SYNTHESIS OF SANGUINARINE, CHELERYTHRINE, AND OXYSANGUINARINE

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Benzo[*c*]phenanthridines *Va* and *Vb* have been prepared by photocyclization of amines *IVa* and *IVb* and transformed into the alkaloids sanguinarine (*VIa*) and chelerythrine (*VIb*). Oxysanguinarine (*XIV*) has been prepared from diazoketone *XVIII*.

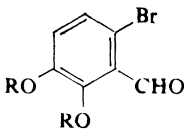
A series of benzo[*c*]phenanthridine alkaloids have already been prepared by total syntheses[1-9]. The methods described in the present communication are simple and suitable for synthesis of larger amounts of these alkaloids.

The key point of this synthesis consisted in solution of preparation of 6-bromo-2,3-methylenedioxybenzaldehyde[10] (*Ia*). From aldehyde *Ia* and naphthylamine[6] *II* the Schiff's base *IIIa* was prepared which was reduced with $NaBH_4$ to amine *IVa*. Photocyclization of amine *IVa* gave benzo[*c*]phenanthridine *Va* in 29% yield. Quaternization of *Va* with dimethyl sulphate gave the corresponding methosulphate which was transformed into sanguinarine chloride (*VIa*). The same reaction sequence gave chelerythrine chloride (*VIb*) from 6-bromo-2,3-dimethoxybenzaldehyde[10] (*Ib*).

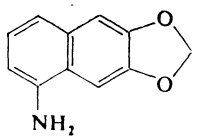
The starting amine can be prepared either by the described way[6,11,12] or by the following procedure. Reaction of safrole (*VIII*) with diborane (prepared *in situ*) and subsequent oxidation of the product with hydrogen peroxide gives the alcohol *IX*. This alcohol reacts with thionyl chloride to produce the chloro derivative *X* which is transformed to the Grignard reagent and, on reaction with carbon dioxide, to the acid *XI*. The alcohol *IX* can also be treated with methanesulphonyl chloride to give the corresponding mesylate, whose reaction with potassium cyanide gives the nitrile which is hydrolyzed to the acid *XI*. The acid *XI* is cyclized to tetralone[6] *XII* by ethyl polyphosphate. The tetralone *XII* is converted to the respective oxime[6] *XIII* which is transformed into amine *II* by action of a mixture of acetic anhydride and phosphoric acid. The last reaction, however, is performed better by the described classical procedure[6] which is simpler and gives comparable yields.

For the synthesis of oxysanguinarine (*XIV*) we chose the procedure described by Cushman[13] and Shamma[3], and we modified it. The condensation of anhydride[10] *XV* with imine[3] *XVI* gave a mixture of *cis*- and *trans*-acids which was epimerized to the pure *trans*-acid *XVII*. The acid *XVII* was transformed into the corresponding

chloride which was converted into diazoketone *XVIII* by reaction with diazomethane. The Wolff rearrangement of *XVIII* gave the acid *XIX*. Its cyclization to ketone *XX* was accomplished by action of ethyl polyphosphate, because this procedure gives better yields than application of polyphosphoric acid[13] or phos-



I



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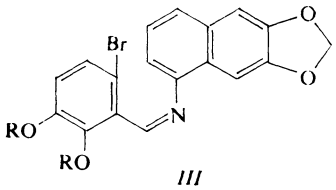

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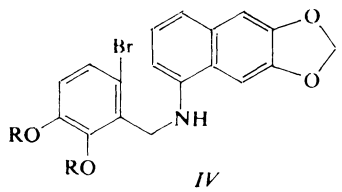

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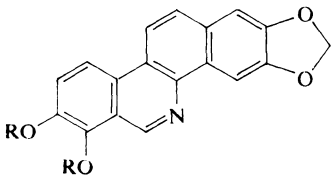
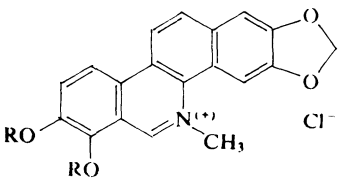
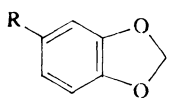


V

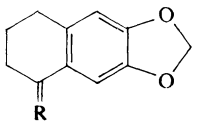


VI

In formulae *I*, *III*–*IV*: *a* RR = CH_2, *b* R = CH_3.



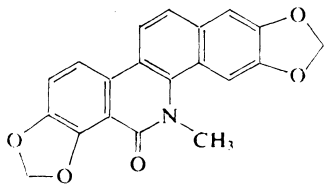
VIII, R = $CH_2CH{=}CH_2$
IX, R = $CH_2CH_2CH_2OH$
X, R = $CH_2CH_2CH_2Cl$
XI, R = $CH_2CH_2CH_2COOH$



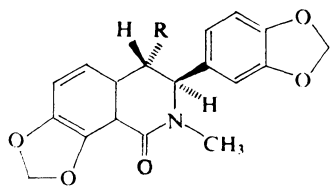
XII, R = O
XIII, R = NOH

phorus pentoxide in methanesulphonic acid[3]. The ketone *XX* was reduced with $NaBH_4$, and the hydroxy derivative *XXI* formed was dehydrogenated to oxysanguinarine (*XIV*). We also tried to prepare oxysanguinarine (*XIV*) by a shorter way, *viz.* by direct cyclization of diazoketone *XVIII* to the 11-oxocompound which should give *XIV* by reduction and dehydrogenation. The cyclization of analogous *cis*-diazo-

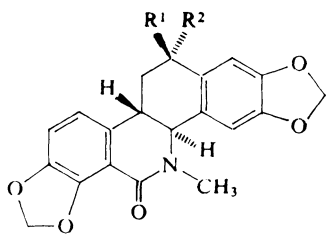
ketone was used in the synthesis of chelidone[14] and corynoline[15]; the cyclization of *trans*-diazoketone was used in synthesis of (±)-13-epi-corynoline[16]. It turned out, however, that, instead of the expected 11-oxocompound, there resulted α-acyloxyketone *XXII* or *XXIII* (depending on the acid used). The ketone *XXII* gives α-hydroxyketone *XXIV* on short boiling in aqueous ethanol. From diazoketone *XXIII* we prepared the α-chloroketone *XXV* whose cyclization to the 11-oxocompound failed, too, although the cyclization of the analogous *cis*-α-chloroketone is described[17].



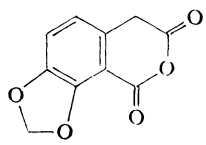
XIV



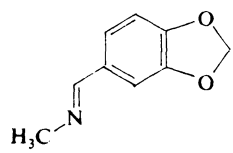
XVII, R = COOH
XVIII, R = $COCHN_2$
XIX, R = CH_2COOH
XXII, R = $COCH_2OCOCF_3$
XXIII, R = $COCH_2OSO_2CH_3$
XXIV, R = $COCH_2OH$
XXV, R = $COCH_2Cl$



XX, $R^1R^2 = O$
XXI, $R^1 = H$, $R^2 = OH$



XV



XVI

The prepared alkaloids *VIa*, *VIb*, and *XIV* were compared with the compounds of natural origin and were found identical.

EXPERIMENTAL

The melting points were determined with a Boetius apparatus. The samples for analyses were dried at 14 Pa pressure over phosphorus pentoxide at room temperature or at 77°C 6 h. Purity

of the substances was checked by TLC on silica gel (Silufol UV_{254}, Kavalier, or GF_{254} plates, Merck) with detection in UV light of the wavelength 254 or 366 nm. The UV spectra were measured with a Unicam SP 8000 spectrophotometer (λ_{max}; log ε), the IR spectra were measured with a Unicam SP 2000 apparatus, (ν, cm^{-1}), and the ^1H NMR spectra were measured with a Tesla 487 C (80 MHz) spectrometer (δ, ppm; J, Hz) using tetramethylsilane as the internal standard. The mass spectra were measured with a Varian MAT 44 S apparatus.

The compounds *VIa*, *VIb*, and *XIV* show no depression when determining the mixed melting points with the respective natural substances. Also in TLC (GF_{254} plates, Merck; chloroform–benzene–ethanol 1 : 1 : 0·1) the synthetized and the natural compounds show identical R_F values. UV and IR spectra of the synthetized alkaloids are identical with those of the natural alkaloids.

N-(6′-Bromo-2′,3′-methylenedioxybenzal)-6,7-methylenedioxy-1-naphthylamine (*IIIa*)

Mixture of 0·58 g (2·5 mmol) 6-bromo-2,3-methylenedioxybenzaldehyde[10] (*Ia*), 0·47 g (2·5 mmol) 6,7-methylenedioxy-1-naphthylamine (*II*), and 25 ml benzene was refluxed 1 h with simultaneous removing of the water formed. The mixture was evaporated to one half of the original volume, filtered, and left to stand, whereupon *IIIa* crystallized as yellow needles. Yield 0·84 g (84%), m.p. 216–218°C. For $C_{19}H_{12}BrNO_4$ (398·2) calculated: 57·30% C, 3·04% H, 20·07% Br, 3·52% N; found: 56·95% C, 3·07% H, 20·42% Br, 3·28% N. UV spectrum (CH_3OH): 246 (4·63), 344 (4·00). Mass spectrum: m/z 397 (M^+, $C_{19}H_{12}BrNO_4$).

N-(6′-Bromo-2′,3′-methylenedioxybenzyl)-6,7-methylenedioxy-1-naphthylamine (*IVa*)

During 15 min 0·08 g (2 mmol) $NaBH_4$ was added portionwise to the stirred solution of 0·80 g (2 mmol) *IIIa* in 12 ml dimethylformamide at 110°C. After 1 h stirring at 110°C, the mixture was cooled, poured in 60 ml water, acidified with 0·2 ml 20% hydrochloric acid, and alkalized with 0·5 ml 20% NaOH. The separated solid was collected by suction, dried, and recrystallized from benzene to give 0·46 g (58%) *IVa*, m.p. 216–218°C. For $C_{19}H_{14}BrNO_4$ (400·2) calculated: 57·01% C, 3·52% H, 19·96% Br, 3·50% N; found: 57·34% C, 3·60% H, 19·67% Br, 3·53% N. UV spectrum (CH_3OH): 244 (4·47), 281 (4·39). Mass spectrum: m/z 399 (M^+, $C_{19}H_{14}BrNO_4$).

2,3,7,8-Bismethylenedioxybenzo[*c*]phenanthridine (*Va*)

Solution of 0·2 g (0·5 mmol) *IVa* in 450 ml benzene was mixed with solution of 40 mg (1 mmol) NaOH in 1 ml water and 50 ml methanol, and the mixture was irradiated with a medium-pressure mercury discharge lamp (125 W) with pyrex filter in argon atmosphere for 2·5 h. The solution was evaporated in vacuum to one half of the original volume, the benzene phase was washed with water, dried with Na_2SO_4, and evaporated. The residue was recrystallized from 2 ml pyridine to give 46 mg (29%) *Va* as needles, m.p. 282–284°C (ref.[1] m.p. 280–281°C). Mass spectrum: m/z 317 (M^+, $C_{19}H_{11}NO_4$).

Sanguinarine chloride (VIa): Quaternization of *Va* by the described procedure[1] gave *VIa* as orange needles in the yield 52%; m.p. 272–274°C (ref.[1] gives m.p. 273–274°C).

N-(6′-Bromo-2′,3′-dimethoxybenzal)-6,7-methylenedioxy-1-naphthylamine (*IIIb*)

The compound *IIIb* was prepared from 6-bromo-2,3-dimethoxybenzaldehyde[10] (*Ib*) and 6,7-methylenedioxy-1-naphthylamine (*II*) in the same way as that given above for *IIIa*. The base *IIIb* was obtained as yellow needles (87%), m.p. 111–113°C (ref.[4], m.p. 94–95°C). For $C_{20}H_{16}$·.$BrNO_4$ (414·3) calculated: 57·98% C, 3·89% H, 19·29% Br, 3·38% N; found: 57·71% C, 4·04% H,

19·22% Br, 3·46% N. UV spectrum (CH_3OH): 216 (4·65), 243 (4·69). ^{1}H NMR spectrum (C^2HCl_3): 8·68 (s, 1 H, CH=N), 7·70 (s, 1 H, 8-H), 7·28 (s, 1 H, 5-H), 7·10 (d, 1 H, J = 9, 5'-H), 6·80 (d, 1 H, J = 9, 4'-H), 6·80–7·60 (m, 3 H, 2,3,4-H), 5·95 (s, 2 H, OCH_2O), 3·91, 3·82 (2 × s, 2 × 3 H, 2 × OCH_3). Mass spectrum: m/z 413 (M^+, 5, $C_{20}H_{16}BrNO_4$), 187 (100%), 148 (18).

N-(6'-Bromo-2',3'-dimethoxybenzyl)-6,7-methylenedioxy-1-naphthylamine (*IVb*)

The compound *IVb* was prepared from *IIIb* (yield 61%) in the same way as the above-described *IVa*. M.p. 122–124°C (ethanol) (ref.[4], m.p. 121–122°C). For $C_{20}H_{18}BrNO_4$ (416·3) calculated: 57·70% C, 4·36% H, 19·19% Br, 3·36% N; found: 57·91% C, 4·45% H, 19·13% Br, 3·57% N. UV spectrum (CH_3OH): 241 (4·43), 264 (4·48). ^{1}H NMR spectrum (C^2HCl_3): 6·60–7·35 (m, 7 H, 2,3,4,5,8,4',5'-H), 5·92, (s, 2 H, OCH_2O), 4·50 (s, 2 H, CH_2—N), 4·40 (bs, 1 H, NH), 3·80 (s, 6 H, 2 × OCH_3). Mass spectrum: m/z 415 (M^+, 85, $C_{20}H_{18}BrNO_4$), 336 (94), 305 (42), 229 (33), 214 (100%), 186 (62), 159 (36).

7,8-Dimethoxy-2,3-methylenedioxybenzo[*c*]phenanthridine (*Vb*)

The compound *Vb* was prepared from *IVb* (yield 23%) in the same way as the above-described *Va* M.p. 213–215°C (ref.[2] gives m.p. 212–214°C; ref.[4], m.p. 208–210°C). For $C_{20}H_{15}NO_4$ (333·3) calculated: 72·06% C, 4·54% H, 4·20% N; found: 71·48% C, 4·62% H, 4·13% N. UV spectrum (CH_3OH): 243 (4·58), 256 (4·55), 276 (4·67), 324 (4·10). Mass spectrum: m/z 333 (M^+, 100%, $C_{20}H_{15}NO_4$), 318 (23), 290 (47), 275 (14), 232(10), 167 (13), 145 (19).

Chelerythrine chloride (VIb): In the same way as *VIa*, the compound *VIb* was prepared from *Vb*. The chloride *VIb* form yellow needles, m.p. 212–214°C, yield 48% (ref.[2] gives m.p. 207 to 209°C).

3-(3,4-Methylenedioxyphenyl)propanol (*IX*)

5·7 g (0·15 mol) $NaBH_4$ was added to solution of 81 g (0·5 mol) 4-allyl-1,2-methylenedioxybenzene (*VIII*) in 250 ml tetrahydrofuran with stirring. The 25·2 ml (0·2 mol) boron trifluoride etherate in 50 ml tetrahydrofuran was added drop by drop at 15–20°C. After 1 h stirring the reaction mixture was treated subsequently with (dropwise added) 10 ml water, then solution of 6·4 g (0·16 mol) NaOH in 50 ml water, and finally 55 ml (0·54 mol) aqueous 30% H_2O_2. After 15 min the mixture was saturated with solid NaCl, the separated organic layer was washed with saturated NaCl solution, dried with $MgSO_4$, and evaporated in vacuum. The residue was distilled in vacuum, and the alcohol *IX* was obtained as a liquid boiling within 130–133°C/120 Pa (ref.[12] gives b.p. 120–122°C/80 Pa) in the yield of 75·2 g (83·5%). 3-(3,4-Methylenedioxyphenyl)-propyl chloride (*X*) was prepared from *IX* by the described procedure[12]. M.p. 59–61°C (ref.[12], m.p. 60–61°C).

4-(3,4-Methylenedioxyphenyl)butyric Acid (*XI*)

a) Solution of the Grignard reagent prepared from 20 g (0·1 mol) *X* and 2·55 g (0·105 mol) Mg in 40 ml ether was added to suspension of 176 g (4 mol) solid CO_2 in 100 ml ether with stirring at −78°C during 5 min. Next day the mixture was decomposed with 40 ml hydrochloric acid (1 : 1) and washed with water. The acid *XI* was extracted with solution of Na_2CO_3 (10%, 2 × 100 ml). The solution of sodium salt of the acid *XI* was acidified with hydrochloric acid (1 : 1), cooled, and the separated acid *XI* was collected by suction. After recrystallization from benzene–heptane mixture yield 14·7 g *XI* (71%), m.p. 78–79°C (ref.[6], m.p. 79–80°C; ref.[12], m.p. 75–76°C).

b) 62 ml (0·8 mol) methanesulphonyl chloride was added drop by drop to solution of 72 g (0·4 mol) *IX* and 80 ml (1 mol) pyridine in 400 ml dichloromethane at 5—10°C with stirring. After 1 h stirring at 10°C, the mixture was neutralized with aqueous ammonia (28%, 34 ml), mixed with 400 ml water, the separated organic layer was washed subsequently with water, hydrochloric acid (1 : 6), and water until neutral. After drying with $CaCl_2$ and evaporation of the solvent, the mesylate of alcohol *X* was obtained as a liquid. Solution of the mesylate in 500 ml ethanol was treated with solution of 24·5 g (0·5 mol) NaCN in 100 ml water, and the mixture was refluxed 12 h. Then a solution of 20 g (0·5 mol) NaOH in 40 ml water was added, and the mixture was refluxed 12 h. Ethanol was evaporated in vacuum, the residue was dissolved in 800 ml water, filtered, acidified with hydrochloric acid (1 : 1), and cooled, and the separated acid *XI* was collected by suction. Recrystallization from benzene–heptane mixture gave 59·9 g (72% with respect to the starting alcohol *IX*) acid *XI*, m.p. 79—80°C, which was identical with the product of the above procedure *a*).

6,7-Methylenedioxy-1-tetralone (*XII*)

62·5 g (0·3 mol) acid *XI* was added slowly to 312 ml ethyl polyphosphate[6] at 20°C with stirring. After 30 min the mixture was heated to 30°C and stirred 1 h. After addition of 1 250 ml water, the mixture was stirred 6 h and extracted with 2 × 400 ml ether. The extract was washed with water and with $NaHCO_3$ solution, dried with Na_2SO_4, and the solvent was evaporated. The residue was recrystallized from ethanol to give 50·2 g (88%) *XII*, m.p. 74—76°C (ref.[6] gives m.p. 75—76°C; ref.[12] m.p. 71—72°C). The ketone *XII* was converted[6] into oxime *XIII*, m.p. 146—148°C (ref.[6], m.p. 145—147°C).

6,7-Methylenedioxy-1-naphthylamine (*II*)

10·2 g (50 mmol) *XIII* was added to mixture of 49 g (0·5 mol) anhydrous phosphoric acid and 51 g (0·5 mol) acetic anhydride with stirring. The mixture was stirred at 80°C 0·5 h, poured in 1 l water, and alkalized with aqueous 20% NaOH solution. The separated precipitate was collected by suction, mixed with 20 ml 37% hydrochloric acid and 180 ml methanol, and refluxed 4 h. Methanol was evaporated in vacuum, the residue was alkalized with 5% NaOH solution, and the separated solid was extracted with 2 × 200 ml ether. Ether was evaporated, and the residue was recrystallized from benzene to give 2·8 g (30%) amine *II*, m.p. 154—156°C (ref.[6] gives m.p. 154—155°C).

trans-N-Methyl-3-(3′,4′-methylenedioxyphenyl)-4-carboxy-7,8-methylenedioxy-3,4-dihydro--1(2*H*)-isoquinolone (*XVII*)

6·2 g (30 mmol) 3,4-methylenedioxyhomophthalic acid anhydride (*XV*) was added to solution of 4·9 g (30 mmol) 3,4-methylenedioxybenzylidenemethylamine (*XVI*) in 30 ml chloroform at 20°C with stirring during 10 min. The exothermic reaction increased slightly the temperature of the solution which was then stirred 30 min and evaporated. The evaporation residue was treated with 150 ml acetic acid, the mixture was refluxed 16 h, evaporated, and the residue was recrystallized from methanol. Yield 10·5 g (95%) acid *XVII*, m.p. 251—253°C (ref.[3] gives m.p. 249—254°C). ^{1}H NMR spectrum ($(C^2H_3)_2SO$): 6·90 (d, 1 H, J = 8·5, 5-H), 6·68 (d, 1 H, J = 8·5, 6-H), 6·40—6·70 (m, 3 H, 2′,5′,6′-H). 6·15 (s, 2 H, OCH_2O), 5·98 (s, 2 H, OCH_2O), 5·16 (bs, 1 H, 3-H), 4·05 (d, 1 H, J = 2·0, 4-H), 3·00 (s, 3 H, N—CH_3).

Methyl Ester of Acid *XVII*

Solution of diazomethane (from 10 mmol N-nitroso-N-methylurea) in 10 ml ether was added to solution of 0·18 g (0·5 mmol) acid *XVII* in 20 ml methanol. After 1 h the solution was evapor-

ated, and the residue was recrystallized from methanol to give 0·12 g (63%) methyl ester of acid *XVII*, m.p. 218–219°C (ref.[3] gives m.p. 213–214°C).

trans-N-Methyl-3-(3′,4′-methylenedioxyphenyl)-4-diazomethylcarbonyl-7,8-methylenedioxy-3,4-dihydro-1(2*H*)-isoquinolone (*XVIII*)

Mixture of 7·4 g (20 mmol) *XVII*, 300 ml dichloromethane, and 4·3 ml (50 mmol) oxalyl chloride was stirred and refluxed for 6 h. After evaporation, the residue (acid *XVII* chloride, m.p. 130 to 132 °C) was dissolved in 50 ml dichloromethane and added dropwise to solution of diazomethane (from 0·1 mol N-nitroso-N-methylurea) in 100 ml ether at 0°C with stirring. After 15 min stirring the separated solid was collected by suction and dried in air. Yield 7·0 g (89%) diazoketone *XVIII*, m.p. 174–176°C. For $C_{20}H_{15}N_3O_6$ (393·3) calculated: 61·07% C, 3·84% H, 10·68% N; found: 60·93% C, 4·02% H, 10·23% N.

trans-N-Methyl-3-(3′,4′-methylenedioxyphenyl)-4-carboxymethyl-7,8-methylenedioxy-3,4-dihydro-1(2*H*)-isoquinolone (*XIX*)

Mixture of 3·9 g (4 mmol) *XVIII*, 500 ml methanol, and 2 g Ag_2O was refluxed 2 h. The mixture was hot filtered, the filtrate was evaporated, and the residue was mixed with 40 ml ethanol and solution of 1 g KOH in 10 ml water. The mixture was refluxed 2 h, cooled, and ethanol was evaporated. The precipitate formed on acidification with hydrochloric acid (1 : 1) was extracted with chloroform, the extract was shaken with sodium hydrogen carbonate solution (5%, 2 × × 120 ml), and the separated aqueous layer was then acidified with hydrochloric acid (1 : 1) and extracted with chloroform. The extract was dried with $MgSO_4$, the solvent was evaporated, and the residue was recrystallized from methanol to give 2·4 g (63%) acid *XIX*, m.p. 244–246°C (ref.[3] gives m.p. 244–246°C).

trans-N-Methyl-2,3,7,8-bismethylenedioxy-6,12-dioxo-4b,5,6,10b-11,12-hexahydrobenzo[*c*]phenanthridine (*XX*)

Mixture of 1·9 g (5 mmol) *XIX* and 38 ml ethyl polyphosphate was stirred and heated on boiling water bath 1 h. The solution was cooled, poured in 200 ml water, and stirred at 40°C for 8 h. The precipitated solid was extracted with chloroform, the extract was washed with aqueous 5% Na_2CO_3, dried with $MgSO_4$, evaporated, and the residue was mixed with 5 ml ethanol. The precipitated solid was collected by suction and recrystallized to give 1·35 g (74%) ketone *XX*, m.p. 276–280°C (ref.[3] gives m.p. 277–280°C).

N-Methyl-2,3,7,8-bismethylenedioxy-12α-hydroxy-6-oxo-4b,5,6,10b-11,12-hexahydrobenzo[*c*]phenanthridine (*XXI*)

Suspension of 0·36 g (1 mmol) *XX* in 500 ml 2-propanol was treated with 0·38 g (10 mmol) $NaBH_4$, and the mixture was stirred at 40°C 8 h. After evaporation, the residue was mixed with water, acidified with hydrochloric acid (10%) and extracted with chloroform. The extract was washed with water, dried with $MgSO_4$, and evaporated. Recrystallization from ethanol gave 0·26 g (72%) *XXI*, m.p. 278–282°C (ref.[3] gives m.p. 281–283°C).

Oxysanguinarine (*XIV*)

Solution of 0·18 g (0·5 mmol) *XXI* and 50 mg *p*-toluenesulphonic acid in 180 ml benzene was refluxed 14 h. Benzene was evaporated, the residue was dissolved in chloroform and washed with $NaHCO_3$ solution. The extract was dried, concentrated, and submitted to column chromato-

graphy (silica gel Kieselgel 60, Merck, 20 g) with chloroform as eluent. The eluate was evaporated, and the residue was recrystallized from chloroform–ether mixture to give 61 mg (35%) *XIV*, m.p. 346–348°C (ref.[3] gives m.p. 347–349°C).

trans-N-Methyl-3-(3′,4′-methylenedioxyphenyl)-4-trifluoroacetoxymethylenecarbonyl-7,8-methylenedioxy-3,4-dihydro-1(2*H*)-isoquinolone (*XXII*)

0·39 g (1 mmol) *XVIII* was added slowly to a stirred mixture of 3·6 ml CH_3CO_2H and 0·4 ml CF_3CO_2H at 17°C under argon atmosphere. When the cooling bath was removed, the reaction mixture liberated slowly nitrogen gas. After 1 h stirring, 50 ml dichloromethane was added, the mixture was washed with 4 × 25 ml water, dried with Na_2SO_4, and evaporated. The evaporation residue was recrystallized from benzene to give 0·29 g (60%) *XXII*, m.p. 196–197°C. For $C_{22}H_{16}F_3NO_8$ (479·4) calculated: 55·12% C, 3·36% H, 11·89% F, 2·92% N; found: 54·97% C, 3·61% H, 11·83% F, 2·65% N. IR spectrum ($CHCl_3$): 1 792 ($COCF_3$), 1 729 ($COCH_2$), 1 640 (CON). ^{1}H NMR spectrum (C^2HCl_3): 6·30–6·80 (m, 5 H, 5,6,2′,5′,6′-H). 6·05 (s, 2 H, 7-OCH_2O-8), 5·79 (s, 2 H, 3′-OCH_2O-4′), 5·02 (bs, 1 H, 3-H), 4·10, 4·50 (d,d-ABq, J = 16·0, 2 H, $COCH_2O$), 3·75 (bs, 1 H, 4-H), 3·00 (s, 3 H, N—CH_3). Mass spectrum: m/z 479 (M^+, $C_{22}H_{16}F_3NO_8$).

trans-N-Methyl-3-(3′,4′-methylenedioxyphenyl)-4-methylsulphonyloxymethylcarbonyl-7,8-methylenedioxy-3,4-dihydro-1(2*H*)-isoquinolone (*XXIII*)

The same procedure as that described for preparation of *XXII* was used to convert *XVIII* to *XXIII* (0·4 ml CH_3SO_3H was used instead of 0·4 ml CF_3CO_2H), m.p. 204–206°C. For $C_{21}H_{19}NO_9S$ (461·4) calculated: 54·66% C, 4·15% H, 3·04% N, 6·95% S; found: 55·04% C, 4·30% H, 3·04% N, 7·18% S. IR spectrum (KBr): 1 180, 1 357 (SO_2—O—), 1 648 ($CONCH_3$), 1 738 ($COCH_2$). ^{1}H NMR spectrum (($C^2H_3)_2SO$): 6·40–7·10 (m, 5 H, 5,6,2′,5′,6′—H), 6·12 (s, 2 H, 7-OCH_2O-8), 5·98 (s, 2 H, 3′-OCH_2O-4′), 5·43, 5·06 (d, d-ABq, J = 17·0, 2 H, $COCH_2O$), 5·10 (bs, 1 H, 3-H), 4·31 (bs, 1 H, 4-H), 3·25 (s, 3 H, SO_2CH_3), 2·95 (s, 3 H, N—CH_3).

trans-N-Methyl-3-(3′,4′-methylenedioxyphenyl)-4-hydroxymethylcarbonyl-7,8-methylenedioxy-3,4-dihydro-1(2*H*)-isoquinolone (*XXIV*)

Mixture of 479 mg (1 mmol) *XXII* and 5 ml 96% ethanol was refluxed 10 min. A part of the solvent was evaporated, and the separated crystalline solid was collected by suction. Recrystallization from ethanol gave 325 mg (85%) *XXIV*, m.p. 192–194°C. For $C_{20}H_{17}NO_7$ (383·4) calculated: 62·65% C, 4·47% H, 3·65% N; found: 63·02% C, 4·63% H, 3·22% N. IR spectrum (KBr): 3 335 (OH), 1 719 ($COCH_2$), 1 628 (CON). ^{1}H NMR spectrum (C^2HCl_3): 6·30–6·80 (m, 5 H, 5,6,2′,5′,6′-H), 6·05 (s, 2 H, 7-OCH_2O-8), 5·80 (s, 2 H, 3′-OCH_2O-4′), 5·08 (bs, 1 H, 3-H), 4·05 (d, J = 17·0, 2 H, $COCH_2$), 3·65 (bs, 1 H, 4-H), 2·98 (s, 3 H, N—CH_3). Mass spectrum: m/z 383 (M^+, $C_{20}H_{17}NO_7$).

trans-N-Methyl-3-(3′,4′-methylenedioxyphenyl)-4-chloromethylcarbonyl-7,8-methylenedioxy-3,4-dihydro-1(2*H*)-isoquinolone (*XXV*)

Hydrogen chloride was bubbled through solution of 393 mg (1 mmol) diazoketone *XVIII* in 10 ml chloroform for 10 min. After 30 min standing, chloroform was evaporated, and the residue was recrystallized from ethanol to give 193 mg (48%) *XXV*, m.p. 245–247°C. For $C_{20}H_{16}ClNO_6$ (401·8) calculated: 59·78% C, 4·01% H, 8·83% Cl, 3·49% N; found: 59·91% C, 4·17% H, 8·53% Cl, 3·23% N. IR spectrum ($CHCl_3$): 1 640 (CON), 1 724 ($COCH_2Cl$). ^{1}H NMR spectrum

($(C^2H_3)_2SO$): 6·91 (d, J = 8·0, 1 H, 5-H), 6·81 (d, J = 8·0, 1 H, 5′-H), 6·78 (d, J = 8·0, 1 H, 6-H), 6·70 (mcs, J = 2·0, 1 H, 2′-H), 6·50 (mcd, J = 8·0, 2·0, 1 H, 6′-H), 6·12 (s, 2 H, 7-OCH_2O-8), 5·97 (s, 2 H, 3′-OCH_2O-4′), 5·12 (bs, 1 H, 3-H), 5·01, 4·61 (d,d-ABq, J = 17·0, 2 H, CH_2Cl), 4·32 (bs, 1 H, 4-H), 2·96 (s, 3 H, N—CH_3). The attempts at cyclization of *XXV* under the described[17] conditions failed, the starting *XXV* being isolated.

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