ATTEMPTS AT THE SYNTHESIS OF 11-METHOXYSUBSTITUTED BENZO[c]PHENANTRIDINES* **

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Experiments aimed at the synthesis of so far unknown 11-methoxybenzo[*c*]phenanthridines (*IIa,b,c*) are described. In the first approach 2,3,7,8-tetramethoxybenzo[*c*]phenanthridine-11-carboxylic acid (*IIIb*) was synthesized using a procedure for the preparation of 2,3,7,8-bismethylenedioxybenzo[*c*]phenanthridine-11-carboxylic acid (*IIIa*). Attempts to convert the carboxyl group of these acids to the methoxyl group were not successful. In the second approach 3-methoxy-6,7-methylenedioxy-1-methylaminonaphthalene (*XX*) was prepared from 1-(3,4-methylenedioxyphenyl)-2-propanone (*IX*) by a multistep synthesis. On acylation of the product with 2,3-dimethoxy-6-nitrobenzoic acid and subsequent hydrogenation N-(3-methoxy-6,7-methylenedioxynaphth-1-yl)-N-methylamide of 6-amino-2,3-dimethoxybenzoic acid (*XXII*) was obtained. The attempts at its cyclization according to Pschorr were unsuccessful.

Among natural benzo[*c*]phenanthridines the alkaloids with five oxygen functions – chelirubine[1] (*Ia*), sanguilutine[2] (*Ib*), chelilutine[1] (*Ic*) and sanguirubine[2] (*Id*) – have a special position not only due to the high degree of substitution, but – as shown over the past decade[3-9] – also to the location of the critical fifth substituent at $C_{(10)}$ in the ring D. Originally a biogenetic relationship of these alkaloids with correspondingly substituted analogues of chelidonine was assumed and the fifth oxygen function was located[10] on the carbon $C_{(11)}$ of the B ring. The subject of this paper is the attempt at the synthesis of the so far unknown 11-methoxysubstituted benzo[*c*]-phenanthridines *IIa,b,c*, isomeric with the natural alkaloids *Ia,b,c*.

In the first approach we intended to introduce a methoxyl group into position 11 by converting the carboxyl function in several steps. The starting compound for the preparation of compound *IIb* was 2,3,7,8-tetramethoxybenzo[*c*]phenanthridine-11-carboxylic acid (*IIIb*) which we prepared by a method described in ref.[11] for the analogoues 2,3,7,8-bismethylenedioxybenzo[*c*]phenanthridine-11-carboxylic acid (*IIIa*). On condensation of 7,8-dimethoxyisoquinolin-4-yl-acetic acid[12] with 4,5-dimethoxy-2-nitrobenzaldehyde[13] we obtained nitro acid *IV* which was converted to amino acid *V* by reduction with iron(II) hydroxide. The amino acid was then cyclized

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by Pschorr's method to acid *IIIb*, characterized as methyl ester *VIb*. From the acid we prepared the corresponding chloride *VIIb* on reaction with thionyl chloride and the product was reacted (without isolation) with hydrazine hydrate to give hydrazide *VIIIb*. When attempting to convert it to the required 11-methoxy derivative *via* azide, isocyanate, amine, diazonium salt and hydroxy derivative, we already failed at the first step, because hydrazide *VIIIb* reacted with nitrous acid under formation of a precipitate, which could not be further worked up owing to its insolubility. The attempt at Curtius' degradation of 2,3,7,8-bismethylenedioxybenzo[*c*]phenanthridine-11-carboxylic acid (*IIIa*), which was prepared according to Sainsbury and coworkers[11] and characterized as methyl ester *VIa*, was also unsuccessful. Therefore we gave up further attempts in this direction and concentrated our attention upon synthesis of the required substances *via* the tricyclic intermediate containing complete rings A, B and D, with suitable substitution.

For the synthesis of the naphthalene component forming the rings A and B we condensed 1-(3,4-methylenedioxyphenyl)-2-propanone[14,15] (*IX*) with diethyl oxalate and the ethyl 5-(3,4-methylenedioxyphenyl)-2,4-dioxopentanoate (*X*) obtained was cyclized, without further isolation, regiospecifically with 85% phosphoric acid to ethyl 3-hydroxy-6,7-methylenedioxy-1-naphthoate (*XI*). The structure is confirmed by spectral properties of *XI* and its product of hydrolysis *XII*, but primarily by the presence of the singlets of the protons on carbons $C_{(5)}$ and $C_{(8)}$ in the ^1H NMR spectra. The conversion of hydroxynaphthoate *XI* to 3-methoxy-6,7-methylenedioxy-1-naphthoic acid (*XIII*) was carried out by methylation with diazomethane to methoxy ester *XIV* and its subsequent hydrolysis. However, a simultaneous one-step methylation with dimethyl sulfate and alkaline hydrolysis proved much more advantageous in respect of the yield. The carboxyl function of acid *XIII* was converted to the methylamino group by a reaction sequence *via* chloride *XV*, azide *XVI* and isocyanate *XVII* (also characterized by its products of hydrolysis *XVIII*), with satisfactory overall yield. This way is more advantageous in all respects than the alternative procedure *via* hydrazide *XIX*. The methylamino derivative *XX* was then acylated with the chloride of 2,3-dimethoxy-6-nitrobenzoic acid[16–18] and the nitro amide *XXI* formed was hydrogenated over palladium to the corresponding amino derivative *XXII*. Under the conditions of Pschorr's cyclization this derivative also afforded only an insoluble precipitate in which we could not detect any benzo[*c*]phenanthridone.

EXPERIMENTAL

The melting points were determined on a Boetius microblock and they are not corrected. The analytical samples were dried over phosphorus pentoxide in a vacuum (27 Pa), at room temperature or at 80°C. The purity of the compounds was checked by thin-layer chromatography on silica gel (Silufol UV_{254}, Kavalier, Czechoslovakia) in chloroform–benzene–ethanol 1 : 1 : 0·1, using detection in UV light of 366 and 254 nm. The UV spectra (λ_{max}, nm (log ε)) were measured on a Unicam SP 8 000 spectrophotometer (Great Britain). The infrared spectra (cm^{-1}) were

recorded on a Unicam SP 2 000 G spectrophotometer (Great Britain). The ^{1}H NMR spectra (80 MHz) (δ, ppm) were obtained with a Tesla BS 487 C instrument (Czechoslovakia). The mass spectra were taken on an AEI 902 spectrometer (70 eV, direct inlet).

2-(7,8-Dimethoxyisoquinolin-4-yl)-3-(4,5-dimethoxy-2-nitrophenyl)propenoic Acid Hydrochloride (*IV*)

A mixture of 4,5-dimethoxy-2-nitrobenzaldehyde[13] (16·9 g, 80·0 mmol), 7,8-dimethoxyisoquinolin-4-ylacetic acid hydrochloride[12] (22·7 g, 80·0 mmol), acetic anhydride (322 ml), triethylamine (215 ml) and anhydrous sodium acetate (6·6 g, 80·0 mmol) was refluxed for 2 h under stirring. After dropwise addition of 1 000 ml of water refluxing was continued for another 10 min. then the reaction mixture cooled and the crystals formed filtered off under suction and recrystallized from 6% hydrochloric acid. Yellow needles (32·6 g, 85%), m.p. 205–207°C. For $C_{22}H_{21}ClN_2O_8$ (476·8) calculated: 55·41% C, 4·44% H, 7·43% Cl, 5·87% N; found: 55·30% C, 4·92% H, 7·30% Cl, 5·64% N. UV spectrum (CH_3OH): 230 (4·68), 256 (4·46), 360 (3·82). IR spectrum (nujol): 1 685 (COOH). ^{1}H NMR spectrum (CF_3COO^2H): 9·85 (1 H, d; $C_{(1)}$—H); 9·05 (1 H, s; $C_{(10)}$—H); 8·54 (1 H, d; $C_{(3)}$—H); 8·16 (2 H, s; $C_{(5)}$—H and $C_{(6)}$—H); 7·90 (1 H, s; $C_{(13)}$—H); 6·58 (1 H, s; $C_{(16)}$—H); 4·30, 4·15, 3·95, 3·49 (4× (3 H, s); 4 OCH_3).

2-(7,8-Dimethoxyisoquinolin-4-yl)-3-(2-amino-4,5-dimethoxyphenyl)propenoic Acid Hydrochloride (*V*)

A solution of iron-II sulfate (44·8 g, 0·161 mol) in water (150 ml) was added to a stirred solution of nitro acid *IV* (8·02 g, 16·8 mmol) in 26% aqueous ammonia (224 ml) and heated in a boiling water bath for 15 min. After filtering the filtrate was cooled and neutralized with acetic acid to pH 7. The next day the precipitate was filtered off under suction and crystallized from 6% hydrochloric acid. Yellow needles (5·5 g, 73%), m.p. 240°C. For $C_{22}H_{23}ClN_2O_6$ (446·8) calculated: 59·13% C, 5·19% H, 7·93% Cl, 6·27% N; found: 58·92% C, 5·21% H, 7·92% Cl, 5·94% N. UV spectrum (CH_3OH): 211 (4·78), 239 (4·47), 254 (4·47), 296 (3·96), 402 (3·96). IR spectrum (nujol): 1 690 (COOH). ^{1}H NMR spectrum ($C^2H_3COO^2H$): 9·90 (1 H, d; $C_{(1)}$—H); 8·84 (1 H, s; $C_{(10)}$—H); 8·50 (1 H, d; $C_{(3)}$—H); 8·18 (2 H, s; $C_{(5)}$—H and $C_{(6)}$—H); 7·34 (1 H, s; $C_{(16)}$—H); 6·25 (1 H, s; $C_{(13)}$—H); 4·30, 4·15, 3·92, 3·06 (4× (3 H, s); 4 OCH_3).

2,3,7,8-Tetramethoxybenzo[*c*]phenanthridine-11-carboxylic Acid (*IIIb*)

Sodium nitrite (0·89 g, 12·9 mmol) in 20 ml of water was added dropwise at 0°C to a stirred suspension of amino acid *V* (2·89 g, 6·47 mmol) in 6% hydrochloric acid (174 ml) and then stirred at this temperature for one hour. The excess of nitrous acid was decomposed by addition of a solution of urea and copper powder (2·89 g) was then added to the reaction mixture. 150 ml of nitrogen (97%) was set free. After 5 h stirring the precipitate was filtered off under suction, stirred with 25 ml of a 5% sodium hydroxide solution and the insoluble material was filtered off. The filtrate was acidified with 6% hydrochloric acid and the precipitate formed was filtered off under suction and dried. Acid *IIIb* was thus obtained in 40% yield (1·1 g), with m.p. 228–230°C. For $C_{22}H_{19}NO_6.2\,H_2O$ (429·4) calculated: 61·53% C, 5·40% H, 3·26% N; found: 61·73% C, 5·31% H, 3·57% N. UV spectrum (CH_3OH): 260 (4·52), 282 (4·52), 291 (4·49), 346 (3·92), 390 (3·62). IR spectrum (nujol): 1 700 (COOH).

Methyl 2,3,7,8-Tetramethoxybenzo[*c*]phenanthridine-11-carboxylate (*VIb*)

A solution of diazomethane in ether (10 ml) was added to a solution of acid *IIIb* (0·10 g, 0·23 mmol) in 3 ml of methanol and allowed to stand overnight. After evaporation and crystal-

lization of the residue from methanol ester *VIb* was obtained (72 mg; 77%), m.p. 208–210°C. For $C_{23}H_{21}NO_6$ (407·4) calculated: 67·80% C, 5·20% H, 3·44% N; found: 67·62% C, 5·43% H, 3·51% N. UV spectrum (CH_3OH): 260 (4·62), 286 (4·64), 347 (3·92), 390 (3·53). IR spectrum ($CHCl_3$): 1 703 ($COOCH_3$). Mass spectrum: *m/z* 407 (M^+; $C_{23}H_{21}NO_6$).

2,3,7,8-Tetramethoxybenzo[*c*]phenanthridine-11-carboxylic Acid Hydrazide (*VIIIb*)

A mixture of acid *IIIb* (0·9 g, 2·1 mmol) and thionyl chloride (4·5 ml) was refluxed for 2 h and then evaporated. The residue (crude acyl chloride *VIIb*) was mixed with 100% hydrazine hydrate (1 ml), heated at 50°C for 10 min and then evaporated. After crystallization of the residue from methanol hydrazide *VIIIb* was obtained (520 mg, 61%), m.p. 230–232°C. For $C_{22}H_{21}N_3O_5$ (407·4) calculated: 64·85% C, 5·20% H, 10·31% N; found: 65·23% C, 5·13% H, 10·30% N. UV spectrum (CH_3OH): 260 (4·64), 282 (4·66), 342 (3·89), 390 (3·46). IR spectrum (nujol): 1 703 ($CONHNH_2$).

Attempts at degradation: A sodium nitrite solution (80 mg, 1·16 mmol) in water (10 ml) was added dropwise to a stirred and cooled (0°C) suspension of hydrazide *VIIIb* (300 mg, 0·73 mmol) in 3% hydrochloric acid (30 ml) and the brown precipitate formed after 30 min was filtered off under suction and then boiled with 6% hydrochloric acid (30 ml) for 20 min. The black precipitate formed was insoluble in water and organic solvents. Further attempts at its processing were unsuccessful.

Methyl 2,3,7,8-bismethylenedioxybenzo[*c*]phenanthridine-11-carboxylate (*VIa*)

This was prepared from 2,3,7,8-bismethylenedioxy[*c*]phenanthridine-11-carboxylic acid[11] (*IIIa*) in 73% yield, using an analogous procedure as for methyl ester *VIb*. Its m.p. was 182–184°C (methanol). For $C_{21}H_{13}NO_6$ (375·3) calculated: 67·20% C, 3·49% H, 3·73% N; found: 67·31% C, 3·24% H, 3·62% N. UV spectrum (CH_3OH): 246 (4·27), 295 (4·16). IR spectrum ($CHCl_3$): 1 710 ($COOCH_3$). Mass spectrum: *m/z* 375 (M^+, $C_{21}H_{13}NO_6$).

Attempts at the Degradation
of 2,3,7,8-Bismethylenedioxybenzo[*c*]phenanthridine-11-carboxylic Acid[11] (*IIIa*)

A solution of triethylamine (0·5 g) in 5 ml of acetone was added to a stirred and cooled (0°C) suspension of acid *IIIa* (1·44 g, 4·0 mmol) in acetone (30 ml), followed by a solution of ethyl chloroformate (0·65 g, 6·0 mmol) in 5 ml of acetone. After 30 min a solution of sodium azide (0·39 g, 6·0 mmol) in 15 ml of water was added and stirred for 1 h. The mixture was poured into 400 ml of water and the precipitated black material was filtered off under suction. It was insoluble in water or organic solvent. Further attempts at its processing were unsuccessful.

Ethyl 5-(3,4-Methylenedioxyphenyl)-2,4-dioxopentanoate (*X*)

A mixture of 1-(3,4-methylenedioxyphenyl)-2-propanone[14,15] (*IX*) (250 g, 1·4 mol) and ethyl oxalate (215 g, 1·47 mol) was added dropwise during 30 min at 5°C into a stirred solution of sodium ethoxide (32·2 g, *i.e.* 1·4 mol of sodium in 1 500 ml of absolute ethanol) and stirred at 10°C for 3 h. Acetic acid (84 g, 1·4 mol) was then added, the mixture poured into 4 500 ml of water and extracted with ether. The combined ethereal extracts (3 100 ml) were washed with water and dried over anhydrous sodium sulfate. After evaporation of the solvent a yellowish oil was obtained (278 g, 71%) which was used without purification for further reaction. TLC: R_F value in chloroform–benzene (50 : 50) 0·5; purity about 95%.

Ethyl 3-Hydroxy-6,7-methylenedioxy-1-naphthoate (*XI*)

Phosphoric acid (85%; 1 100 ml) was added to ester *X* (278·2 g, 1·0 mol) under vigorous stirring over 5 min and the mixture was stirred at room temperature for another 15 min. After 30 min standing water (2 000 ml) and ether (2 000 ml) were added under stirring and the ethereal layer was separated, washed with water, sodium hydrogen carbonate solution and again with water. After drying over sodium sulfate the solvent was evaporated. Yellow needles (83·2 g, 32%), m.p. 154–156°C (benzene). For $C_{14}H_{12}O_5$ (260·2) calculated: 64·61% C, 4·65% H; found: 64·71% C, 4·58% H. UV spectrum (CH_3OH): 355 (3·86), 303 (3·67), 233 (4·67). IR spectrum (nujol): 3 320 (OH), 1 682 (ester). ^{1}H NMR spectrum ($C^2H_3COO^2H$): 8·10 (1 H, s; $C_{(8)}$—H); 7·60 (1 H, d, J = 2·5 Hz; $C_{(2)}$—H); 7·21 (1 H, d, J = 2·5 Hz; $C_{(4)}$—H); 6·95 (1 H, s; $C_{(5)}$—H); 5·92 (2 H, s; —OCH_2O—); 4·29 (2 H, q, J = 7·0 Hz; CH_3—CH_2—O); 1·35 (3 H, t, J = 7·0 Hz; CH_2—CH_3).

3-Hydroxy-6,7-methylenedioxy-1-naphthoic Acid (*XII*)

A solution of ester *XI* (1·04 g, 4·0 mmol), 1·0 g of sodium hydroxide, 5 ml of water and 5 ml of methanol was refluxed for 3 h. After cooling the pH of the solution was adjusted to 7 with dilute hydrochloric acid (1 : 2), the solution was filtered and allowed to stand in a refrigerator, yielding crystals (0·58 g, 62·5%) with m.p. 263–265°C (water). For $C_{12}H_8O_5$ (232·2) calculated: 62·07% C, 3·47% H; found: 61·90% C, 3·49% H. UV spectrum (CH_3OH): 352 (3·84), 299 (3·68), 233 (4·74). IR spectrum (nujol): 1 696 (COOH). ^{1}H NMR spectrum ($C^2H_3SOC^2H_3$): 8·20 (1 H, s; $C_{(8)}$—H); 7·63 (1 H, mcs, J = 3·0 Hz; $C_{(2)}$—H); 7·25 (1 H, mcs, J = 3·0 Hz; $C_{(4)}$—H); 7·19 (1 H, s; $C_{(5)}$—H); 6·10 (2 H, s; —OCH_2O—).

Ethyl 3-Methoxy-6,7-methylenedioxy-1-naphthoate (*XIV*)

Ethereal diazomethane solution (600 ml) prepared from 0·6 mol of nitrosomethylurea was added to a solution of hydroxy ester *XI* (52·0 g, 0·2 mol) in methanol (500 ml) and the mixture allowed to stand for 20 h. The solvent was distilled off and the residue was crystallized twice from ethanol. Yield, 41·0 g (75%), m.p. 74–75°C. For $C_{15}H_{14}O_5$ (274·3) calculated: 65·69% C, 5·15% H; found: 65·27% C, 5·36% H. UV spectrum (CH_3OH): 350 (3·84), 297 (3·63), 241 (4·58), 233 (4·68). IR spectrum (nujol): 1 702 (ester). ^{1}H NMR spectrum (C^2HCl_3): 8·20 (1 H, s; $C_{(8)}$—H), 7·67 (1 H, d, J = 3·0 Hz; $C_{(2)}$—H); 7·12 (1 H, d, J = 3·0 Hz; $C_{(4)}$—H); 6·96 (1 H, s; $C_{(5)}$—H); 5·98 (2 H, s; —OCH_2O—); 4·38 (2 H, q, J = 6·5 Hz; CH_3—CH_2—O); 3·85 (3 H, s; OCH_3); 1·40 (3 H, t, J = 6·5 Hz; CH_2—CH_3).

3-Methoxy-6,7-methylenedioxy-1-naphthoic Acid (*XIII*)

a) A 10% aqueous potassium hydroxide solution (50 ml) was added to a solution of 3·0 (10·9 mmol) of methoxy ester *XIV* in 12 ml of ethanol and the mixture was refluxed for 5 h. After cooling it was extracted twice with 50 ml of ether and the extract was dried over anhydrous magnesium sulfate and evaporated. Yield, 2·4 g (88%) of compound *XIII*, m.p. 242–244°C (50% ethanol). For $C_{13}H_{12}O_5$ (248·2) calculated: 62·90% C, 4·87% H; found: 63·05% C, 4·61% H. UV spectrum (CH_3OH): 349 (3·83), 299 (3·64), 233 (4·94). IR spectrum (nujol): 1 688 (COOH). ^{1}H NMR spectrum ($C_5{}^2H_5N$): 13·13 (1 H, bs; —COOH); 8·86 (1 H, s; $C_{(8)}$—H); 8·18 (1 H, d, J = 3·0 Hz; $C_{(2)}$—H); 7·32 (1 H, d, J = 3·0 Hz; $C_{(4)}$—H); 7·52 (1 H, s; $C_{(5)}$—H); 5·90 (2 H, s; —OCH_2O—); 3·65 (3 H, s; OCH_3).

b) A sodium hydroxide solution (11·0 g in 55 ml of water) was added to a stirred solution of hydroxy ester *XI* (65·0 g, 0·25 mol) in 500 ml of methanol and dimethyl sulfate (31·5 g, 0·25 mol)

was then added dropwise at 35°C. After 2 h stirring sodium hydroxide (100 g) in 400 ml of water was added and the reaction mixture was refluxed for 3 h. After cooling the solution was filtered and acidified with hydrochloric acid. The precipitate formed was crystallized from 80% ethanol. Yield, 50·8 g (83%) of acid *XIII*, identical with that obtained under *a*).

3-Methoxy-6,7-methylenedioxy-1-naphthoic Acid Hydrazide (*XIX*)

A mixture of 10·4 g (38·0 mmol) of ester *XIV* and 14·1 g of hydrazine hydrate was heated for 10 h in a water bath. After cooling ethanol was added until a clear solution was obtained and the mixture was allowed to stand for crystallization. Yield, 8·9 g (90%), m.p. 223–225°C. For $C_{13}H_{12}N_2O_4$ (260·2) calculated: 59·99% C, 4·65% H, 10·77% N; found: 60·26% C, 4·85% H, 10·75% N. UV spectrum (CH_3OH): 342 (3·86), 291 (3·72), 280 (3·76), 234 (4·46).

3-Methoxy-6,7-methylenedioxy-1-naphthoyl Chloride (*XV*)

A mixture of acid *XIII* (24·8 g, 0·1 mol) and thionyl chloride (119·0 g, 1·0 mol) was refluxed for 2 h and thionyl chloride evaporated. The yellow crystals (26·6 g) obtained were washed with light petroleum, (m.p. 135–138°C) and used directly for the subsequent reaction.

3-Methoxy-6,7-methylenedioxy-1-naphthoic Acid Azide (*XVI*)

a) Hydrazide *XIX* (2·5 g, 9·6 mmol) was added to 40 ml of cooled (−3°C) hydrochloric acid (9·6 mmol) and 40 ml of a 0·5 mol l^{-1} solution of sodium nitrite were added to it dropwise over 30 min. The precipitated crystals were suction-dried after 2 h standing, yield, 2·3 g (88%), m.p. 156–159°C, identical with the m.p. of isocyanate *XVII* as a result of the thermal decomposition of *XVI* to *XVII*. The product was used without purification for the next step.

b) Chloride *XV* (26·6 g) was added slowly to a stirred solution of sodium azide (13·0 g, 0·20 mol) in 80 ml of water and 150 ml of dioxane cooled at 4°C and the stirring was continued for 30 min. The azide *XVI* precipitated after addition of 200 ml of ice water, was washed with ice, water, filtered and dried over phosphorus pentoxide (26·5 g, 97%). It was identical with the substance obtained under *a*). The product was used for further reaction without previous purification.

3-Methoxy-6,7-methylenedioxynaphth-1-yl Isocyanate (*XVII*)

A suspension of azide *XVI* (27·1 g, 0·1 mol) in 500 ml of benzene was heated slowly to boiling point and then refluxed for another hour. After addition of charcoal the solution was filtered and the filtrate concentrated to 100 ml volume and allowed to stand for crystallization. Yield, 16·1 g (66%) of yellow needles, m.p. 156–159°C. For $C_{13}H_9NO_4$ (243·2) calculated: 64·20% C, 3·73% H, 5·76% N; found: 64·72% C, 4·07% H, 5·76% N. IR spectrum (nujol): 1 642 (C=N), 1 041, 1 091 (C–O–).

1-Amino-3-methoxy-6,7-methylenedioxynaphthalene (*XVIII*)

Concentrated hydrochloric acid (40 ml) was added to a solution of isocyanate *XVII* (6·1 g, 25 mmol) in 1 000 ml of dioxane and the mixture was refluxed for 1 h. After cooling it was diluted with 500 ml of water, the separated impurities were filtered off and the filtrate alkalized with a sodium carbonate solution. The precipitate formed was filtered off under suction, washed with water and crystallized from ethanol. Yield of *XVIII* 3·6 g (66%), m.p. 176–178°C. For $C_{12}H_{11}\cdot NO_3$ (217·2) calculated: 66·35% C, 5·10% H, 6·45% N; found: 66·52% C, 5·46% H, 6·20% N. UV spectrum (CH_3OH): 260 (4·10), 225 (4·21). IR spectrum (nujol): 3 450 (NH_2). ^1H NMR

spectrum ($C^2H_3SOC^2H_3$): 7·42 (1 H, s; $C_{(5)}$—H); 7·04 (1 H, s; $C_{(8)}$—H); 6·46 (1 H, d, J = = 2·5 Hz; $C_{(4)}$—H); 6·25 (1 H, d, J = 2·5 Hz; $C_{(2)}$—H); 6·04 (2 H, s; —OCH_2O—); 3·75 (3 H, s; OCH_3).

3-Methoxy-1-methylamino-6,7-methylenedioxynaphthalene (*XX*)

A solution of isocyanate *XVII* (12·2 g, 0·05 mol) in 250 ml of benzene was added dropwise into a solution of 4·0 g (0·10 mol) of lithium aluminum hydride in 250 ml of ether and the mixture was refluxed for 1 h. After cooling to 0°C 4 ml of water were added for the decomposition of reaction mixture, followed by 4 ml of 15% sodium hydroxide and 12 ml of water. The precipitate formed was filtered off under suction and washed with ether. The filtrate was dried over anhydrous sodium sulfate and evaporated. The needles of amine *XX* (9·5 g, 82%) melted at 135—137°C. For $C_{13}H_{13}NO_3$ (213·2) calculated: 67·52% C, 5·67% H, 6·06% N; found: 67·52% C, 5·38% H, 5·80% N. UV spectrum (CH_3OH): 342 (3·61), 303 (3·84), 264 (4·43), 221 (4·40). IR spectrum ($CHCl_3$): 3 450 (NH). ^{1}H NMR spectrum (C^2HCl_3): 6·98 (2 H, s; $C_{(5)}$—H and $C_{(8)}$—H); 6·44 (1 H, d, J = 2·5 Hz; $C_{(4)}$—H); 6·17 (1 H, d, J = 2·5 Hz; $C_{(2)}$—H); 5·94 (2 H, s; —OCH_2O—); 3·85 (1 H, bs, disappears after addition of ^2H_2O; —NH—); 3·80 (3 H, s; OCH_3); 2·86 (3 H, s; N—CH_3).

Hydrochloride: Obtained on dissolution of base *XX* in boiling 3M-HCl; m.p. 194—195°C. For $C_{13}H_{13}NO_3.HCl.1/2\,H_2O$ (276·7) calculated: 56·30% C, 5·09% H, 5·06% N, 12·80% Cl; found: 56·38% C, 5·51% H, 4·62% N, 12·54% Cl. UV spectrum (CH_3OH): 337 (3·86), 287 (4·12), 270 (4·17). IR spectrum (nujol): 3 400 (NH).

N-(3-Methoxy-6,7-methylenedioxynaphth-1-yl)-N-methylamide of 2,3-Dimethoxy-6-nitrobenzoic Acid (*XXI*)

Thionyl chloride (1·34 ml) was added to a suspension of 3·6 g (15·8 mmol) of 2,3-dimethoxy-6-nitrobenzoic acid[16—18] (m.p. 187—189°C) in 50 ml of chloroform and when the acid has dissolved after 2 h the mixture was refluxed for another 2 h. The volatile components were distilled off and the crystalline residue was washed with light petroleum and dried in a vacuum. 2,3-Dimethoxy-6-nitrobenzoyl chloride (3·5 g, 90%), m.p. 168—170°C. ^{1}H NMR spectrum: C^2H_3. COC^2H_3): 7·94 (1 H, d, J = 9·5 Hz; $C_{(5)}$—H); 7·18 (1 H, d, J = 9·5 Hz; $C_{(4)}$—H); 3·95 and 3·76 (2 × 3 H, s); 2 OCH_3). Powdered potassium carbonate (1·17 g, 8·4 mmol) and 1·38 g (5·64 mmol) of 2,3-dimethoxy-6-nitrobenzoyl chloride were added gradually to a solution of 1·3 g (5·64 mmol) of 3-methoxy-1-methylamino-6,7-methylenedioxynaphthalene (*XX*) in 70 ml of ether and the mixture was refluxed for 3 h. Ether was evaporated and 150 ml of water were added to the mixture. The substance was extracted with 150 ml of chloroform. The extract was dried over anhydrous sodium sulfate, filtered through 30 g of silica gel, the filtrate was evaporated and the residue crystallized from ethanol. Yellow crystals (2·1 g, 84·5%), m.p. 181—183°C. For $C_{22}H_{20}N_2O_8$ (440·4) calculated: 60·00% C, 4·58% H, 6·36% N; found: 60·11% C, 4·52% H, 6·24% N. UV spectrum (CH_3OH): 342 (3·97), 270 (4·09), 234 (4·64). IR spectrum ($CHCl_3$): 1 652 (amide). Mass spectrum: m/z 440 (M^+, $C_{22}H_{20}N_2O_8$).

N-(3-Methoxy-6,7-methylenedioxynaphth-1-yl)-N-methylamide of 6-Amino-2,3-dimethoxybenzoic Acid (*XXII*)

A solution of nitro amide *XXI* (1·76 g, 3·0 mmol) in ethanol (210 ml) was hydrogenated at atmospheric pressure in the presence of 0·6 g of 5% Pd/$CaCO_3$. After 6 h 103% of the theoretical amount of hydrogen were absorbed. After filtration off of the catalyst ethanol was evaporated in a vacuum. The glassy amide *XXII* was homogeneous according to TLC, 1·53 g (93·5%).

For $C_{22}H_{22}N_2O_6$ (410·4) calculated: 64·38% C, 5·40% H, 6·83% N; found: 64·71% C, 5·57% H, 6·91% N. UV spectrum (CH_3OH): 345 (3·99), 270 (3·98), 236 (4·68). IR spectrum ($CHCl_3$): 1 654 (amide). Mass spectrum: m/z 410 (M^+, $C_{22}H_{22}N_2O_6$).

Attempts at Pschorr's closure: A solution of sodium nitrite (0·47 g, 6·82 mmol) was added dropwise to a stirred solution of amide *XXII* (1·4 g, 3·41 mmol) in 6% hydrochloric acid kept at 0°C and the mixture stirred for one hour. The excess of nitrous acid was decomposed with urea. Powdered copper (1·45 g) was then added and the mixture stirred for 5 h. The black precipitate formed was insoluble in water and in organic solvents. Further attempts at its processing were unsuccessful.

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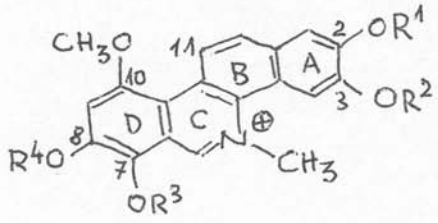

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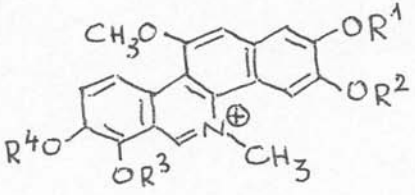

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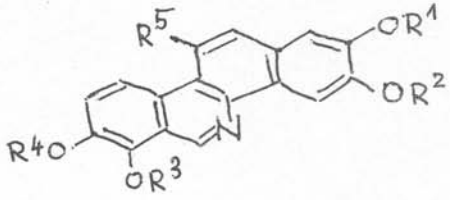
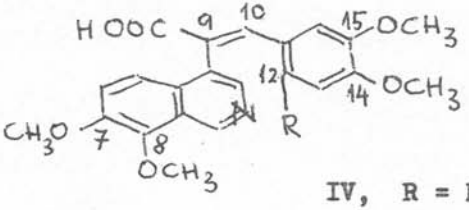
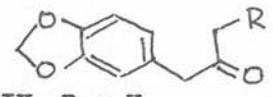


IIIa, R^5 = COOH
IIIb, R^5 = COOH
VIa, R^5 = $COOCH_3$
VIb, R^5 = $COOCH_3$
VIIb, R^5 = COCl
VIIIb, R^5 = $CONHNH_2$

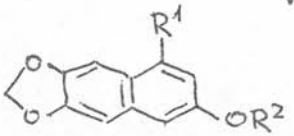
a, $R^1R^2 = R^3R^4 = CH_2$
b, $R^1 = R^2 = R^3 = R^4 = CH_3$
c, $R^1R^2 = CH_2$, $R^3 = R^4 = CH$
d, $R^1 = R^2 = CH_3$, $R^3R^4 = CH$



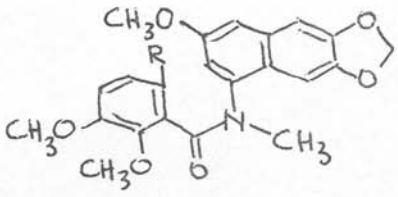
IV, R = NO_2
V, R = NH_2



IX, R = H
X, R = $COCOOC_2H_5$



XI, R^1 = $COOC_2H_5$, R^2 = H
XII, R^1 = COOH, R^2 = H
XIII, R^1 = COOH, R^2 = CH_3
XIV, R^1 = $COOC_2H_5$, R^2 = CH_3
XV, R^1 = COCl, R^2 = CH_3
XVI, R^1 = CON_3, R^2 = CH_3
XVII, R^1 = NCO, R^2 = CH_3
XVIII, R^1 = NH_2, R^2 = CH_3
XIX, R^1 = $CONHNH_2$, R^2 = CH_3
XX, R^1 = $NHCH_3$, R^2 = CH_3



XXI, R = NO_2
XXII, R = NH_2