6.38 (each d, each $J = 7.7$ Hz, each 1H, 1-H and 3-H), 4.31–4.26 (m, 10-H), 3.63 (t, $J = 7.9$ Hz, 5-H), 3.37–3.27, 2.99–2.95, 2.86–2.82 (each m, each 1H, 5a-H, 6a-H, and 10a-H), 2.72 (s, 4-N–CH_3), 2.69–2.58 (m, 3H, 5-H and 2×8-H), 2.38 (dd, $J = 6.3/13.6$ Hz, 6-H), 2.35 (s, 7-N–CH_3), 1.92–1.81, 1.70–1.62 (each m, 2H and 1H, 9-H/OH and 9-H), 1.41 (ddd, $J = 4.5/10.3/13.6$ Hz, 6-H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 152.95$, 133.36, 131.50 (each s, each 1C, C-3a, C-10c, and C-10b), 127.88, 115.90, 105.51, 67.22 (each d, each 1C, C-2, C-1, C-3, and

C-10), 65.50 (t, 1C, C-5), 57.47 (d, 1C, C-6a), 48.84 (t, 1C, C-8), 46.37 (d, 1C, C-10a), 42.80, 36.86 (each q, each 1C, 7- and 4-N–CH_3), 32.85 (d, 1C, C-5a), 30.38, 27.04 (each t, each 1C, C-9 and C-6) ppm.

(5aS,6aS,9R,10aR/5aR,6aR,9S,10aS)-4,7-Dimethyl-4,5,5a,6,6a,7,8,9,10,10a-decahydroindolo[4,3-fg]quinolin-9-ol (**15a**; $C_{16}H_{22}N_2O$)

Yield: 62 mg (16%); m.p.: 155°C (Et_2O/*n*-hexane/$CHCl_3$); IR (film): $\tilde{\nu}$ = 3415 (OH) cm^{-1}; MS: a) CI: *m/z* (%) = 287 ($M^{+\bullet}$ + 29, 2), 259 ($M^{+\bullet}$ + 1, 100), 241 ($M^{+\bullet}$ + 1 – H_2O, 20); b) EI: *m/z* (%) = 258 ($M^{+\bullet}$, 100), 257 ($M^{+\bullet}$ – 1, 70), 243 ($M^{+\bullet}$ – CH_3, 30), 208 (10), 182 (15), 170 (30), 144 (40); ^{1}H NMR ($CDCl_3$): δ = 7.06 (dt, *J* = 0.9/7.7 Hz, 2-H), 6.67, 6.35 (each d, each *J* = 7.7 Hz, 1-H and 3-H), 3.70–3.63 (m, 9-H), 3.57 (t, *J* = 7.7 Hz, 5-H), 3.34–3.23, 3.06–3.02 (each m, each 1H, 5a-H and 10a-H), 2.92 (ddd, *J* = 2.1/4.1/10.5 Hz, 8-H_{eq}), 2.71 (s, 4-N–CH_3), 2.60 (dd, *J* = 7.7/12.8 Hz, 5-H), 2.61–2.53, 2.48–2.44 (each m, each 1H, 10-H_{ax} (br) and 6a-H), 2.40 (dt, *J* = 4.8/13.1 Hz, 6-H), 2.30 (s, 7-N–CH_3), 2.08 (br s, OH), 2.04 (dd, *J* = 9.5/10.5 Hz, 8-H_{ax}), 1.58, 1.47 (each ddd, *J* = 5.3/10.8/12.7 and 2.4/11.9/13.1 Hz, 10-H_{eq} and 6-H) ppm; ^{13}C NMR ($CDCl_3$): δ = 152.75, 134.85, 131.65 (each s, each 1C, C-3a, C-10c and C-10b), 127.88, 114.86, 104.98 (each d, each 1C, C-2, C-1, and C-3), 64.82 (t, 1C, C-5), 64.67 (d, 1C, C-9), 63.23 (t, 1C, C-8), 61.05 (d, 1C, C-6a), 43.02 (q, 1C, 7-N–CH_3), 37.79 (d, 1C, C-10a), 36.95 (q, 1C, 4-N–CH_3), 36.13 (t, 1C, C-10), 32.58 (d, 1C, C-5a), 28.90 (t, 1C, C-6) ppm.

(5aS,6aS,9S,10aR/5aR,6aR,9R,10aS)-4,7-Dimethyl-4,5,5a,6,6a,7,8,9,10,10a-decahydroindolo[4,3-fg]quinolin-9-ol (**15b**; $C_{16}H_{22}N_2O$)

Yield: 28 mg (7%); m.p.: 117°C (Et_2O/*n*-hexane/$CHCl_3$); MS: a) CI: *m/z* (%) = 287 ($M^{+\bullet}$ + 29, 10), 259 ($M^{+\bullet}$ + 1, 100), 241 ($M^{+\bullet}$ + 1 – H_2O, 20); b) EI: *m/z* (%) = 258 ($M^{+\bullet}$, 100), 257 ($M^{+\bullet}$ – 1, 70), 243 ($M^{+\bullet}$ – CH_3, 20), 208 (10), 182 (15), 170 (25), 144 (30); ^{1}H NMR ($CDCl_3$): δ = 7.08 (dt, *J* = 0.9/7.7 Hz, 2-H), 6.74, 6.35 (each d, each *J* = 7.70 Hz, 1-H and 3-H), 3.92–3.88 (m, 9-H), 3.60 (t, *J* = 7.7 Hz, 5-H), 3.48–3.38, 2.94–2.90 (each m, 5a-H and 10a-H), 2.88 (ddd, *J* = 2.2/3.6/11.5 Hz, 8-H), 2.72 (s, 4-N–CH_3), 2.62 (dd, *J* = 7.7/12.6 Hz, 5-H), 2.64–2.58, 2.57–2.54 (each m, 10-H and 6a-H), 2.47 (dt, *J* = 4.7/13.3 Hz, 6-H), 2.39 (dd, *J* = 1.9/11.5 Hz, 8-H), 2.34 (s, 7-N–CH_3), 2.15 (br s, OH), 1.85, 1.47 (each ddd, *J* = 3.0/6.2/14.1 and 2.4/11.9/13.3 Hz, 10-H and 6-H) ppm; ^{13}C NMR ($CDCl_3$): δ = 152.82, 135.59, 131.11 (each s, each 1C, C-3a, C-10c and C-10b), 127.98, 116.33, 104.75, 66.26 (each d, each 1C, C-2, C-1, C-3, and C-9), 64.83, 62.29 (each t, each 1C, C-5 and C-8), 61.81 (d, 1C, C-6a), 42.96, 36.91 (each q, each 1C, 7-N–CH_3 and 4-N–CH_3), 35.66 (d, 1C, C-10a), 33.47 (t, 1C, C-10), 32.41 (d, 1C, C-5a), 29.92 (t, 1C, C-6) ppm.

Oxoergolines **16** *and* **17**

To a solution of 30 mg (0.12 mmol) of the required hydroxy compound **14** or **15** in 5 cm^3 dry CH_2Cl_2 100 mg grounded molecular sieves (3 Å/4 Å) and, after stirring for 5 min, 20 mg tetra-*n*-propylammonium perruthenate were added under N_2. Stirring was continued for further 20 min. The reaction mixture was purified by FC: ($CHCl_3$:MeOH = 19:1) without removing the solvent. After evaporation of the eluates *in vacuo* the residue was crystallized by treatment with a small amount of Et_2O.

(5aS,6aS,10aR/5aR,6aR,10aS)-4,7-Dimethyl-4,5,5a,6a,7,8,9,10a-octahydro-6H-indolo[4,3-fg]quinolin-10-one (**16**; $C_{16}H_{20}N_2O$)

Yield: 10 mg (33%); TLC (eluent: see FC): R_f = 0.77 (educt: R_f = 0.07); IR (KBr): $\tilde{\nu}$ = 1703 (C=O) cm^{-1}; MS: a) CI: *m/z* (%) = 297 ($M^{+\bullet}$ + 41, 2), 285 ($M^{+\bullet}$ + 29, 7), 257 ($M^{+\bullet}$ + 1, 100); b) EI: *m/z* (%) = 256 ($M^{+\bullet}$, 100), 241 ($M^{+\bullet}$ – CH_3, 20), 213 (10), 199 (10), 170 (50), 144 (25); ^{1}H NMR

($CDCl_3$): $\delta = 7.02$ (dt, $J = 1.0/7.7$ Hz, 2-H), 6.40, 6.39 (each d, each $J = 7.7$ Hz, 1-H and 3-H), 3.63 (t, $J = 7.8$ Hz, 5-H), 3.54–3.51, 3.46–3.36 (each m, 10a-H and 5a-H), 3.11 (ddd, $J = 2.6/6.1/11.4$ Hz, 8-H), 2.83–2.80 (m, 6a-H), 2.79–2.70 (ddd, $J = 6.1/13.1/13.9$ Hz, 9-H), 2.72 (s, 4-N–CH_3), 2.66 (dd, $J = 7.8/12.8$ Hz, 5-H), 2.50 (ddd, $J = 2.6/11.4/13.1$ Hz, 8-H), 2.46 (dt, $J = 3.3/13.5$ Hz, 6-H), 2.40 (s, 7-N–CH_3), 2.29 (dq, $J = 2.6/13.9$ Hz, 9-H), 1.41 (ddd, $J = 2.0/12.3/13.5$ Hz, 6-H) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 209.53$ (s, 1C, C=O), 153.36, 131.00, 128.51 (each s, each 1C, C-3a, C-10c, and C-10b), 128.27, 115.34, 105.85 (each d, each 1C, C-2, C-1, and C-3), 64.74 (t, 1C, C-5), 62.44 (d, 1C, C-6a), 55.93 (t, 1C, C-8), 53.88 (d, 1C, C-10a), 42.25 (q, 1C, 7-N–CH_3), 39.81 (t, 1C, C-9), 36.85 (q, 1C, 4-N–CH_3), 31.84 (d, 1C, C-5a), 29.94 (t, 1C, C-6) ppm.

(5aS,6aS,10aR/5aR,6aR,10aS)-4,7-Dimethyl-5,5a,6,6a,7,8,10,10a-octahydro-4H-indolo[4,3-fg]quinolin-9-one (**17**; $C_{16}H_{20}N_2O$)

Yield: 10 mg (33%); TLC (eluent: see **16**): R_f identical with that of **16**; IR (nujol): $\tilde{\nu} = 1714$ (C=O) cm^{-1}; MS: a) CI: m/z (%) = 285 ($M^{+\bullet} + 29$, 7), 257 ($M^{+\bullet} + 1$, 100); b) EI: m/z (%) = 256 ($M^{+\bullet}$, 100), 241 ($M^{+\bullet} - CH_3$, 10), 227 (20), 170 (40), 145 (30), 144 (30); ^{1}H NMR ($CDCl_3$): $\delta = 7.06$ (dt, $J = 0.8/7.7$ Hz, 2-H), 6.55, 6.36 (each d, each $J = 7.7$ Hz, 1-H and 3-H), 3.66 (t, $J = 7.9$ Hz, 5-H), 3.37–3.29 (m, 5a-H), 3.31 (d, $J = 15.9$ Hz, 8-H), 2.97–2.93 (m, 6a-H/10a-H), 2.90 (d, $J = 15.9$ Hz, 8-H), 2.89 (dd, $J = 5.0/15.5$ Hz, 10-H), 2.72 (dd, $J = 0.8/15.4$ Hz, 10-H, overlapped), 2.72 (s, 4-N–CH_3), 2.75–2.70 (m, 6a-H/10a-H), 2.66 (dd, $J = 7.9/12.3$ Hz, 5-H), 2.50 (dt, $J = 4.7/13.6$ Hz, 6-H), 2.41 (s, 7-N–CH_3), 1.60 (ddd, $J = 3.7/11.5/13.6$ Hz, 6-H) ppm.

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