225. Benz[*cd*]indoles

Part III

A New Stereospecific Synthesis of Dihydrolysergic Acid and an Entry to 14-Substituted Derivatives[1])

by **Walter E. Haefliger**

Preclinical Research, *Sandoz Ltd.*, CH-4002 Basel

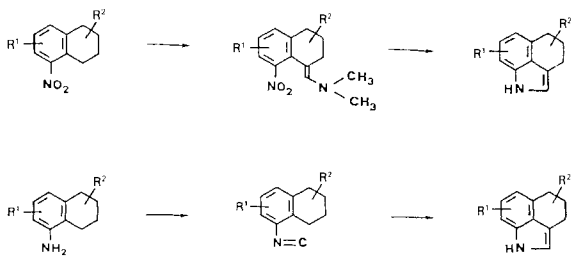
(14.VIII.84)

Summary

A new convenient synthesis of dihydrolysergic acid is described, which allows the preparation of substituted derivatives, especially those with different substituents in the aromatic ring. Starting from appropriately substituted 5-nitro-2-tetralones, the synthesis leads *via* a tricyclic isonitrile to the indole-ring closure as the last step, thus circumventing the troublesome protection/deprotection of the latter.

In our previous papers [1] [2], we reported two methods of preparing annelated indoles, the principles being shown in *Scheme 1*. These proved to be versatile and straightforward entries to tricyclic indoles. It was obvious, then, to try to extend this scheme to tetracyclic derivatives such as the ergot alkaloids which are 3,4-disubstituted

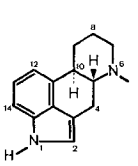
Scheme 1



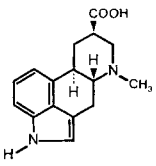
derivatives of indole, the majority of which possess the tetracyclic ring structure designated as ergoline (**1**), a partly hydrogenated indolo[4,3-*fg*]quinoline [3].

In this publication, we describe a new synthesis of dihydrolysergic acid (**2**) [4] [5] and of 14-substituted derivatives, a substitution pattern not previously accessible by other methods.

[1]) Part of this work has been presented at the 'Herbstversammlung der Schweizerischen Chemischen Gesellschaft' at Berne, on October 18, 1982.



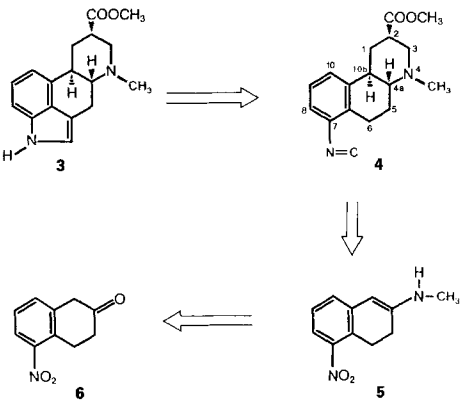
1



2

The continuing interest in the lysergic-acid field is manifested by at least half a dozen total syntheses [6] [7] and a plethora of publications and patents about their activities as CNS-agents, prolactin inhibitors, vasodilators, hypotensives *etc.* [3] [8]. All synthetic approaches to the dihydrolysergic acid as well as to lysergic acid itself use as starting material a derivative with intact indole ring which may be adequately substituted or protected. Since it is well known that the indole ring of the ergoline structure is by far the most sensitive part, it is desirable to elaborate it last. This would at the same time circumvent the problem of protecting the indole nucleus by reduction, acylation, tosylation *etc.* Both above mentioned methods of indole-ring closure offer the possibility of keeping the designated indole at the level of an amino- or nitrobenzene to the very end of the synthetic sequence. In addition, many substituents may be carried into the final product by varying the starting material.

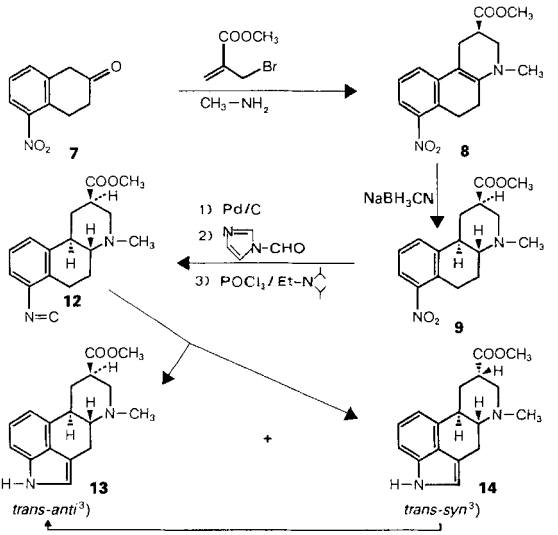
Scheme 2



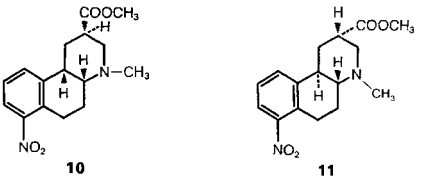
Using the isocyanide route, the retrosynthetic sequence shown in *Scheme 2* can be envisaged. For the realization of the key step **4**→**3**, the tricyclic system **4** had to be constructed, and this was done following the ring-closure procedure[2]) described by *Grob & Renk* [9] starting from a tetralone. To this end, a solution of 5-nitro-2-tetralone (**7**) [1] in benzene was condensed with methylamine and methyl 2-(bromomethyl)acrylate in a water separator for about 40 h to furnish methyl *N*-methyl-7-nitro-1,2,3,4,5,6-hexahydrobenzo[*f*]quinoline-2-carboxylate (**8**) as dark red crystals *(Scheme 3)*. Reduction of the enamino-ester **8** with sodium cyanoborohydride at pH

[2]) A literature search revealed a parent compound lacking only the substituent in position 7 of compound **4**. Thus, ethyl *trans-anti*-4-methyl-1,2,3,4,4a,5,6,10b-octahydrobenzo[*f*]quinoline-2-carboxylate[3]) has been elaborated by *Horii et al.* [10] [11] in their studies on ergot alkaloids. An analogous scheme was followed by *Cassady* [12] in the synthesis of methyl DL-dihydrolysergate from a protected dihydrobenz[*cd*]indoline.

Scheme 3



3.8–5.4 (bromocresole green) gave as the predominant product the expected *trans-anti* ester **9**, together with some *cis*-epimer **10** and a trace of the *trans-syn* ester **11**[3]). All products were easily separable by chromatography on silica gel with toluene/AcOEt (gradient) and were identified mainly by their NMR spectra. The crucial protons H–C(2), H–C(4a), and H–C(10b) could be unambiguously assigned by double-resonance experiments. The structure is further proved later in the synthesis through identification of the main products **13** and **14** (racemates) by comparison with an authentic sample of natural origin. Since only compound **9** was of interest to us, all the following synthetic steps were done exclusively with **9**.



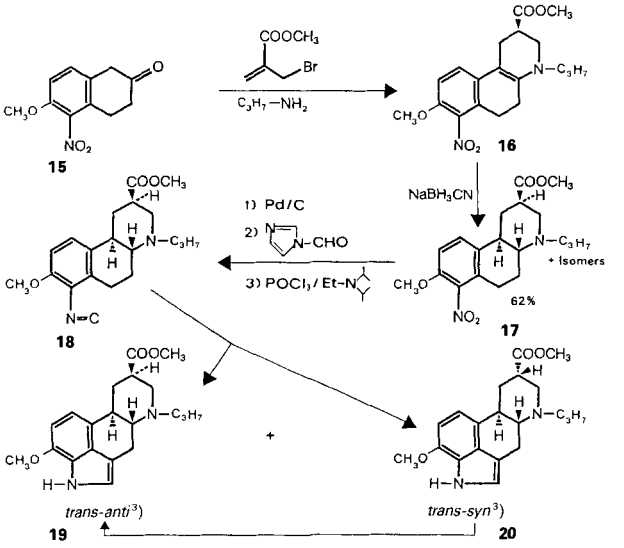
Reduction of the nitro group of **9** with Pd/C gave the corresponding amine quantitatively, which was treated with *N*-formylimidazole to give methyl 7-formylamino-*N*-methyl-1,2,3,4,4a,5,6,10b-octahydrobenzo[*f*]quinoline-2-carboxylate. Dehydration with $POCl_3$ and *N*-ethyl-*N*-isopropyl isopropylamine furnished the isonitrile **12** in high overall yield. The stage was now set for the crucial cyclization step. We knew already from our experience with the benz[*cd*]indoles [1] [2] [13] that cyclization depends heavily on the substituent in the aromatic ring. Thus, a CH_3O-substituent in the *o*-position favors the ring closure, while the unsubstituted compound cyclizes very slowly or

[3]) For the nomenclature of the different isomers compare [10]. Systematic nomenclature in the *Exper. Part.*

not at all. The isonitrile **12** in diglyme was first treated at $-70°$ with lithium diisopropylamide (LDA), then warmed up to $-20°$ and quenched with a buffer solution (pH 7) to give – to our initial surprise – not 1 but 2 products in about equal amount. They were identified spectroscopically and by comparison with authentic samples as the (±)-methyl dihydrolysergates **13** and **14**, epimeric at C(8). Apparently, the strongly alkaline conditions used in the cyclization step not only created a benzylic anion but also caused epimerization of the α-carboxylate center.

Of more interest to us were 14-substituted ergolines not accessible by other methods. Thus, we synthesized 14-methoxy-6-propyldihydrolysergate **19** starting from the known [2] β-tetralone **15** and using essentially the same reaction sequence (→**16**, **17**, **18**, *Scheme 4*) as described above. Again, both 8α- and 8β-esters **19** and **20** were obtained, in even better yield than in the unsubstituted series.

Scheme 4



In an attempt to avoid the epimerization at C(8), the ester group of **17** was reduced with $LiAlH_4$ and the resulting alcohol **21** was protected as tetrahydropyranyl ether **22** *(Scheme 5)*. Cyclization of the corresponding isocyanide **23** indeed furnished as the only product the expected 8β-ergoline **24**. A thorough investigation of the relative configuration of alcohol **25** was undertaken. With double-resonance experiments in the 360-MHz NMR, all protons on the tetracyclic C-skeleton could be assigned. A ^{13}C-NMR comparison with dihydrolysergol *(Table)* showed the close proximity of the signals of corresponding C-atoms. Finally, an X-ray analysis[4]) of the (±)-14-methoxy-6-propyl-ergolin-8-methyl mesylate **26** confirmed the above-made assumptions in every detail (see *Fig.*).

[4]) Private communication of Drs. *H. P. Weber, M. Kohler,* and *A. Widmer* of this department.

Scheme 5

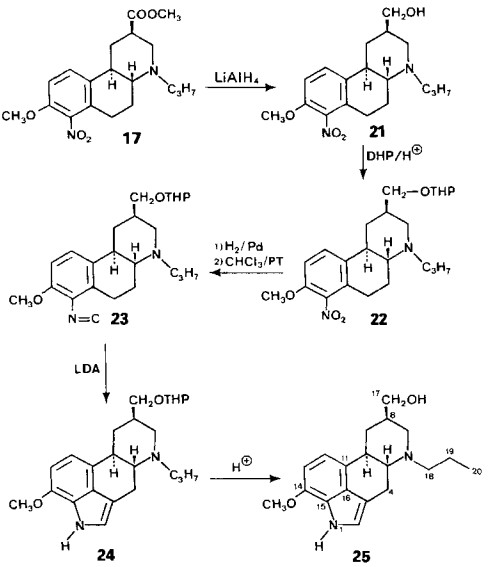
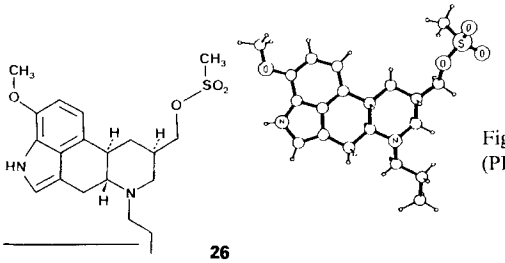


Table. *Comparison of* ^{13}*C-NMR Chemical Shifts of* **25** *and Dihydrolysergol in DMSO*

C-Atom	Dihydrolysergol	**25**	$\Delta\sigma$	Remarks
C(2)	117.9	118.3	− 0.4	
C(3)	109.7	110.7	− 1.0	
C(4)	26.5	26.5	0	
C(5)	67.0	64.2	+ 2.8	γ-effect of C(19)
C(7)	60.5	56.5	+ 4.0	γ-effect of C(19)
C(8)	38.1	38.1	0	
C(9)	30.7	31.1	− 0.4	
C(10)	39.9	40.0	− 0.1	
C(11)	132.3	125.8	+ 6.5	*p*-effect of CH_3O
C(12)	111.3	112.3	− 1.0	*m*-effect of CH_3O
C(13)	121.3	102.5	+ 18.8	*o*-effect of CH_3O
C(14)	108.0	144.3	− 36.3	α-effect of CH_3O
C(15)	132.6	123.0	+ 9.6	*o*-effect of CH_3O
C(16)	125.4	127.6	− 2.2	*m*-effect of CH_3O
C(17)	64.3	64.6	− 0.3	
C(18)	42.8	55.0	− 12.2	
C(19)	not present	17.3	new	$N-CH_3 \rightarrow N$
C(20)	not present	11.8	new	$N-CH_3 \rightarrow N$
CH_3O	not present	54.8	new	



26

Fig. *Molecular formula and perspective view of* **26** (PLUTO plot[5])

[5]) PLUTO: A program for plotting molecular and crystal structures, Sam Motherwell, University Chemical Lab, Lensfield Road, Cambridge, CB1 2EW (England).

Conclusion. – The ergoline skeleton can be synthesized from readily accessible tricyclic compounds. Substituents on the aromatics ring can be brought along with the tetralone system, but influence the yield of the cyclization step leading to the indole. The substituents on N(6) are without influence on the ring-closing procedure – as far as they are compatible with LDA. If the C(8)-substituent is an acidifying group, the product configuration can be α or β or both depending on the reaction conditions.

The synthetic methods described here should in principle be applicable to other annelated indoles.

We wish to thank the following persons for their help: Dr. *H. Braunschweiger* and *F. Seemann* for the supply of intermediates, *T. Zardin* (NMR spectra) and Prof. Dr. *D. Seebach* for a review of the manuscript.

Experimental Part

with *Edgar Kloeppner* and *Helmut Knecht*

General. Melting points (m.p.) (uncorrected): *Büchi 510*. IR: *Perkin Elmer 720* (in cm^{-1}); intensities as weak (*w*), medium (*m*), strong (*s*); broad (br.), shoulder (sh). ^{1}H-NMR: *Varian A60* (60 MHz), *Bruker HX90* (90 MHz), *Varian HA* (100 MHz), *Bruker WH360* (360 MHz); chemical shifts are given in ppm with internal tetramethylsilane (TMS) reference at 0.0 ppm, multiplicities as singlet (*s*), doublet (*d*), triplet (*t*), quadruplet (*q*), multiplet (*m*), coupling constants (*J*) in Hz. MS: *AEI MS30* for low resolution (LR) and *Varian MAT 212* for high resolution (HR) and field desorption (FD), measurements effected at 70 eV (electron energy). For column chromatography, silica gel 0.063–0.2 mm is used.

1. *Methyl 4-Methyl-7-nitro-1,2,3,4,5,6-hexahydrobenzo[f]-quinoline-2-carboxylate* (**8**). A solution of benzene (104 ml) being 1.57N in $MeNH_2$ is diluted with additional benzene (100 ml) and cooled to 5–10°. To this is added dropwise a solution of methyl 2-(bromomethyl)acrylate (14.86 g, 83 mmol) in benzene (50 ml). A white precipitate is formed. The mixture is stirred an additional 20 min at 5–10° and then treated dropwise during 5 min with 5-nitro-3,4-dihydro-2(1*H*)-naphthalenone (12.7 g, 66.4 mmol) in benzene (50 ml). The solution is then refluxed for 40 h under continuous azeotropic distillation of H_2O. The mixture is cooled to r.t., evaporated, diluted with AcOEt (100 ml), and shaken with 2N HCl (200 ml). The aq. phase is made alkaline with sat. $NaHCO_3$ and reextracted with CH_2Cl_2 (300 ml), the combined org. phase dried over Na_2SO_4, and the solvent evaporated. The dark-red oil is filtered rapidly through 70 g of silica gel with CH_2Cl_2 to give 13 g (64%) of **8**, which is crystallized from petroleum ether, m.p. 93–95°. IR (CH_2Cl_2): 2950–2850*w*, 1730*s*, 1610*s*, 1600*s*, 1550*m*, 1520*s*. ^{1}H-NMR (DMSO, 360 MHz): 2.2–2.5 (*m*, 2H, 2H–C(5)); 2.53 (*m*, 2H, 2H–C(1)); 2.78 (*m*, 1H, 1H–C(2)); 2.82 (*s*, 3H, CH_3N); 2.85–3.1 (*m*, 2H, 2H–C(6)); 3.15 (*t*, J = 10, 1H, H_{ax}–C(3)); 3.35 (*dd*, J = 10, 2, 1H, H_{eq}–C(3)); 3.68 (*s*, 3H, $COOCH_3$); 7.15 (*dd*, J = 14, 2, 1H, H–C(10)); 7.27 (*t*, J = 14, 1H, H–C(9)); 7.37 (*dd*, J = 14, 2, 1H, H–C(8)). Anal. calc. for $C_{16}H_{18}N_2O_4$ (302.33): C 63.6, H 6.0, N 9.3, O 21.2; found: C 63.5, H 5.9, N 9.1, O 21.4.

2. *Methyl (2RS,4aRS,10bSR)-4-Methyl-7-nitro-1,2,3,4,4a,5,6,10b-octahydrobenzo[f]quinoline-2-carboxylate* (**9**). To a cooled (5–10°) solution of **8** (6 g, 19.8 mmol) in THF (80 ml) and MeOH (30 ml) under N_2 and stirring, a trace of bromocresol green and $NaBH_3CN$ (2.5 g, 39.7 mmol) are added. To this mixture is added dropwise 1N HCl/MeOH so that the color of the solution remains in the pH range of the indicator (blue-brown to yellow-brown). At the end of the reaction, the yellow color just persisted. After 1 h stirring, the mixture is poured in sat. aq. $NaHCO_3$ and extracted with CH_2Cl_2 (500 ml), the combined org. phase dried over Na_2SO_4 and evaporated under vacuum. The residue is chromatographed on silical gel (200 g) with toluene/AcOEt 2:1 and then with toluene/AcOEt 1:1. The *cis-anti*[3]) ester **10** is eluted first, followed by the *trans-syn*[3]) ester **11** and finally by the desired *trans-anti*[3]) ester **9** as the main product. **9**: 3.2 g (53%), m.p. 110–112°. IR (CCl_4): 2950–2800*w*, 1735*s*, 1520*s*. ^{1}H-NMR (DMSO, 360 MHz): 1.28 (*q*, J = 12, 1H, H_{ax}–C(1)); 1.8 (*tt*, J = 10, 2, 1H, H–C(4a)); 2.12 (*t*, J = 11, 1H, H_{ax}–C(3)); 2.3 (*s*, 3H, CH_3N); 2.25–2.35 (*m*, 1H, H–C(5)); 2.66 (*tt*, J = 11, 3, 1H, H–C(10b)); 2.78 (*dt*, 1H, H–C(1)); 2.85 (*tt*, J = 12, 3, 1H, H–C(2)); 2.9–3.0 (*m*, 2H, 2H–C(6)); 3.1 (*dd*, J = 12, 3, 1H, H_{eq}–C(3)). 3.66 (*s*, 3H, $COOCH_3$); 7.2–7.8 (*m*, 3H, arom. H). Anal. calc. for $C_{16}H_{20}N_2O_4$ (304.3): C 63.1, H 6.6, N 9.2, O 21.0; found: C 63.3, H 6.8, N 9.2, O 20.9.

Methyl (2RS,4aRS,10bRS)-4-Methyl-7-nitro-1,2,3,4,4a,5,6,10b-octahydrobenzo[f]quindine-2-carboxylate (**10**): 1.2 g (20%), m.p. 98–102°. IR (CCl_4): 2950–2800*w*, 1735*s*, 1530*s*. ^{1}H-NMR ($CDCl_3$, 360 MHz): 1.77 (*m*,

1H, H_{ax}–C(1)); 2.0 (*m*, 1H, H_{ax}–C(5)); 2.15 (*m*, 1H, H_{eq}–C(1)); 2.35 (*s*, 3H, CH_3N); 2.5 (*m*, 4H, H_{ax}–C(3), H–C(4a), H_{eq}–C(5), H_{ax}–C(6)); 2.85 (*tt*, *J* = 18, 5, 1H, H–C(2)); 2.97 (*d*, *J* = 8, 1H, H_{eq}–C(6)); 3.12 (*dd*, *J* = 12, 6, 1H, H_{eq}–C(3)); 3.2 (*q*, *J* = 10, 1H, H–C(10b)); 3.11 (*s*, 3H, $COOCH_3$); 7.2–7.8 (*m*, 3H, arom. H). Anal. calc. for $C_{16}H_{20}N_2O_4$ (304.3): C 63.1, H 6.6, N 9.2, O 21.0; found: C 63.1, H 6.7, N 9.4, O 21.3.

*Methyl (2*RS,*4a*SR,*10b*RS*)-4-Methyl-7-nitro-1,2,3,4,4a,5,6,10b-octahydrobenzo[*f*]quinoline-2-carboxylate* (**11**): 0.23 g (4%), m.p. 108–113°. IR (CCl_4): 2950–2800*w*, 1740*s*, 1530*s*. ^{1}H-NMR (DMSO, 360 MHz): 1.37 (*m*, 2H, H_{ax}–C(1), H_{ax}–C(5)); 1.8 (*td*, *J* = 11, 3, 1H, H–C(4a)); 2.2 (*s*, 3H, CH_3N); 2.3 (*dd*, *J* = 14, 3, 1H, H_{ax}–C(3)); 2.4–2.6 (*m*, 1H, H_{eq}–C(5)); 2.75 (*tt*, *J* = 12, 3, 1H, H–C(10b)); 2.82 (*dd*, *J* = 12, 3, 1H, H_{eq}–C(1)); 2.92 (*m*, 2H, 2H–C(6), H–C(2)); 3.3 (*dd*, *J* = 10, 2, 1H, H_{eq}–C(3)); 3.68 (*s*, 3H, $COOCH_3$); 7.3–7.8 (*m*, 3H, arom. H). Anal. calc. for $C_{16}H_{20}N_2O_4$ (304.3): C 63.1, H 6.6, N 9.2, O 21.0; found: C 63.4, H 6.6, N 9.2, O 20.8.

3. *Methyl (2*RS,*4a*RS,*10b*SR*)-7-Formylamino-4-methyl-1,2,3,4,4a,5,6,10b-octahydrobenzo[f]quinoline-2-carboxylate.* A solution containing **9** (2 g, 6.6 mmol) in MeOH (120 ml) and 0.8 g 10% Pd/C is hydrogenated at r.t. After 2 h, it was filtered through talc and evaporated *in vacuo*. The residue was taken up in THF (40 ml), and formylimidazole (0.94 g, 9.8 mmol) in THF (10 ml) is added dropwise during 1 h. The solution is stirred for 3 h and then evaporated, the residue is taken up in CH_2Cl_2 (100 ml) and extracted 3 × with buffer solution of pH 7, and the org. phase dried over Na_2SO_4 and evaporated. The product crystallizes from petroleum ether: 1.8 g (90%), m.p. 143–147°. IR (CH_2Cl_2): 3100–2800*w*, 1735*s*, 1695*s*, 1590*m*, 1475*m*. ^{1}H-NMR (DMSO, 360 MHz): 1.2 (*q*, *J* = 12, 1H, H_{ax}–C(1)); 1.4 (*m*, 1H, H_{ax}–C(5)); 1.73 (*td*, *J* = 10, 4, 1H, H_{ax}–C(4a)); 2.12 (*t*, *J* = 11, 1H, H_{ax}–C(3)); 2.25–2.35 (*dd*, 1H, H_{eq}–C(5)); 2.3 (*s*, 3H, CH_3N); 2.5–2.9 (*m*, 5H, 2H–C(6), H–C(2), H–C(1), H–C(10b)); 3.08 (*dd*, *J* = 11, 3, 1H, H_{eq}–C(3)); 3.65 (*s*, 3H, $COOCH_3$); 7.1–7.6 (*m*, 3H, arom. H); 8.35 (*m*, 1H, CHO); 9.5 (*m*, 1H, NHCO). Anal. calc. for $C_{17}H_{22}N_2O_3$ (302.37): C 67.5, H 7.3, N 9.3, O 15.9; found: C 67.4, H 7.3, N 9.2, O 16.0.

4. *Methyl (2*RS,*4a*RS,*10b*SR*)-7-Isocyano-4-methyl-1,2,3,4,4a,5,6,10b-octahydrobenzo[f]quinoline-2-carboxylate* (**12**). Methyl 7-formylamino-4-methyl-1,2,3,4,4a,5,6a,10b-octahydrobenzo[*f*]quinoline (1.7 g, 5.6 mmol) is dissolved in CH_2Cl_2 (20 ml) under stirring and cooling with an ice bath. To this solution are added *N*-ethyl-*N*-isopropylisopropylamine (3.9 ml, 2.2 mmol) and then dropwise $POCl_3$ (0.56 ml, 0.62 mmol) in CH_2Cl_2 (5 ml) during 10 min. After 4 h at r.t., the mixture is poured on buffer solution of pH 7 (100 ml). The CH_2Cl_2-phase is extracted 2 × with H_2O, dried over Na_2SO_4, evaporated *in vacuo*, and filtered through silica gel (30 g) with CH_2Cl_2/MeOH 97:3: 1.4 g (88%), m.p. 91–93°, from petroleum ether. IR (CH_2Cl_2): 2950–2800*w*, 2250*m*, 1730*s*, 1460–1430*m*. ^{1}H-NMR (DMSO, 360 MHz): 1.2 (*q*, *J* = 12, 1H, H_{ax}–C(1)); 1.45 (*m*, 1H, H_{ax}–C(5)); 1.78 (*tt*, *J* = 10, 3, 1H, H–C(4a)); 2.11 (*t*, *J* = 11, 1H, H_{ax}–C(3)); 2.3–2.4 (*dd*, 1H, H_{eq}–C(5)); 2.3 (*s*, 3H, CH_3N); 2.6 (*td*, *J* = 9, 3, 1H, H–C(10b)); 2.7–2.9 (*m*, 3H, H_{eq}–C(1), H–C(2), H_{ax}–C(6)); 2.95 (*dd*, *J* = 1,8, 4, 1H, H_{eq}–C(6)); 3.1 (*dd*, *J* = 11, 3, 1H, H_{eq}–C(3)); 3.65 (*s*, 3H, $COOCH_3$); 7.2–7.6 (*m*, 3H, arom. H). Anal. calc. for $C_{17}H_{20}N_2O_2$ (284.4): C 71.8, H 7.1, N 9.9, O 11.3; found: C 71.9, H 7.4, N 10.0, O 11.3.

5. *Methyl 8β,8α-Dihydrolysergates (= Methyl (6a*RS,*9*RS,*10a*SR*)- and (6a*RS,*9*SR,*10a*SR*)-7-Methyl-4,6,6a,7,8,9,10,10a-octahydroindolo[4,3-fg]quinoline-9-carboxylate; **13** and **14**, resp.).* In a thoroughly dried flask under N_2, dry diglyme (5 ml) is placed and cooled to − 78°. With a syringe, 1.65N BuLi in hexan (4.3 ml, 7 mmol) is added dropwise. A white precipitate is formed. After 10 min of stirring, diisopropylamine (0.99 ml, 7 mmol) in diglyme (3 ml) is added. To this solution is added dropwise, after 15 min at − 78°, a solution of **12** (0.4 g, 1.41 mmol) in diglyme (8 ml). The red solution is again stirred for 20 min, warmed up to − 20° and left at − 20° for 45 min. The mixture is then poured on buffer solution of pH 7 (200 ml) and extracted with CH_2Cl_2. The org. phase is dried over Na_2SO_4, evaporated under vacuum, and chromatographed on silica gel with CH_2Cl_2/MeOH 98:2. First, **14** is eluted. Mixed fractions are chromatographed again on a silica-gel column with BuOH/AcOH/H_2O 4:1:2, where a better separation of **13** and **14** is obtained. On this column, **13** is eluted first. **13**: 100 mg (25%), m.p. 135–140°. **14**: 110 mg (28%), m.p. 146–153°. IR, MS: identical with those of authentic methyl dihydrolysergate. TLC (silica gel, BuOH/AcOH/H_2O 4:1:2, *Van Urk*'s reagent) and ^{1}H-NMR (360 MHz, double resonance) further corroborate the assignment structure.

6. *6-Methoxy-5-nitro-3,4-tetrahydro-2(1*H*)-napthalenone* (**15**). To DMSO (19 ml; 0.268 mol) and CH_2Cl_2 (250 ml) at − 78° is added dropwise during 15 min trifluoracetic anhydride (28 ml, 0.2 mol). After stirring for 30 min at − 78°, 6-methoxy-5-nitro-1,2,3,4-tetrahydro-2-naphthol [14] (30.0 g, 0.135 mol) in CH_2Cl_2 250 ml is added dropwise, stirred for an additional 30 min and then *N*-ethyl-*N*-isopropylisopropylamine (66.0 ml, 0.383 mol) is added dropwise. The cooling bath is then removed and the mixture left to reach r.t. (1–2 h). The solution is poured on H_2O (1 l), extracted 3 × with CH_2Cl_2, the combined org. phases are dried over Na_2SO_4, evaporated under vacuum, and the residue is filtered through silica gel (100 g) with CH_2Cl_2 to yield 23 g (76%) of **15** which crystallized from Et_2O/hexane, m.p. 103–105°. IR (CH_2Cl_2): 3000 (br.), 1720*s*, 1620*m*, 1590*m*, 1540*s*, 1500*s*, 1380*s*, 1290*s*, 1080*s*, 980*s*, 810*s*. ^{1}H-NMR ($CDCl_3$, 90 MHz): 2.55 (*q*, *J* = 6, 2H, $H_2C(3)$); 2.95 (*q*, *J* = 6,

2H, $H_2C(4)$); 3.55 (*s*, 2H, $H_2C(1)$); 3.9 (*s*, 3H,CH_3O); 7.05 (*AB*, *J* = 8, 2H, arom. H). Anal. calc. for $C_{11}H_{11}NO_4$ (221): C 60.0, H 4.9, N 6.3, O 28.9; found: C 60.1, H 4.9, N 6.4, O 28.6.

7. *Methyl (*RS*)-8-Methoxy-7-nitro-4-propyl-1,2,3,4,5,6-hexahydrobenzo[*f*]quinoline-2-carboxylate* (**16**). To benzene (300 ml) and propylamine (31 ml, 0.38 mol) under N_2 is added dropwise at 5–10° methyl 2-(bromomethyl) acrylate (31.7 g, 0.177 mol). After stirring for 30 min, **15** (34 g, 0.154 mol) in benzene (300 ml) is added and the mixture refluxed on a water separation apparatus for 26 h (→deep yellow solution). The mixture is extracted 3 × with 2N HCl and AcOEt, the aq. phase adjusted to pH 8 with $NaHCO_3$, reextracted with AcOEt (500 ml), dried over Na_2SO_4, and evaporated *in vacuo*. The residue is crystallized from MeOH (100 ml) to yield 34 g (62%) of deep red crystals, m.p. 117–118°. UV: 318 (21931). IR (CH_2Cl_2): 2950–2800*w*, 1720*s*, 1605*s*, 1530*s*, 1485*s*, 1370*s*. ^{1}H-NMR ($CDCl_3$, 90 MHz): 0.88 (*t*, *J* = 7, 3H, $CH_3CH_2CH_2N$); 1.3–1.7 (*m*, 2H); 2.2–3.4 (*m*, 11H); 3.75 (*s*, 3H, $COOCH_3$); 3.82 (*s*, 3H, CH_3O); 6.7–7.1 (*AB*, *J* = 9, arom. H). Anal. calc. for $C_{19}H_{24}N_2O_5$ (358.44): C 63.7, H 6.7, N 7.8, O 22.3; found: C 63.6, H 6.6, N 7.8, O 22.1.

8. *Methyl (2*RS,*4a*RS,*10b*SR*)-8-Methoxy-7-nitro-4-propyl-1,2,3,4,4a,5,6,10-octahydrobenzo[*f*]-2-carboxylate* (**17**). A solution of **16** (45 g, 0.123 mol) in THF (900 ml) and MeOH (350 ml) is cooled with an ice bath, and a trace of bromocresol green and $NaBH_3CN$ (15.8, 0.25 mol) is added under stirring. To this mixture is added dropwise 1N HCl/MeOH so that the color of the solution remains in the pH range of the indicator (green-yellow). When all **16** is consumed (TLC), the mixture is worked up and chromatographed as under *2*: 26 g (58%) of **17** after recrystallization from Et_2O, m.p. 168–170°. IR (CH_2Cl_2): 2950–2800 (br.), 1725*s*, 1610*w*, 1575*w*, 1530*s*, 1490*m*, 1370*m*. ^{1}H-NMR ($CDCl_3$, 360 MHz): 0.89 (*t*, *J* = 7, 3H, $CH_3CH_2CH_2N$); 1.38 (*q*, *J* = 12, 1H, H_{ax}–C(1)); 1.5 (*m*, 3H); 2.12 (*td*, *J* = 10, 3, 1H, H–C(4a)); 2.3 (*m*, 1H, H–C(5)); 2.39 (*t*, *J* = 12, H_{ax}–C(3)); 3.72 (*s*, 3H, $COOCH_3$); 3.87 (*s*, 3H, CH_3O); 6.88 (*d*, *J* = 6, H–C(9)); 7.35 (*d*, *J* = 7, H–C(10)). Anal. calc. for $C_{19}H_{26}N_2O_5$ (362.45): C 63.0, H 7.2, N 7.7, O 22.1; found: C 63.1, H 7.2, N 7.6, O 22.3.

The *cis-anti*[3]) ester (corresponding to **10**; (2*RS*,4a*RS*,10b*RS*)-isomer of **17**) is isolated in 18% yield (8 g) after recrystallization from Et_2O, m.p. 108–109°. IR (CH_2Cl_2): 2950–2800 (br.), 1725*s*, 1610*w*, 1575*w*, 1530*s*, 1490*m*, 1375*m*. ^{1}H-NMR ($CDCl_3$, 360 MHz): 0.88 (*t*, *J* = 7, 3H, $CH_3CH_2CH_2N$); 1.48 (*m*, 2H); 1.7 (*m*, 1H, H_{ax}–C(5)); 2.1 (*m*, 3H, 2H–C(1), H_{eq}–C(5)); 2.4 (*m*, 2H, CH_2N); 2.5 (*m*, 2H, H_{ax}–C(3), H–C(2)); 2.8 (*m*, 4H, 2H–C(6), H_{eq}–C(3), H–C(4a)); 3.2 (*m*, 1H, H–C(10a)); 3.21 (*s*, 3H, $COOCH_3$); 3.85 (*s*, 3H, CH_3O); 6.88 (*d*, *J* = 7, H–C(9)); 7.3 (*d*, *J* = 7, H–C(10)). Anal. calc. for $C_{19}H_{26}N_2O_5$ (362.45): C 63.0, H 7.2, N 7.7, O 22.1; found: C 62.9, H 7.1, N 7.7, O 21.9.

The *trans-syn*[3]) ester (corresponding to **11**; (2*RS*,4a*SR*,10b*RS*)-isomer of **17**) is isolated in 13% yield (6 g) after recrystallization from Et_2O, m.p. 140–141°. IR (CH_2Cl_2): 2950–2800 (br.), 1730*s*, 1610*w*, 1575*w*, 1530*s*, 1490*m*, 1370*m*. ^{1}H-NMR ($CDCl_3$, 360 MHz): 0.88 (*t*, *J* = 7, 3H, $CH_3CH_2CH_2N$); 1.35 (*td*, *J* = 12, 4, 1H, H–C(1)); 1.45 (*q*, 2H, *J* = 7, $CH_3CH_2CH_2N$); 1.5 (*m*, 1H, H_{ax}–C(5)); 2.05 (*td*, 1H, *J* = 11, 2, H–C(4a)); 2.3 (*m*, 1H, H_{eq}–C(5)); 2.35 (*m*, 2H, H_{ax}–C(3), H_{ax}–C(6)); 2.75 (*m*, 5H, H_{eq}–C(6), H–C(3), H–C(10a), CH_2N); 2.9 (*m*, 1H, H_{eq}–C(1)); 3.5 (*d*, *J* = 12, H_{eq}–C(3)); 3.75 (*s*, 3H, $COOCH_3$); 3.85 (*s*, 3H, CH_3O); 6.88 (*d*, *J* = 9, H–C(9)); 7.40 (*d*, *J* = 6, H–C(10)). Anal. calc. for $C_{19}H_{26}N_2O_5$ (362.45): C 63.0, H 7.2, N 7.7, O 22.1; found: C 63.2, H 7.3, N 7.6, O 22.4.

9. *Methyl (2*RS,*4a*RS,*10b*SR*)-7-Formylamino-8-methoxy-4-propyl-1,2,3,4,4a,5,6,10b-octahydrobenzo[*f*]quinoline-2-carboxylate*. A solution of **17** (18 g, 0.049 mol) in MeOH (400 ml) containing 10% Pd/C (1.8 g) is hydrogenated for 16 h. Then the solution is filtered through talc and evaporated *in vacuo*. The residue is dissolved in THF (250 ml) and *N*-formylimidazole (4.1 g, 0.043 mol) in THF (50 ml) is added dropwise during 5–8 h. After additional stirring for 2 days, the mixture is evaporated *in vacuo* and filtered through silica gel (100 g) with $CHCl_3$/MeOH 95:5 to yield 11.5 g (64%) of the title compound; m.p. 147–148°, recrystallized from AcOEt. IR (CH_2Cl_2): 3400*w*, 3100–2800 (br.), 1730*s*, 1700*s*, 1605*w*, 1585*w*, 1500*m*. ^{1}H-NMR ($CDCl_3$, 90 MHz): 0.9 (*t*, *J* = 6, 3H, $CH_3CH_2CH_2N$); 1.0–1.8 (*m*, 4H); 2.0–3.4 (*m*, 11H); 3.7 (*s*, 3H, $COOCH_3$); 3.8 (*s*, 3H, CH_3O); 6.6–7.3 (*m*, 3H, arom. H); 8.3 (*m*, 1H, CHO). Anal. calc. for $C_{20}H_{28}N_2O_4$ (360.45): C 66.6, H 7.8, N 7.8, O 17.8; found: C 66.4, H 7.9, N 8.0, O 18.0.

10. *Methyl (2*RS,*4a*RS,*10b*SR*)-7-Isocyano-8-methoxy-4-propyl-1,2,3,4,4a,5,6,10b-octahydrobenzo[*f*]quinoline-2-carboxylate* (**18**). To a cooled (0°) solution of methyl 7-formylamino-8-methoxy-4-propyl-1,2,3,4,4a,5,6,10b-octahydrobenzo[*f*]quinoline-2-carboxylate (7.3 g, 20 mmol) in CH_2Cl_2 (300 ml) are added under stirring *N*-ethyl-*N*-isopropyl-isopropylamine (13.9 ml, 80.8 mmol) and then dropwise $POCl_3$ (2.04 ml, 22.3 mmol). The mixture is kept for 20 min at 0° and then for 28 h at r.t. The solution is then poured on H_2O, extracted 3 × with 100 ml of CH_2Cl_2, dried over Na_2SO_4 and evaporated *in vacuo*. The residue is chromatographed on silica gel with CH_2Cl_2/MeOH 98:2 to yield 5.4 g (75%) of **18**, m.p. 137–138°. IR (CH_2Br_2): 2950–2800 (br.), 2250*m*, 1730*s*, 1605*w*, 1580*w*, 1500*s*. ^{1}H-NMR ($CDCl_3$, 100 MHz): 0.9 (*t*, *J* = 7, 3H, $CH_3CH_2CH_2N$); 1.2–1.8 (*m*, 4H); 2.0–3.4 (*m*, 11H); 3.7 (*s*, 3H, CH_3O); 3.85 (*s*, 3H, $COOCH_3$); 6.7–7.3 (*m*, 2H,

arom. H). MS (LR): 342 (M^+), 313, 238, 185, 142, 105, 82, 55. Anal. calc. for $C_{20}H_{26}N_2O_3$ (342.44): C 70.2, H 7.7, N 8.2, O 14.0; found: C 70.2, H 7.7, N 8.2, O 14.2.

11. *Methyl 14-Methoxy-6-propylergoline-8-carboxylates (= Methyl (6a*RS,*9*RS,*10a*SR)- *and (6a*RS,*9*SR,*10a*SR)-*3-Methoxy-7-propyl-4,6,6a,7,8,9,10,10a-octahydroindolo[4,3-*fg*]*quinoline-9-carboxylate;* **19** *and* **20** *resp.* To diglyme (40 ml; dried over aluminium oxide under dry N_2) is added dropwise BuLi (30.3 ml, 50 mmol) at $-40°$. Stirring is continued for 10 min, then diisopropylamine (7.1 ml, 50 mmol) is added and the solution stirred for an additional 15 min. Then, ester **18** (1.71 g, 5 mmol) as a suspension in diglyme is added dropwise (→deep red). After 15 min at $-40°$, the mixture is warmed to $-20°$, left for 30 min at $-20°$ (red→brown), poured on buffer solution of pH 7 (500 ml), extracted with AtOEt, dried over Na_2SO_4 and evaporated under vacuum. Chromatography on a silica gel column with CH_2Cl_2/MeOH 98:2 yields 1.4 g (82%) of **19**/**20** which is separated by repeated chromatography on silica gel with CH_2Cl_2/MeOH 99:1 to furnish **19** and **20** in a proportion of *ca.* 1:1. **19**: m.p. 139–140°. IR (CH_2Cl_2): 3400*m*, 2950–2800 (br.), 1730*s*, 1520*m*. ^{1}H-NMR ($CDCl_3$, 360 MHz): 0.91 (*t*, J = 7, 3H, $CH_3CH_2CH_2N$); 1.55 (*m*, 3H, H_{ax}–C(9), $CH_3CH_2CH_2N$); 2.55 (*t*, J = 11, 1H, H_{ax}–C(7)); 2.0 (*td*, 1H, H–C(5)); 2.7 (*dd*, J = 12, 10, 1H, H_{ax}–C(4)); 2.81 (*t*, J = 7, 2H, $CH_3CH_2CH_2N$); 2.83–3.0 (*m*, 3H, H–C(8), H–C(9), H–C(10)); 3.25–3.4 (*m*, 2H, H_{eq}–C(7), H_{eq}–C(4)); 3.78 (*s*, 3H, $COOCH_3$); 3.93 (*s*, 3H, CH_3O); 6.5–7.0 (*m*, 3H, H–C(2), arom. H); 8.2 (br., 1H, NH). MS (LR): 342 (M^+), 327, 313, 282, 267, 223, 184, 148, 115, 91. Anal. calc. for $C_{20}H_{26}N_2O_3$ (342.44): C 70.2, H 7.7, N 8.2, O 14.0; found: C 70.3, H 7.8, N 8.1, O 14.2.

20: m.p. 153–154°. IR (CH_2Cl_2): 3450*m*, 2950–2800 (br.), 1730*s*, 1520*m*. ^{1}H-NMR ($CDCl_3$, 360 MHz): 0.9 (*t*, J = 7, $CH_3CH_2CH_2N$); 1.5 (*m*, J = 7, 2H, $CH_3CH_2CH_2N$); 1.58 (*td*, J = 14, 4, 1H, H_{ax}–C(9)); 2.42 (*td*, J = 8, 4, 1H, H–C(5)); 2.51 (*dd*, J = 12, 3, 1H, H_{ax}–C(7)); 2.65 (*m*, 1H, H_{ax}–C(4)); 2.55–2.9 (*m*, 2H, $CH_3CH_2CH_2N$); 2.8 (*m*, 1H, H–C(8)); 3.0–3.15 (*m*, 2H, H_{eq}–C(9), H–C(10)); 3.3 (*dd*, J = 14, 4, 1H, H_{eq}–C(4)); 3.52 (*d*, J = 12, 1H, H_{eq}–C(7)); 3.75 (*s*, 3H, $COOCH_3$); 3.92 (*s*, 3H, OCH_3); 6.5–6.9 (*m*, 3H, arom. H, H–C(2)); 8.0 (br., 1H, NH). MS (LR): 342 (M^+), 327, 313, 282, 267, 223, 184, 148, 115, 91. Anal. calc. for $C_{20}H_{26}N_2O_3$ (342.44): C 70.2, H 7.7, N 8.2, O 14.0; found: C 70.1, H 7.8, N 8.3, O 14.1.

12. (2RS,*4a*RS,*10b*SR)*-8-Methoxy-7-nitro-4-propyl-1,2,3,4,4a,5,6,10b-octahydrobenzo[*f*]quinoline-2-methanol* (**21**). To a solution of **17** (3.2 g, 8.84 mmol) in THF (150 ml) under N_2 and stirring at 0° is added $LiAlH_4$ (1.3 g, 34 mmol). After 90 min, the mixture is poured on aq. NH_4Cl, extracted 3 × with 100 ml of AcOEt, dried over Na_2SO_4, and evaporated under vacuum. The residue is crystallized from Et_2O to yield 2.9 g (94%) of **21**, m.p. 140–142°. IR (CH_2Cl_2): 3600*w*, 3000–2800*m*, 1540*s*, 1500*m*, 1380*m*, 1290*m*, 1080*m*. ^{1}H-NMR ($CDCl_3$, 360 MHz): 0.88 (*t*, J = 8, 3H, $CH_3CH_2CH_2N$); 0.95 (*q*, J = 12, 1H, H_{ax}–C(1)); 1.5 (*m*, 2H, $CH_3CH_2CH_2N$); 1.6 (*m*, 1H, H_{ax}–C(5)); 2.01 (*m*, 1H, H_{ax}–C(3)); 2.02 (*m*, 1H, H–C(2)); 2.1 (*dd*, J = 11, 3, 1H, H–C(4a)); 2.32 (*tt*, J = 7, 1H, H_{eq}–C(5)); 2.51 (*dd*, J = 11, 2, 1H, H_{eq}–C(1)); 2.6 (*td*, J = 12, 3, 1H, H–C(10b)); 2.6 (*m*, 2H, CH_2N); 2.8 (*m*, 2H, $H_2C(6)$); 3.16 (*dd*, J = 9, 3, 1H, H_{eq}–C(3)); 3.58 (*AB* of *ABX*, J = 11, 6, 2H, CH_2OH); 3.86 (*s*, 3H, CH_3O); 6.9 (*d*, H–C(9)); 7.3 (*d*, J = 9, H–C(10)). MS (LR): 334 (M^+), 305, 275, 258, 205, 189, 128, 115, 91, 72. Anal. calc. for $C_{18}H_{26}N_2O_4$ (334.42): C 64.7, H 7.8, N 8.4, O 19.1; found: C 64.6, H 8.1, N 8.3, O 19.0.

13. *(2*RS,*4a*RS,*10b*SR)*-8-Methoxy-7-nitro-4-propyl-2-(tetrahydro-2*H*-2-pyranyloxy)methyl-1,2,3,4,4a,5,6,10b-octahydrobenzo[f]quinoline* (**22**). Anh. TsOH (1.5 g, 8.7 mmol) is added to **21** 2.5 g (7.5 mmol) in CH_2Cl_2 (100 ml) at 0°. To this, 3,4-dihydro-2H-pyran (1 ml, 11 mmol) is added, the mixture kept at r.t. for 5 h, then poured on sat. aq. $NaHCO_3$, and extracted 3 × with 50 ml of CH_2Cl_2. The org. phase is dried over Na_2SO_4, evaporated under vacuum, and the residue chromatographed on silica gel (50 g) with CH_2Cl_2/MeOH 95:5 to yield 2.7 g (64%) of **22**; crystallized from hexane, m.p. 93–94°. IR (CH_2Cl_2): 2950 (br.), 1540*s*, 1500*m*, 1380*m*, 1290*m*. ^{1}H-NMR ($CDCl_3$, 100 MHz): 0.9 (*t*, J = 6, 3H, $CH_3CH_2CH_2N$); 1.3–3.0 (*m*, 19H); 3.0–4.1 (*m*, 6H); 3.85 (*s*, 3H, CH_3O); 4.6 (*m*, 1H, OCHO); 7.1 (*AB*, J = 9, arom. H). Anal. calc. for $C_{23}H_{34}N_2O_5$ (402.55): C 68.6, H 8.4, N 7.0, O 19.9; found: C 68.4, H 8.5, N 6.9, O 19.8.

14. *(2*RS,*4a*RS,*10b*SR)*-7-Isocyano-8-methoxy-4-propyl-2-(tetrahydro-2*H*-2-pyranyloxy)methyl-1,2,3,4,4a,5,6,10b-octahydrobenzo[f]quinoline* (**23**). A solution of **22** (19 g, 46.2 mmol) in MeOH (50 ml) containing 10% Pd/C (1.5 g) is hydrogenated for 5 h. The mixture is filtered through talc and evaporated *in vacuo* to yield 17 g of *7-amino-8-methoxy-4-propyl-2-(tetrahydro-2*H*-2-pyranyloxy)methyl-1,2,3,4,4a,5,6,10b-octahydrobenzo[f]quinoline.* To a mixture of 50% aq. KOH (21.7 ml), CH_2Cl_2 (12 ml), and benzyltributylammonium bromide (215 mg) is added dropwise under efficient mixing with a vibromixer at 20° the above amine (17 g, 44.6 mmol) in CH_2Cl_2 (12 ml) and $CHCl_3$ (8.7 ml). After 16 h, the mixture is diluted with H_2O, extracted 3 × with CH_2Cl_2, and the org. phase dried over Na_2SO_4 and evaporated under vacuum. The residue is chromatographed over silica gel (200 g) with CH_2Cl_2/MeOH 95:5 and crystallized from Et_2O/hexane: 10 g (55%), m.p. 70–71°. IR (CH_2Cl_2): 2900 (br.), 2250*m*, 1600*w*, 1495*s*. ^{1}H-NMR ($CDCl_3$, 90 MHz): 0.9 (*t*, J = 8, 3H, $CH_3CH_2CH_2N$);

1.4–3.8 (*m*, 25H); 3.9 (*s*, 3H, CH_3O); 4.6 (*s*, 1H, OCHO); 7.0 (*AB*, J = 9, arom. H). MS (LR): 398 (M^+), 369, 313, 285, 255, 185, 172, 85. Anal. calc. for $C_{24}H_{34}N_2O_3$ (398.55): C 72.3, H 8.6, N 7.0, O 12.0; found: C 72.1, H 8.8, N 7.1, O 11.8.

15. *14-Methoxy-6-propyl-8-(tetrahydro-2*H*-2-pyranyloxy)methyl-ergolin (= (6a*RS,*9*RS,*10a*SR*)-3-Methoxy-7-propyl-9-(tetrahydro-2*H*-2-pyranyloxy)methyl-4,6,6a,7,8,9,10,10a-octahydroindolo[4,3-*fg*]quinoline;* **24**). To diglyme (dried over aluminium oxide) under Ar is added dropwise BuLi (30.4 ml, 50.2 mmol) at – 78°. After 15 min stirring, diisopropylamine (7.2 ml, 50.2 mmol) is added dropwise, and after an additional 15 min, **23** (2 g, 5.1 mmol) in diglyme (20 ml) is added in the same way. The solution is stirred for 30 min at – 78°, warmed up to – 25°, and kept for 4 h at – 20 to – 25°. The mixture is then poured on buffer solution of pH 7, extracted 5 × with AcOEt, dried over Na_2SO_4, evaporated under vacuum, and chromatographed on a silica gel column with CH_2Cl_2/MeOH 95:5 to yield 1.85 g (92%) of **24**; m.p. 77–80°, after recrystallization from Et_2O/hexane. IR (CH_2Cl_2): 3400*m*, 2900 (br.), 1520*m*. ^{1}H-NMR ($CDCl_3$, 90 MHz): 0.9 (*t*, J = 7, 3H, $CH_3CH_2CH_2N$); 1.1–3.8 (*m*, 23H); 3.9 (*s*, 3H, CH_3O); 4.6 (*s*, 1H, OCHO); 6.6 (*AB*, J = 8, arom. H); 3.82 (*s*, 1H, H–C(2)); 8.25 (*s*, 1H, NH). MS (LR): 398 (M^+), 383, 369, 313, 297, 285, 269, 226, 154, 85. Anal. calc. for $C_{24}H_{34}N_2O_3$ (398.55): C 72.3, H 8.6, N 7.0, O 12.0; found: C 72.5, H 8.4, N 6.9, O 11.9.

16. *14-Methoxy-6-propylergolin-8-methanol (= (6a*RS,*9*RS,*10a*SR*)-3-Methoxy-7-propyl-4,6,6a,7,8,9,10,10a-octahydroindolo[4,3-*fg*]quinoline-9-methanol* **25**). To a solution of **24** (160 mg, 0.4 mmol) in MeOH (5 ml) is added TsOH · H_2O (84 mg, 0.44 mmol) under stirring. After 2 h, the mixture is evaporated, sat. aq. $NaHCO_3$ (10 ml) is added and extracted 5 × with 10 ml of AcOEt. The org. phase is dried over Na_2SO_4, evaporated under vacuum and treated with Et_2O. The resulting crude material is dissolved in i-PrOH (5 ml), evaporated to half the volume, and left to crystallize: 113 mg (90%), m.p. 210–211°. IR (CH_2Cl_2): 3620*w*, 3400*m*, 2900 (br.), 1520*m*. ^{1}H-NMR ($CDCl_3$, 360 MHz): 0.91 (*t*, J = 7, 3H, $CH_3CH_2CH_2N$); 1.11 (*q*, J = 12, 1H, H_{ax}–C(9)); 1.57 (*m*, 2H, $CH_3CH_2CH_2N$); 1.7 (br., 1H, OH); 2.15 (*m*, 1H, H–C(8)); 2.2 (*t*, J = 12, 1H, H_{ax}–C(7)); 2.48 (*td*, J = 11, 4, 1H, H–C(5)); 2.65 (*m*, 1H, H_{eq}–C(9)); 2.75 (*m*, 1H, H_{eq}–C(4)); 2.81 (*m*, 2H, $CH_3CH_2CH_2N$); 2.95 (*td*, J = 14, 3, 1H, H–C(10)); 3.21 (*dd*, J = 10, 3, 1H, H_{eq}–C(7)); 3.37 (*dd*, J = 14, 4, 1H, H_{eq}–C(4)); 3.62 (*AB* of *ABX*, J = 10, 6, 2H, CH_2OH); 3.93 (*s*, 3H, CH_3O); 6.6 (*d*, J = 9, 1H, H–C(13)); 6.8 (*d*, J = 9, 1H, H–C(14)); 6.9 (*s*, H–C(2)); 8,1 (br., 1H, NH). MS (LR): 314 (M^+), 299, 285, 210, 184, 105, 77. Anal. calc. for $C_{19}H_{26}N_2O_2$ (314.43): C 72.6, H 8.3, N 8.9, O 10.2; found: C 69.8, H 8.1, N 8.3, O 11.4.

17. *14-Methoxy-6-propylergolin-8-methyl Methanesulfonate (= (6a*RS,*9*RS,*10a*SR*)-3-Methoxy-7-propyl-4,6,6a,7,8,9,10,10a-octahydroindolo[4,3-*fg*]quinoline-9-methyl Methanesulfonate;* **26**). To a suspension of **25** (2.4 g, 7.6 mmol) in pyridin (35 ml) is added dropwise under stirring a solution of MsCl (1.17 ml, 10 mmol) in pyridin (20 ml). After 1 h, the mixture is evaporated under vacuum at 30°, 5% aq. $NaHCO_3$ (10 ml) added, and the mixture extracted 3 × with AcOEt. The org. phase is dried over Na_2SO_4, evaporated under vacuum, and treated with Et_2O. The product crystallizes from AcOEt: 2.54 g (85%), m.p. 184–185°. IR (CH_2Cl_2): 3460*m*, 2900 (br.), 1520*m*, 1070*m*. ^{1}H-NMR ($CDCl_3$, 90 MHz): 0.9 (*t*, J = 7, 3H, $CH_3CH_2CH_2N$); 1.0–3.6 (*m*, 13H); 3.05 (*s*, 3H, CH_3SO_3); 3.93 (*s*, 3H, CH_3O); 4.2 (*t*, J = 4, 2H, CH_2O); 6.65 (*AB*, J = 8, arom. H); 6.85 (*s*, 1H, H–C(2)); 8.1 (*s*, 1H, CHO). Anal. calc. for $C_{20}H_{28}N_2O_4S$ (392.52): C 61.2, H 7.2, N 7.1, O 16.3, S 8.2; found: C 60.9, H 7.0, N 7.1, O 16.2, S 8.2.

REFERENCES

[1] *W. Haefliger & H. Knecht*, Tetrahedron Lett. *1984*, 285.
[2] *W. Haefliger & H. Knecht*, Tetrahedron Lett. *1984*, 289.
[3] *B. Berde & H.O. Schild*, 'Handbook of Experimental Pharmacology', Vol. 49, Springer Verlag, Berlin-Heidelberg, 1978, p. 29.
[4] *D.C. Horwell*, Tetrahedron *36*, 3123 (1980).
[5] *A.P. Kozikowski*, Heterocycles *16*, 267 (1981).
[6] *T. Kiguchi, Ch. Hashimoto, T. Naito & I. Ninomiya*, Heterocycles *19*, 2279 (1982).
[7] *D.F. Tai & J. Rebek*, Tetrahedron Lett. *1983*, 859 and ref. therein.
[8] *P.A. Stadler*, Chem. Ind. *29*, 207 (1980).
[9] *C.A. Grob & E. Renk*, Helv. Chim. Acta *44*, 1531 (1961).
[10] *Z. Horii, T. Kurihara, S. Yamamoto, M.-Ch. Hsü, Ch. Iwata, I. Ninomiya & Y. Tamura*, Chem. Pharm. Bull. *14*, 1227 (1966).
[11] *Z. Horii, T. Watanabe, T. Kurihara & Y. Tamura*, Chem. Pharm. Bull. *13*, 420 (1965).
[12] *A.M. Crider, J.M. Robinson, H.G. Floss & J.M. Cassady*, J. Med. Chem. *20*, 1473 (1977).
[13] *W. Haefliger*, unpublished results.