274. Selective Ether Cleavage in the Aporphine Series. Conversion of (*S*)-Bulbocapnine into (*S*)-Corytuberine and (*S*)-Corydine Methyl Ether[1])

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Summary. Bulbocapnine methyl ether (**2**), on treatment with boron halides, affords the aporphine-1,2-diol (**3**), the novel aporphines **5** and **6** or the phenanthrene derivative **11** depending on the reaction conditions. **3** can be further transformed into corydine methyl ether (**4**); **6** has been converted to corytuberine (**8**). Similarly, dehydrobulbocapnine methyl ether **9** was converted to **10**.

The aporphine alkaloid, (*S*)-bulbocapnine (**1**), can be easily isolated from the roots of *Corydalis cava*. Its substitution pattern, a methylenedioxy group on ring A, a hydroxy and a methoxy group on ring D, offers the possibility of manifold selective transformations to different semisynthetic aporphines.

For our present studies, we decided to start from the known bulbocapnine methyl ether (**2**). Following earlier work with β-hydrastine [1], we used boron trichloride as reagent, rather than boron tribromide, which seems to be less selective.

As expected, the treatment of bulbocapnine methyl ether (**2**) with 2 mol of boron trichloride in dichloromethane at room temperature affords the known catechol **3** [2–4], which can be O-methylated to the known corydine [3] and corydine methyl ether (**4**) [2]. Under the conditions chosen, only a part of **2** is cleaved to the catechol **3**. An increase of the ratio of boron trichloride to substrate does not improve the yield of **3**, but rather favours the formation of the novel aporphine **6**. Similarly, treatment of **2** with boron tribromide affords the diphenol **5**. In both cases, the original methylenedioxy group opens and subsequently cyclizes to the oxygen at C(11), forming a 7-membered ring. The diphenol **5** can also be obtained, although in lower yield, directly from bulbocapnine (**1**) and boron tribromide.

The structure assignements of compounds **5** and **6** containing a newly formed 7-membered, instead of the original 5-membered ring, is based on spectral as well as chemical evidences. In the ^{1}H-NMR. spectrum, the signals of the two protons of the methylenedioxy group, which appear as two well separated doublets, are very characteristic. In the 5-membered ring compounds **1** and **2**, the coupling constant is in the order of about 1.5 Hz [5], but increases significantly to *ca.* 6 Hz in the 7-membered ring compounds **5** and **6**. Both compounds can be methylated to the same dimethyl ether **7**. Prolonged hydrolysis of **7** with dilute hydrochloric acid gives the known aporphine alkaloid (*S*)-corytuberine (**8**) [6].

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[1]) Presented in part by one of us (M. G.) at the meeting of the Swiss Chemical Society held in Aarau, Switzerland, on October 3, 1975.

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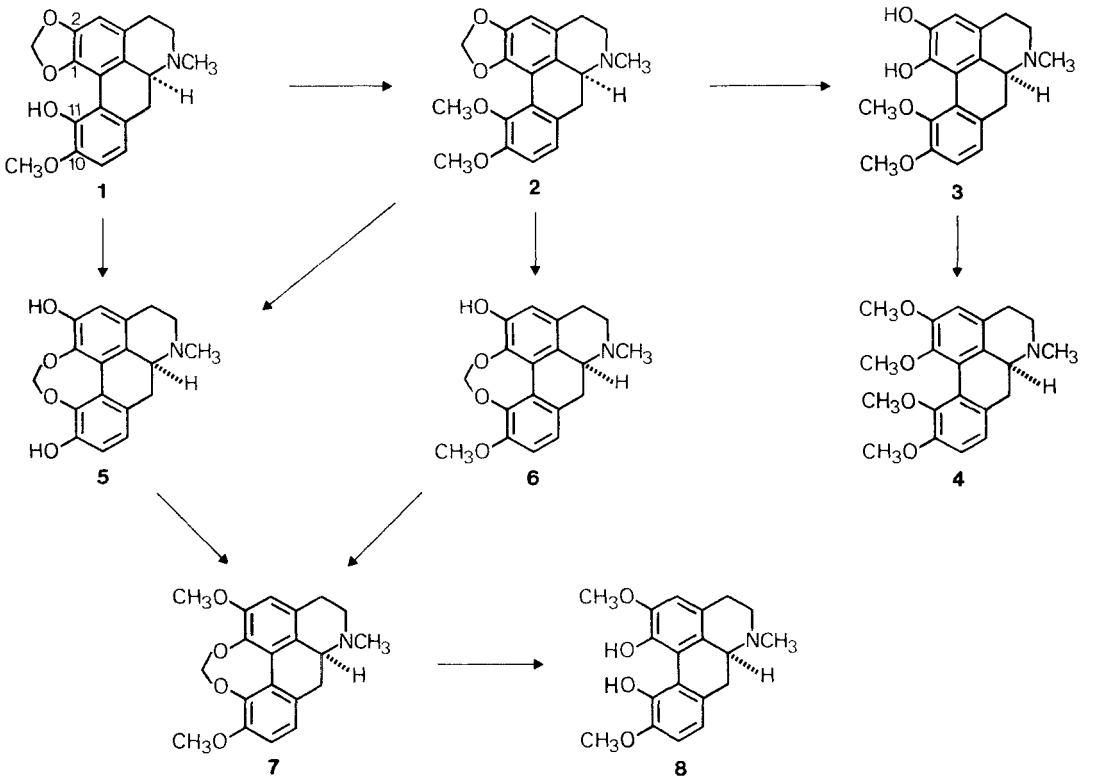
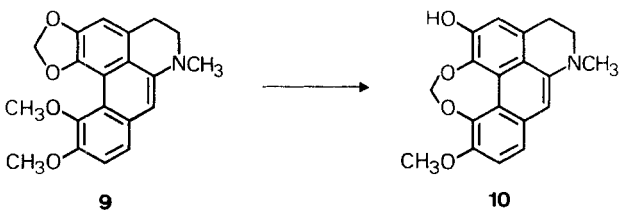
Scheme 1



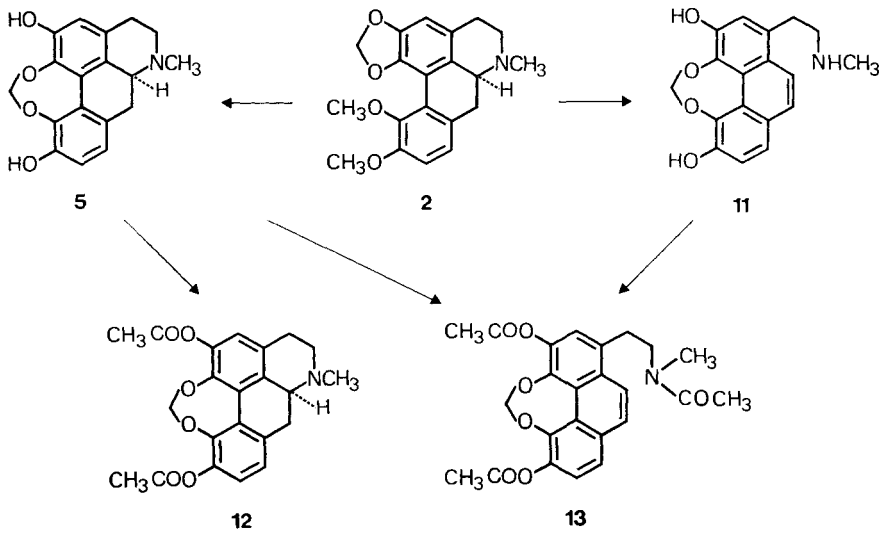
The reactions described above have all been carried out in analytical grade dichloromethane containing about 0.3% of ethanol as a stabilizer. Under the conditions chosen, enough boron halide is ethanolysed to form the hydrohalides of the aporphines. After the formation of the hydrohalide salts, the boron halide seems to attack the oxygen atom of the methylenedioxy group at C(2). Further addition of boron halide favours the formation of the dioxepin ring, possibly due to the very close vicinity of the two oxygens at C(1) and C(11). The great ease of formation of the 7-membered ring may be further illustrated by the conversion of dehydrobulbocapnine methyl ether (**9**) to the highly strained **10** with boron trichloride under similar conditions.

Scheme 2



In dichloromethane free of ethanol [7], treatment of bulbocapnine methyl ether with boron tribromide affords a mixture of the diphenol **5** and the phenanthrene derivative **11**. Acetylation of the mixture of **5** and **11** with acetic anhydride and triethylamine at room temperature affords a mixture of the diacetoxy aporphine **12** and the N,O,O-triacetylphenanthrene derivative **13**, which can be separated by chromatography. Both compounds can be obtained in pure from from the diphenol **5** by treatment with acetic anhydride and triethylamine at room temperature, or by refluxing in acetic anhydride respectively.

Scheme 3



The formation of either **5** or **11** in ethanol-free dichloromethane can be influenced by addition of acids or bases. The hydrobromide of **2**, when treated with boron tribromide, affords only diphenol **5**, whereas reaction of the free base **2** with the same reagent, in the presence of a strong base (for instance 1,8-bis(dimethylamino)naphthalene) gives mainly the ring B-opened compound **11**. Therefore, addition of boron tribromide on the nitrogen of **2** seems to be the initial step for opening of ring B. (Boron trichloride, under the same conditions, leaves the ring B intact.) This type of reaction could be of general use for preparing secondary amines, at least in the aporphine field.

We wish to express our gratitude to Prof. *A. Battersby*, Cambridge, for fruitful discussions. We are also grateful to our Central Research Units, in particular to Dr. *W. Arnold*, Dr. *L. Chopard-dit-Jean*, Dr. *A. Dirscherl*, Dr. *G. Englert*, Dr. *M. Grosjean*, Mr. *W. Meister* and Dr. *W. Vetter* for the analytical and spectral data and their interpretation.

Experimental Part

General remarks. Melting points (m.p.) were taken on a *Tottoli* apparatus and are not corrected. UV. spectra: taken in ethanol, λ_{max} in nm (log ε). IR. spectra: *Beckmann* IR 9, KBr, max in cm^{-1}. ^1H-NMR. spectra: *Varian* A-60, *Varian* HA 100, *Bruker* HX 90 E, *Bruker* HX 270. Chemical shifts in ppm (internal standard: tetramethylsilane, $\delta = 0$ ppm). Abbreviations: s = singulet, d = doublet, m = multiplet, br. = broad, AB = AB-system (Δ-values calculated according to [8]), J = coupling constant (Hz). Mass spectra: *AEI* MS 902, mass numbers in m/e, relative

intensity in %in parentheses. Reactions were routinely monitored by TLC. (silicagel F 254 DC plates, chloroform/2-propanol/acetic acid/water 2:2:0.6:0.4). Other abbreviations: RT. = room temperature.

(6*a*S)-*1,11-(Methylenedioxy)aporphine-2,10-diol* (**5**) *from* **1**. A solution of (+)-bulbocapnine (**1**) (3.25 g) in dichloromethane[4] (320 ml) was stirred at RT. under argon and then treated with a solution of boron tribromide (5.67 ml) in dichloromethane (25 ml). The mixture was stirred at RT. over night, carefully treated with methanol and evaporated to dryness. The residue was dissolved in methanol, heated for 5 min under reflux and evaporated again. This operation was repeated once more, the residue was then dissolved in methanol and this solution concentrated to 80 ml. The precipitated crystals were filtered off to give 1.46 g (37%) of **5** as the hydrobromide. Recrystallization from methanol gave the analytical sample: colorless crystals, m.p. 253–255°, $[\alpha]_D^{22°}$ +39.2° (*c* = 0.50, H_2O). – NMR. (100 MHz, d-DMSO): 3.07 (*s*, NCH_3); 5.53, 5.67 (*AB*, 2H, *J* = 6, $-OCH_2O-$); 6.74 (*s*, 1H, H–C(3)); 6.84, 6.96 (*AB*, 2H, *J* = 8, H–C(8) and H–C(9)); 9.15, 9.42 (2*s*, 1H each, 2OH). – MS.: 311 (M^+, 43), 310 (100), 309 (51), 268 ($M - CH_3NCH_2$, 71), 79 (14), 44 (79).

$C_{18}H_{17}NO_4 \cdot HBr$ (392.2) Calc. C 55.02 H 4.63 N 3.57% Found C 55.03 H 4.58 N 3.32%

5 *from* **2**. A solution of (+)-bulbocapnine methyl ether (1.53 g) in dichloromethane (150 ml) was stirred at RT. under argon and then treated with a solution of boron tribromide (2.58 ml) in dichloromethane (9.0 ml). The mixture was stirred at RT. over night and then worked up and crystallized as described above to give 1.45 g (81%) of **5**-hydrobromide.

(6*a*S)-*10-Methoxy-1,11-(methylenedioxy)aporphin-2-ol* (**6**) *from* **2**. A solution of (+)-bulbocapnine methyl ether (8.0 g) in dichloromethane (800 ml) was stirred at 10° under argon and then treated with 120 ml of 1.96 M boron trichloride in dichloromethane solution. The temperature increased to 15° and the reaction mixture was stirred at this temperature for 1 h. 150 ml of methanol was added carefully and the resulting solution evaporated to dryness. The crystalline residue was heated in 85 ml of methanol under reflux for 5 min and the precipitated crystals filtered off to give 7.6 g (89%) of **6** as hydrochloride. A sample was suspended in methanol and stirred at RT. for 5 h, after which it was filtered off to give the analytical sample as colorless crystals: m.p. 247–250°, $[\alpha]_D^{22°}$ +42.5° (*c* = 1.0, H_2O). – UV. (EtOH): 274 (4.06), 305 (3.68); (EtOH/0.01 N NaOH): 252 (4.22), 282 (4.06), 336 sh (3.53). – IR.: 3256 (OH), 2538 (N^+H), 1615, 1593, 1579, 1492 (aromatic rings), 1298, 1253, 1124, 1018 (aryl ethers), 829 (ortho-H arom.). – NMR. (90 MHz, d-DMSO): 3.02 (*s*, NCH_3); 3.80 (*s*, 3H, OCH_3); 5.49, 5.70 (*AB*, 2H, *J* = 5.5, $-OCH_2O-$); 6.74 (*s*, 1H, H–C(3)); 7.01, 7.09 (*AB*, 2H, *J* = 8.5, H–C(8) and H–C(9)); 9.58 (*s*, 1H, OH). – MS.: 325 (M^+, 46), 324 (100), 310 ($M - CH_3$, 8), 293 (17), 282 ($M - CH_3NCH_2$, 35), 252 (8).

$C_{19}H_{19}NO_4 \cdot HCl$ (361.8) Calc. C 63.07 H 5.57 N 3.87% Found C 62.87 H 5.64 N 3.63%

(6*a*S)-*2,10-Dimethoxy-1,11-(methylenedioxy)aporphine* (**7**) *from* **6**. 6 g of **6**-hydrochloride was treated with saturated sodium hydrogen carbonate solution and extracted with benzene to give 5.4 g of the free base. This material was dissolved in ether (100 ml), methanol (10 ml) and diazomethane solution (100 ml). The mixture was stirred at RT. for 3 days, evaporated to dryness and the residue crystallized from ether to give a first pure crop of **7** (2.7 g) as colorless crystals. The mother liquor was evaporated and the residue chromatographed on aluminium oxide (60 g, activity grade III). Elution with benzene/hexane mixtures and with benzene alone gave, after evaporation, 2.5 g of crude **7**. After crystallization from benzene/hexane, one obtains a second pure crop of **7** (2.0 g). Total amount of **7**: 4.7 g (83%). Recrystallisation from ether gave the analytical sample as colorless crystals: m.p. 136–138°, $[\alpha]_D^{22°}$ +143° (*c* = 1.0, $CHCl_3$). – UV.: 276 (4.16), 305 (3.78). – IR.: 2794 (N-alkyl-CH), 1599, 1580, 1490 (aromatic rings), 1260, 1140, 1080, 1018 (aryl ethers), 828 (ortho-H arom.). – NMR (90 MHz, d-DMSO): 2.44 (*s*, 3H, NCH_3); 3.78 (*s*, 6H, $2OCH_3$); 5.45, 5.70 (*AB*, 2H, *J* = 6, $-OCH_2O-$); 6.75 (*s*, 1H, H–C(3)); 6.92, 6.98 (*AB*, 2H, *J* = 8.5, H–C(8) and H–C(9)). – MS.: 339 (M^+, 53), 338 (100), 324 ($M - CH_3$, 14), 307 (18), 296 ($M - CH_3NCH_2$, 28).

$C_{20}H_{21}NO_4$ (339.4) Calc. C 70.78 H 6.24 N 4.13% Found C 70.48 H 6.39 N 3.86%

[4] When not otherwise stated, analytical grade dichloromethane containing about 0.3% of ethanol (from *Merck AG* Darmstadt) was used. Ethanol can be easily detected by GLC.

7 *from* **5**. 1.4 g of **5** (as the free base) was suspended in ether (200 ml), methanol (30 ml) and treated with 80 ml of diazomethane solution. The mixture was stirred at RT. for 4 days and then evaporated to dryness. After crystallization from benzene/hexane, one obtains 970 mg of **7** as colorless crystals, m.p. 135–137°.

(S)-*Corytuberine* (**8**) *from* **7**. 3.0 g of **7** hydrochloride were dissolved in 1 N hydrochloric acid (60 ml) and heated under reflux for 24 h under argon. The reaction mixture was cooled, neutralized with saturated sodium hydrogen carbonate solution (70 ml) and extracted with two portions of 150 ml of benzene. The combined extracts were washed with water (20 ml), saturated sodium chloride solution (50 ml), dried over sodium sulfate, filtered and evaporated to dryness to give 2.2 g of a crystalline residue. TLC. (benzene/methanol 4:1) showed this residue to contain mainly the starting material **7** plus a small amount of **6**. This crude was treated with diazomethane for several hours, evaporated and crystallized from ether/hexane to give 2.05 g (75%) of pure recovered **7**. The aqueous phase of the above work-up was extracted with six portions of chloroform (120 ml each). The combined extracts were washed with saturated sodium chloride solution, dried over sodium sulfate, filtered and evaporated to dryness to give 438 mg of a crude oil. This oil was dissolved in 50 ml of ethanol and this solution concentrated to 20 ml. The precipitated crystals were filtered off to give **8** (0.2 g) as grey-tanned crystals: m.p. 235–238°, $[\alpha]_D^{22°}$ +334° (c = 0.1, ethanol). Recrystallization from ethanol gave the analytical sample as colorless crystals: m.p. 238–240°, $[\alpha]_D^{22°}$ +344° (c = 0.1, methanol). – UV. (EtOH/0.01 N HCl): 225 (4.59), 268 (4.14), 276 sh (4.11), 304 (3.85); (EtOH/0.01 N NaOH): 228 sh (4.58), 272 (3.99), 280 (3.99), 318 (3.93). – IR.: 3642 (OH), 1249 (aryl ether). – NMR. (100 MHz, d-DMSO): 2.57 (s, 3H, NCH_3); 3.74 (s, 6H, $2OCH_3$); 6.63 (s, 1H, H–C(3)); 6.65, 6.79 (AB, 2H, J = 8, H–C(8) and H–C(9)); 10.15 (br., 2H, 2OH). – MS.: 327 (M^+, 100), 312 ($M-CH_3$, 81), 284 ($M-CH_3NCH_2$, 22), 44 (6).

$C_{19}H_{21}NO_4$ (327.4) Calc. C 69.71 H 6.47 N 4.28% Found C 69.83 H 6.58 N 4.24%

When the reaction time was prolonged to 72 h and stronger acid (2 N HCl) was used, some racemisation was observed.

(*6a* S)-*10,11-Dimethoxyaporphine-1,2-diol* (**3**) *from* **2**[5]. A solution of (+)-bulbocapnine methyl ether (3.06 g) in dichloromethane (306 ml) was stirred at RT. under argon and then treated with 5.8 ml of 2.34 M boron trichloride in dichloromethane solution. The mixture was stirred at RT. for 18 h, carefully treated with methanol and evaporated to dryness. The residue was dissolved in methanol and this solution heated under reflux for 5 min and again evaporated to dryness. This operation was repeated twice to give a crude product, which by TLC. (silicagel; chloroform/2-propanol/acetic acid/water 2:2:0,6:0.4) contains two main products (**2** and **3**) and a minor product (**6**). This crude was mixed with 5% borax solution (150 ml) and ethyl acetate (250 ml) and stirred for 3 h. The borax solution was separated and the ethyl acetate layer treated again with 5% borax solution as described above. This operation was repeated once more, after which the combined ethyl acetate layers were washed with saturated sodium chloride solution, dried over sodium sulfate, filtered and evaporated to dryness to give 2.3 g (75%) of recovered **2**. The combined borax solutions were acidified with hydrochloric acid and extracted with chloroform for 18 h in a continous extraction apparatus. Evaporation of the chloroform and crystallisation of the residue from methanol/ether gave 0.71 g of **3**-hydrochloride. Recrystallization from methanol/ether gave the analytical sample as colorless crystals: m.p. 215–218°, $[\alpha]_D^{22°}$ +178.9° (c = 1.0, methanol). – NMR. (100 MHz, d-DMSO): 2.98 (s, NCH_3); 3.66 (s, 3H, OCH_3); 3.83 (s, 3H, OCH_3); 6.72 (s, 1H, H–C(3)); 7.07, 7.19 (AB, 2H, J = 8.5, H–C(8) and H–C(9)); 8.55, 9.20 (2s, 1H each, 2OH); 11.5 (br., 1H, HCl). – MS.: 327 (M^+, 100), 326 (47), 312 ($M-CH_3$, 66), 296 ($M-OCH_3$, 89).

$C_{19}H_{21}NO_4 \cdot HCl$ (363.8) Calc. C 62.72 H 6.09 N 3.85% Found C 62.72 H 6.06 N 3.73%

(S)-*Corydine methyl ether* (**4**) *from* **3**. From 0.9 g of **3**-hydrochloride the free base was prepared in the usual way and dissolved in methanol (60 ml). Diazomethane solution (250 ml) was added and the mixture was allowed to stand at RT. for several days. The solution was evaporated and the residue chromatographed on aluminium oxide (act. grade III). Elution with benzene and benzene/methanol 95:5 mixture afforded 0.8 g of an oil. The hydrochloride was prepared in

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[5] The first trials for this ether cleavage were done by Dr. *S. Teitel* from *Hoffmann-La Roche Inc.*, Nutley N.J., USA. We thank our colleague for the communication of his results (*cf.* [4]).

acetone to give 457 mg of colorless crystals. Recrystallization from methanol/ether and heating under reflux in acetone gave the analytical sample of **4**-hydrochloride: m.p. 262°, $[\alpha]_D^{22°}$ +209.4° (c = 1.0, methanol). – UV.: 224 (4.61), 270 (4.16), 300 sh (3.71). – NMR. (90 MHz, d-DMSO): 2.97 (s, 3H, NCH_3); 3.59, 3.62, 3.82, 3.84 (4s, 3H each, $4OCH_3$); 6.93 (s, 1H, H–C(3)); 7.03, 7.09 (AB, 2H, J = 8.5, H–C(8) and H–C(9)); 11.6 (br., 1H, HCl). – MS.: 355 (M^+, 58), 354 (21), 340 ($M-CH_3$, 95), 324 ($M-CH_3O$, 100).

$C_{21}H_{25}NO_4 \cdot HCl$ (391.9) Calc. C 64.36 H 6.69 N 3.57% Found C 64.42 H 6.64 N 3.50%

(6*a* S)-*1,11-(Methylenedioxy)aporphine-2,10-diol diacetate* (**12**) *from* **5**. A suspension of **5**-hydrobromide (0.6 g) in dichloromethane (60 ml) was treated with triethylamine (4.3 ml) and acetic anhydride (1.45 ml). The mixture was stirred at RT. for 3 h, washed with water, dried over sodium sulfate, filtered and evaporated to dryness. The residue (0.6 g) was chromatographed on silicagel (20 g, 0.2–0.5 mm). Elution with benzene containing 1 to 3% methanol afforded 0.5 g of an oil which was crystallized from isopropyl ether to give 379 mg of crystalline **12**, m.p. 121–125°. Two recrystallizations from 2-propanol gave the analytical sample: m.p. 125–127°, $[\alpha]_D^{22°}$ –18.4° (c = 0.91, $CHCl_3$). – UV. (EtOH): 275 (3.96), 313 sh (3.42); (EtOH/0.01 N NaOH): 248 (4.25), 281 (3.90), 325 (3.51). – IR.: 2820 (N-alkyl-CH), 1772, 1598, 1504, 1498 (aromatic rings), 1218 (ester), 1132, 1022 (aryl ether). – NMR. (100 MHz, $CDCl_3$): 2.30 (s, 6H, $2COCH_3$); 2.53 (s, 3H, NCH_3); 5.37, 5.58 (AB, 2H, J = 6, $-OCH_2O-$); 6.77 (s, 1H, H–C(3)); 6.94 (s, 2H, H–C(8) and H–C(9)). – MS.: 395 (M^+, 43), 394 (48), 352 ($M-CH_3NHCH_2$, 100), 336 (352 – C_2H_2O, 16); 310 (65), 268 (310 – C_2H_2O, 26), 238 (268 – CH_2O, 17).

$C_{22}H_{21}NO_6$ (395.4) Calc. C 66.83 H 5.35 N 3.54% Found C 66.78 H 5.40 N 3.40%

1-[2-(Methylacetamido)ethyl]-4,5-methylenedioxyphenanthrene-3,6-diol diacetate (**13**) *from* **5**. **5**-hydrobromide (0.6 g), acetic anhydride (30 ml) and pyridine (0.35 ml) were heated together under reflux for 3 h and then evaporated to dryness. The residue was dissolved in benzene, washed with saturated sodium hydrogen carbonate solution, dried over sodium sulfate, filtered and evaporated to dryness. After recrystallization from isopropyl ether, one obtains 590 mg of **13** as beige tanned crystals, m.p. 122–127°. Recrystallization from ether gave the analytical sample: m.p. 126–130°. – UV.: 255 (4.64), 283 (4.31), 302 (4.16), 316 (4.21), 330 sh (3.35), 347 (3.49), 365 (3.51). – IR.: 1776, 1765, 1220 (ester), 1646 (amide), 1596, 1539, 1510, 1478 (aromatic rings), 1133, 1014 (aryl ether), 852 (ortho-H arom.). – NMR. (60 MHz, $CDCl_3$): 1.90 (s, 1/4H, $NCOCH_3$, rotamer I); 2.06 (s, 3/4H, $NCOCH_3$, rotamer II); 2.38 (s, 6H, $2OCH_3$); 2.76 (s, 3/4H, NCH_3, rotamer II); 2.96 (s, 1/4H, NCH_3, rotamer I); 3.1 to 3.8 (m, 4H, CH_2CH_2); 5.59 (s, 2H, $-OCH_2O-$); 7.17 (s, 1/4H, H–C(2), rotamer I); 7.23 (s, 3/4H, H–C(2), rotamer II); 7.33, 7.59 (AB, 2H, J = 9, H–C(7) and H–C(8)); 7.71, 8.08 (AB, 2H, J = 9, H–C(9) and H–C(10)). – MS.: 437 (M^+, 9), 395 ($M-C_2H_2O$, 12), 364 ($M-CH_3NHCOCH_3$, 19), 322 (364 – C_2H_2O, 42), 309 (15), 280 (322 – C_2H_2O, 100), 267 (38), 44 (63).

$C_{24}H_{23}NO_7$ (437.4) Calc. C 65.90 H 5.30 N 3.20% Found C 65.97 H 5.28 N 3.04%

Mixture of **5** *and* **11** *from* **2**. A solution of (+)-bulbocapnine methyl ether (1.02 g) in dichloromethane (100 ml, made ethanol-free by filtering through basic aluminium oxide (act. grade I [7])) was stirred at RT. unter argon and then treated with a solution of boron tribromide (1.2 ml) in dichloromethane (6 ml, purified as above). The mixture was stirred at RT. for 18 h, carefully treated with methanol and evaporated to dryness. The residue was dissolved in methanol, heated 5 min under reflux and again evaporated to dryness. After this operation was repeated once more, the residue was dissolved in methanol and this solution concentrated to 50 ml. The precipitated crystals were filtered off to give 0.9 g of a mixture of the hydrobromides of **5** and **11**. To acetylate this material, it was suspended in dichloromethane (100 ml) and treated with triethylamine (6.5 ml) and acetic anhydride (2.2 ml). The mixture was stirred at RT. for 2 h, washed with water, dried over sodium sulfate, filtered and evaporated to dryness at 35°. The residue was chromatographed on silicagel (0.2–0.5 mm). The chromatogramm was monitored by TLC. (silicagel; benzene/triethylamine/methanol 6:3.5:0.5). The fractions eluted with benzene containing 0.5 to 1% of methanol gave, after evaporation, 345 mg of an oil, which was crystallized from isopropyl ether to give pure **13** (0.3 g) as colorless crystals: m.p. 125–130°. This material was identical with a sample prepared directly from **5**. Latter fractions of the chromatography eluted with benzene containing 5% of methanol gave, after evaporation, 149 mg of an oil which was

crystallized from isopropyl ether to give pure **12** (93 mg) as colorless crystals: m.p. 119–125°. This material was identical with the product prepared directly from **5**.

When instead of the free base, the hydrobromide of **2** was used and treated as above, only **5** and no **11** was formed.

1-[2-(Methylamino)ethyl]-4,5-methylenedioxyphenanthrene-3,6-diol (**11**) *from* **2**. (+)-Bulbocapnine methyl ether (339 mg) and 1,8-bis(dimethylamino)naphthalene (235 mg) [9] in dichloromethane (34 ml, made ethanol-free as described above) were stirred at RT. under argon, and then treated with boron tribromide (0.57 ml). The mixture was stirred at RT. for 18 h, carefully treated with methanol and evaporated to dryness. The residue was dissolved in methanol, heated under reflux for 5 min and evaporated again. This operation was repeated once more, after which the residue was dissolved in methanol and this solution concentrated to 20 ml. The precipitated crystals were filtered off to give 0.2 g of **11**-hydrobromide. Recrystallization from methanol gave the analytical sample as grey-tanned crystals: m.p. 280–283°. – UV. (EtOH/0.01 N HCl): 244 (4.49), 262 (4.71), 298 (4.00), 311 (4.13), 324 (4.21), 345 (3.38), 363 (3.58), 382 (3.67); (EtOH/0.01 NaOH): 252 (4.65), 271 (4.64), 340 sh (4.21), 351 (4.26), 385 (3.75). – NMR. (270 MHz, d-DMSO): 2.63 (*s*, 3H, NCH_3); 3.10 to 3.24 and 3.28 to 3.42 (*2m*, 2H each, CH_2CH_2); 5.67 (*s*, 2H, $-OCH_2O-$); 7.20 (*s*, 1H, H–C(2)); 7.26, 7.57 (*AB*, 2H, $J = 8.3$, H–C(7) and H–C(8)); 7.59, 7.74 (*AB*, 2H, $J = 9.5$, H–C(9) and H–C(10)); 8.64 (br., 2H, N^+H_2); 9.37, 9.40 (*2s*, 1H each, 2OH). – MS.: 311 (M^+, 6), 268 ($M - CH_3NCH_2$, 78), 237 (6), 165 (4), 152 (9), 44 ($CH_2{=}N^+HCH_3$, 100).

$C_{18}H_{17}NO_4 \cdot HBr$ (392.2) Calc. C 55.12 H 4.63 N 3.57% Found C 55.10 H 4.59 N 3.35%

6a,7-Didehydro-10-methoxy-1,11-(methylenedioxy)aporphin-2-ol (**10**) *from 6a,7-didehydrobulbocapnine methyl ether* (**9**). A solution of didehydrobulbocapnine methyl ether (**9**, 337 mg) [10] in dichloromethane (35 ml) was stirred at –10° under argon and then treated with 5.3 ml of 1.89 M boron trichloride in dichloromethane solution. The mixture was stirred for 0.5 h at RT. and then again treated with 1.0 ml of 1.89 M boron trichloride solution. The mixture was stirred for another 0.5 h, carefully treated with methanol and evaporated to dryness. The residue was dissolved in methanol, heated under reflux for 5 min and evaporated again. The resulting residue was crystallized from methanol/dichloromethane to give 235 mg of crude **10** as the hydrochloride, m.p. 206–210° (dec.). The free base was prepared with saturated sodium hydrogen carbonate solution and extracted with chloroform. The chloroform was evaporated and the residue chromatographed on 5 g of aluminium oxide (activity grade III). Elution with dichloromethane and dichloromethane/methanol 4:1 afforded, after evaporation,146 mg of **10** as an oil. – NMR. (100 MHz, $CDCl_3$): 3.03 (*s*, 3H, NCH_3); 3.15 to 3.35 (*m*, 4H, CH_2CH_2); 3.95 (*s*, 3H, OCH_3); 5.69 (*s*, 2H, $-OCH_2O-$); 6.51 (*s*, 1H, H–C(7)); 7.00 (*s*, 1H, H–C(3)); 7.18, 7.30 (*AB*, 2H, $J = 8.5$, H–C(8) and H–C(9)). – MS.: 323 (M^+, 83), 308 ($M - CH_3$, 100), 280 ($M - CH_3NCH_2$, 6), 161 (9).

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