Abnormal Products from Phenolic Oxidation of a Dihydroxy-1-benzyl-1,2,3,4-tetrahydroisoquinoline

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Phenolic oxidation of 1,2,3,4-tetrahydro-7-hydroxy-1-(3-hydroxy-4,5-dimethoxybenzyl)-6-methoxy-2-methylisoquinoline (III) unexpectedly afforded 3-hydroxy-4,5-dimethoxybenzaldehyde (XVII) and a cyclopent[*ij*]isoquinolinone (XVIII), whose structures were elucidated by spectral determinations.

In a previous paper [1] phenolic oxidative coupling of 1-(3,4-dihydroxybenzyl)-1,2,3,4-tetrahydro-7-hydroxy-6-methoxy-2,2-dimethylisoquinolinium iodide (I) gave 1,9,10-trihydroxy-2-methoxyaporphine methopicrate (II), which was methylated with diazomethane to give glaucine methopicrate (IIa). No attempts to obtain the aporphines of type (IV) by phenolic oxidation of the 1,2,3,4-tetrahydroisoquinolines which have three substituents at the 3-, 4-, and 5-positions of the 1-benzyl group (III) have been carried out.

Franck and Schlingloff [2] have already reported the formation of the aporphine (IIb) by phenolic oxidation of (Ia), and the compound (IIc) cyclised at the position *ortho* to the hydroxy-group was not formed. Jackson and Martin [3] also reported that the oxidation of (IIIa) with potassium ferricyanide did not afford the aporphine (IVa) but the compound (IVb) cyclised at the position *para* to the hydroxy-group.

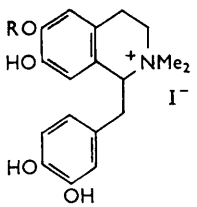
These facts suggest that the cyclisation proceeds preferentially at the *para*-position with respect to the hydroxy-group.

The purpose of this investigation is to study the phenolic oxidation of compound (III) in order to discover whether the formation of 1,2,9,10,11-pentasubstituted aporphines would be possible or not and whether the characteristic radical coupling would occur or not.

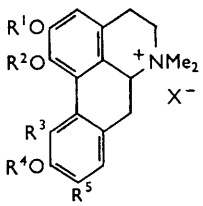
The starting material (III) was synthesised as follows. Chlorination with thionyl chloride of the alcohol (Vb), which was obtained by reduction of methyl 3-benzyloxy-4,5-dimethoxybenzoate (Va) [4] with lithium aluminium hydride, afforded the chloride (Vc), which was converted into the cyanide (Vd).

Hydrolysis of the above cyanide (Vd) gave the homo-acid (Ve), whose condensation with phenethylamine (VI)

[1] T. Kametani and I. Noguchi, *J. Chem. Soc.* (*C*), 1967, 1440.
[2] B. Franck and G. Schlingloff, *Annalen*, 1962, **659**, 123.
[3] A. H. Jackson and J. A. Martin, *J. Chem. Soc.* (*C*), 1966, 2061.
[4] Y. Inubushi and Y. Fujitani, *J. Pharm. Soc. Japan*, 1958, **78**, 486.



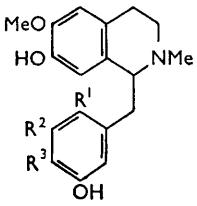
(I)



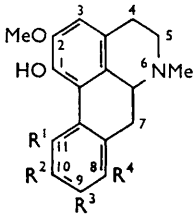
(II)

(I) R = Me
a; R = H

(II) R^1 = Me, R^2 = R^3 = R^4 = H, R^5 = OH, X = $C_6H_2(NO_2)_3O^-$
a; R^1 = R^2 = R^4 = CH_3, R^3 = H, R^5 = OCH_3, X = $C_6H_2(NO_2)_3O^-$
b; R^1 = R^2 = R^3 = R^4 = H, R^5 = OH, X = Cl^-
c; R^1 = R^2 = R^4 = R^5 = H, R^3 = OH, X = Cl^-



(III)



(IV)

(III) R^1 = H, R^2 = R^3 = OMe
a; R^1 = Br, R^2 = H, R^3 = OMe

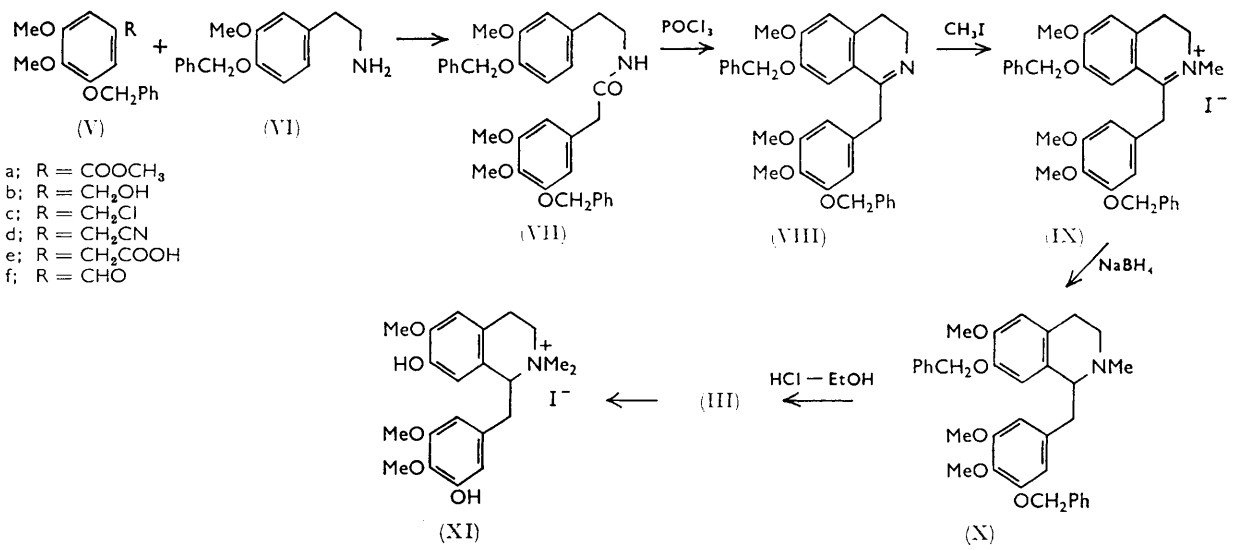
(IV) R^1 = R^2 = OMe, R^3 = OH, R^4 = H
a; R^1 = OH, R^2 = OMe, R^3 = H, R^4 = Br
b; R^1 = R^4 = H, R^2 = OMe, R^3 = OH

by heating at 190° for 2 hours afforded the amide (VII). Methylation with methyl iodide of the 3,4-dihydroisoquinoline (VIII), which was cyclised by Bischler–Napieralski reaction with phosphoryl chloride, afforded the methiodide (IX). Reduction of (IX) with sodium borohydride gave 1,2,3,4-tetrahydroisoquinoline (X), which was characterised as its oxalate. Debenzylation of (X) with ethanolic concentrated hydrochloric acid solution gave the expected compound (III), which was also characterised as its methiodide (XI) by microanalysis and spectral determinations.

In order to obtain the cyclised compounds (XIIa—b) and (XIIIa—b), oxidation of (III) was investigated under a variety of conditions. On treatment with potassium ferricyanide of the hydrochloride of (III) according to Jackson and Martin's methods,[3,5] no spots besides the starting material could be detected on t.l.c. Furthermore, oxidation of (III) in phosphate buffer by the method of Chan and Maitland [6] was tried, but only starting material was recovered.

Therefore, since there would be a strong steric hindrance to the formation of aporphine derivatives (XIIa) and (XIIb) or morphine derivatives (XIIIa) and (XIIIb), oxidation of (III) under drastic conditions was investigated in order to overcome this hindrance. Thus, a solution of the hydrochloride of (III) was treated with 35 molar equivalents of ferric chloride hexahydrate at room temperature for 20 hours with stirring, a novel spot besides the starting material being observed on t.l.c. The reaction was therefore continued at 60—80° for an additional 48 hours, after which no spot of (III) was detected. After working up as usual, column chromatography of the resultant dark reddish syrup using silicic acid afforded a mixture of two substances (XVII) and (XVIII). The former compound, 3-hydroxy-4,5-dimethoxybenzaldehyde, was obtained in 3·3% yield by evaporation of the first eluate ($CHCl_3$) to give a colourless oil, which was identical with an authentic sample (mixed melting point and spectral determination). The authentic sample was prepared by debenzylation of 3-benzyloxy-4,5-dimethoxybenzaldehyde (Vf) which was obtained according to Inubushi's method.[4]

The latter compound (XVIII) was obtained from the eluate (chloroform–methanol, 97 : 3) as pale yellow fine needles, which were comparatively labile in the air. At



(V) (VI) (VII) (VIII) (IX) (XI) (III) (X)

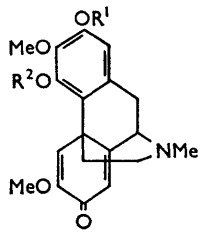
a; R = $COOCH_3$
b; R = CH_2OH
c; R = CH_2Cl
d; R = CH_2CN
e; R = CH_2COOH
f; R = CHO

[5] A. H. Jackson and J. A. Martin, *J. Chem. Soc.* (*C*), 1966, 2222.

[6] W. Wan-Chiu Chan and P. Maitland, *J. Chem. Soc.* (*C*), 1966, 753.

first this compound (XVIII) was expected to be one of the oxidised compounds (XIIa), (XIIb), (XIIIa), or (XIIIb).

(XII)a; $R^1 = H$, $R^2 = Me$
b; $R^1 = Me$, $R^2 = H$



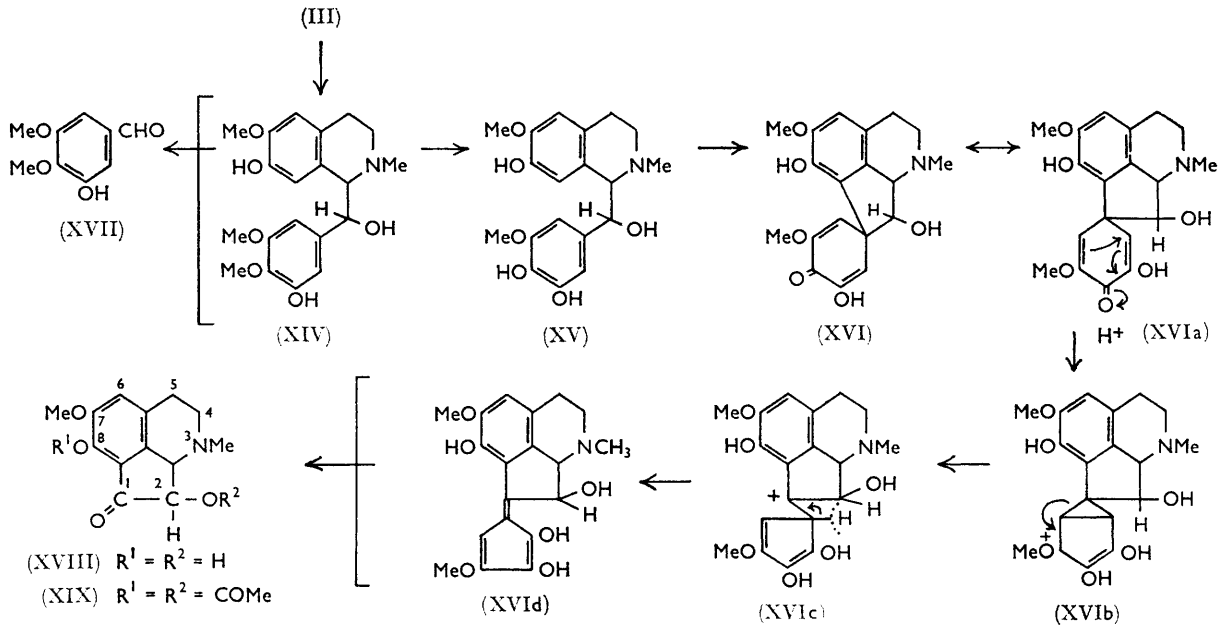
(XIII)a; $R^1 = H$, $R^2 = Me$
b; $R^1 = Me$, $R^2 = H$

The n.m.r. spectrum (p.p.m. from tetramethylsilane, in $CDCl_3$) of compound (XVIII) showed one proton due to the chelated hydroxy-group at 12·80 p.p.m. as a broad signal, one aromatic proton at 6·81 p.p.m., methoxy-protons at 3·87 p.p.m., a hydroxy-proton at 3·25 p.p.m., and an *N*-methyl group at 2·51 p.p.m. as singlets; the signals at 12·80 and 3·25 p.p.m. disappeared on substitution with deuterium oxide. On the other hand, in the n.m.r. spectrum of the acetyl derivative (XIX), the signals at 12·80 and 3·25 p.p.m. could not be detected and a signal of six protons due to two acetyl groups was observed at 2·36 p.p.m. Furthermore, the signal of the methoxy-group at 3·87 p.p.m. in (XVIII) shifted to higher field at 3·81 p.p.m. by acetylation.[7] These facts support the structure of (XVIII).

Furthermore, the mass spectrum of (XVIII) supported the molecular formula of $C_{13}H_{15}NO_4$ and showed strong peaks at *m/e* 249 (M^+), 248 ($M-1$), 247 ($M-2$). In addition, the peak at *m/e* 231 ($M - H_2O$) shows the presence of an alcoholic hydroxy-group having hydrogen at the α-position. Moreover, a strong peak at *m/e* 204 seems to be formed through retro-Diels–Alder cleavage of the ion ($M-2$) and the ion ($M-58$) of the isoquinoline nucleus appears at *m/e* 191 as the base peak. These facts also prove the oxidised compound (XVIII) to have an isoquinoline ring substituted at the 1- and 8-positions.

The i.r. spectrum (in $CHCl_3$) of (XVIII) showed a broad hydroxy-absorption, attributable to hydrogen bonding [8] with the lone pair of nitrogen, at 3350—3100 cm.$^{-1}$ and a broad absorption due to the chelation [9] at 2750—2550 cm.$^{-1}$. The absorptions of the *N*-methyl group and the chelated carbonyl group [9,10] were shown at 2795 and 1635 cm.$^{-1}$. On the other hand, in the i.r. spectrum (in $CHCl_3$) of the acetyl derivative (XIX) the two characteristic broad absorption bands at 3350—3100 and 2750—2500 cm.$^{-1}$ disappeared and the above band due to the chelated carbonyl group at 1635 cm.$^{-1}$ was shifted to the normal conjugated carbonyl frequency of 1685 cm.$^{-1}$. A broad absorption due to the *O*-acetyl groups was observed at 1755 cm.$^{-1}$.

The u.v. spectrum of (XVIII) in chloroform or dioxan showed $\lambda_{max.}$ 358 mμ, but $\lambda_{max.}$ in methanol was 364 mμ, showing a bathochromic shift. Since this is closely similar to the characteristic bathochromic shift of *O*-hydroxyacetophenone derivatives [11,12] due to solvation with a hydroxylic solvent and the chelation effect [13,14] of hydrogen bonding, the structure of (XVIII) was also proved to be correct.



[7] A. R. Battersby, R. B. Bradbury, R. B. Hervert, M. H. G. Munro, and R. Ramage, *Chem. Comm.*, 1967, 450.
[8] T. Kametani and T. Kikuchi, *J. Pharm. Soc. Japan*, 1967, **87**, 682.
[9] K. Nakanishi and L. F. Fieser, *J. Amer. Chem. Soc.*, 1952, **74**, 3910.
[10] T. Kametani, K. Ohkubo, and I. Noguchi, *J. Chem. Soc.* (*C*), 1966, 715.
[11] R. A. Morton and Z. Sawires, *J. Chem. Soc.*, 1940, 1052.
[12] R. A. Morton and A. L. Stubbs, *J. Chem. Soc.*, 1940, 1347.
[13] L. H. Conover, *Chem. Soc. Special Publ.*, 1950, No. 5, 48.
[14] A. I. Scott, 'Ultraviolet Spectra of Natural Products, Pergamon, London, 1964, p. 114.

The simplest mechanism to explain the formation of the two abnormal oxidation products (XVII) and (XVIII) would initially involve the oxidation of the α-position of the benzyl group to afford (XVII) by oxidative cleavage of (XIV). On the other hand, ether cleavage would occur in acid media at the methoxy-group *ortho* to the hydroxy-group to afford an intermediate (XV), whose oxidation seems to give the dienone (XVI).

This would be further oxidised to give (XVIII), after conversion into (XVId) by protonation by way of (XVIa) ⟶ (XVIb) ⟶ (XVIc).

EXPERIMENTAL

Nuclear magnetic resonance spectra were measured on Varian A-60 and Hitachi H-60 spectrometers with deuteriochloroform and dimethyl sulphoxide as solvents and tetramethylsilane as an internal reference.

The mass spectrum was measured with a Hitachi mass spectrometer RMU-6D equipped with a direct inlet system: chamber voltage 70 ev; total emission 80μA; evaporation temp., 80—90°; ion-chamber temp., 250°.

3-*Benzyloxy*-4,5-*dimethoxybenzyl Cyanide* (Vd).—To a cooled suspension of lithium aluminium hydride (4.0 g.) in dry ether (100 ml.) was added dropwise with stirring a solution of methyl 3-benzyloxy-4,5-dimethoxybenzoate (Va) [4] (10 g.) in dry tetrahydrofuran (40 ml.). The mixture was stirred at room temperature for 1 hr. and then refluxed for a further 30 min. The excess of reagent was decomposed with 40% potassium hydroxide solution and the resultant mixture was filtered.

Concentration of the filtrate gave the residue, which was extracted with benzene. The solvent was washed with 10% sodium hydroxide solution and water, dried (K_2CO_3), and distilled to give 3-*benzyloxy*-4,5-*dimethoxybenzyl alcohol* (Vb) (7·0 g.) as a colourless oil, b. p. 205°/0·09 mm., $\nu_{max.}$ (KBr) 3420 (OH) and 1060 cm.$^{-1}$ (C–O).

To a solution of the above alcohol (Vb) (5·0 g.) in dry benzene (30 ml.) was added thionyl chloride (7·0 g.), and the mixture was allowed to stand at room temperature for 1 hr. and then refluxed for an additional 1 hr. Removal of the excess of reagent afforded the *chloride* (Vc) as a reddish-brown syrup, which was used in the following reaction without purification.

A mixture of the preceding chloride (Vc), ethyl methyl ketone (200 ml.), sodium iodide (6·0 g.), and sodium cyanide (7·0 g.) was heated with stirring at 75—80° for 5 hr. After the reaction mixture had been added to water, the solvent layer separated was washed with saturated sodium chloride solution, dried (K_2CO_3), and distilled to give a yellow oil (4·5 g.), b. p. 200—205°/0·5 mm.

Recrystallisation from ether afforded the *cyanide* (Vd) as colourless prisms, m. p. 58—59° (Found: C, 72·4; H, 6·4; N, 5·25. $C_{17}H_{17}NO_3$ requires C, 72·05; H, 6·05; N, 4·95%), $\nu_{max.}$ (KBr) 2260 (C≡N) and 755 and 695 cm.$^{-1}$ (monosubstituted benzene), δ ($CDCl_3$) 7·48 (5H, broad singlet, monosubstituted benzene), 6·54 (2H, broad singlet, 2- and 6-*H*), 5·10 (2H, singlet, OCH_2Ph), 3·85 (6H, singlet, 4- and 5-OCH_3), and 3·61 p.p.m. (2H, singlet, CH_2CN).

N-(4-*Benzyloxy*-3-*methoxyphenethyl*)-3-*benzyloxy*-4,5-*dimethoxyphenylacetamide* (VII).—A mixture of the above cyanide (Vd) (5·0 g.), methanol (45 ml.), potassium hydroxide (10·6 g.), water (10 ml.), and dioxan (30 ml.) was refluxed on a water-bath for 20 hr., and the solvent was then removed by distillation to give a residue, which was extracted with cold water. The resultant aqueous layer was washed with ether, acidified with 10% hydrochloric acid solution, and extracted with chloroform. The extract was washed with water, dried (Na_2SO_4), and evaporated to give the phenylacetic acid derivative (Ve) (3·2 g.) as a yellow oil, $\nu_{max.}$ ($CHCl_3$) 1695 cm.$^{-1}$ (C=O).

A mixture of the acid (Ve) (2·0 g.) and phenethylamine (3·0 g.) was fused under reduced pressure at 190° for 2 hr. After cooling, the reaction mixture was extracted with chloroform. The extract was washed with 10% hydrochloric acid and 10% sodium hydroxide solution, dried (K_2CO_3), and evaporated to give a yellowish-brown syrup (3·8 g.), whose recrystallisation from methanol–ether afforded the *amide* (VII) as colourless cubes, m. p. 106—107° (Found: C, 72·85; H, 6·55; N, 2·6. $C_{38}H_{35}NO_6$ requires C, 73·15; H, 6·5; N, 2·6%), $\nu_{max.}$ (KBr) 3390 (NH) and 1655 cm.$^{-1}$ (C=O).

7-*Benzyloxy*-1-(3-*benzyloxy*-4,5-*dimethoxybenzyl*)-3,4-*dihydro*-6-*methoxyisoquinoline* (VIII) *Hydrochloride*.—A mixture of the amide (VII) (1·0 g.), dry benzene (20 ml.), and phosphoryl chloride (2 ml.) was heated under reflux in an oil-bath for 2 hr. After the reaction, the mixture was poured into n-hexane (500 ml.), and an oil precipitated was separated and washed with n-hexane. Recrystallisation of the above insoluble residue from ethanol–ether gave the 3,4-*dihydroisoquinoline* (VIII) *hydrochloride* (0·6 g.) as colourless prisms, m. p. 203—205° (decomp.) (Found: C, 70·8; H, 6·1; N, 2·35. $C_{33}H_{33}NO_5$,HCl requires C, 70·75; H, 6·1; N, 2·5%), $\nu_{max.}$ (KBr) 2350—2650 (≡$\overset{+}{N}$H) and 1645 cm.$^{-1}$ (C=$\overset{+}{N}$).

The Methiodide (IX) *of* (VIII).—A suspension of the hydrochloride of (VIII) (500 mg.) in benzene was made basic with 10% ammonium hydroxide solution and the solvent layer was separated. The extract was washed with water, dried (K_2CO_3), and distilled to give the free base (VIII) as an oil, which was dissolved in methyl iodide (3 ml.). The resultant solution was allowed to stand at room temperature for 2 hr. Removal of the excess of methyl iodide gave a yellowish-brown syrup, which solidified on being triturated with methanol. Collection by filtration and recrystallisation from methanol–ether afforded the *methiodide* (IX) (400 mg.) as pale yellow needles, m. p. 142—143·5° (Found: C, 61·3; H, 5·75; N, 2·05. $C_{33}H_{33}NO_5$,CH_3I requires C, 61·3; H, 5·45; N, 2·1%), $\nu_{max.}$ (KBr) 1630 cm.$^{-1}$ (C=$\overset{+}{N}$).

7-*Benzyloxy*-1-(3-*benzyloxy*-4,5-*dimethoxybenzyl*)-1,2,3,4-*tetrahydro*-6-*methoxy*-2-*methylisoquinoline* (X).—To a solution of the methiodide (IX) (150 mg.) in methanol (50 ml.) containing 2 drops of water was added portionwise sodium borohydride (150 mg.), and the mixture was allowed to stand at room temperature for 30 min. After 0·5 hr. refluxing, removal of the solvent gave the residue, which was treated with water (10 ml.) and extracted with benzene. The extract was washed with water, dried (K_2CO_3), and evaporated to give a colourless oil (100 mg.), $\nu_{max.}$ ($CHCl_3$) 2798 cm.$^{-1}$ (N–Me).

Recrystallisation of the *oxalate* of (X) from ethanol afforded colourless prisms, m. p. 182—184° (Found: C, 68·3; H, 6·2; N, 2·2. $C_{34}H_{37}NO_5$,$C_2H_2O_4$ requires C, 68·65; H, 6·25; N, 2·2%).

1,2,3,4-*Tetrahydro*-7-*hydroxy*-1-(3-*hydroxy*-4,5-*dimethoxybenzyl*)-6-*methoxy*-2-*methylisoquinoline methiodide* (XI).—

A mixture of the above isoquinoline (X) (500 mg.), ethanol (16 ml.), and concentrated hydrochloric acid was refluxed for 2 hr. After the reaction, the ethanol was distilled off to give the residue, which was mixed with water (20 ml.) and washed with ether. The resulting aqueous solution was made basic with ammonia and extracted with ether. The extract was washed with saturated sodium chloride solution, dried (K_2CO_3), and evaporated to give the hydroxyisoquinoline (III) as a pale yellow oil (312 mg.), δ (in $CDCl_3$) 6·52 (1H, singlet, 5-*H*), 6·48 (1H, doublet, J = 2·5 c./sec., 6′-*H*), 6·40 (1H, singlet, 8-*H*), 6·20 (1H, doublet, J = 2·5 c./sec., 2′-*H*), 4·35 (2H, broad singlet, O*H*), 3·84, 3·82 (6H, two singlets, 6- and 4′-OCH_3), 3·73 (3H, singlet, 5′-OCH_3), and 2·44 p.p.m. (3H, singlet, N-CH_3).

After a mixture of hydroxyisoquinoline (III) (100 mg.), methanol (3 ml.), and methyl iodide (3 ml.) had been allowed to stand at room temperature for 30 min., removal of the solvent gave a pale yellow oil, which solidified on being triturated with ether.

Recrystallisation from methanol–ether afforded the *methiodide* (95 mg.) as colourless prisms, m. p. 242—244° (Found: C, 50·5; H, 5·9; N, 2·75. $C_{20}H_{25}NO_5,CH_3I$ requires C, 50·25; H, 5·6; N, 2·8%), $\nu_{max.}$ (KBr) 3380 cm.$^{-1}$ (OH), δ $(CO_3)_2SO$ 8·93 (1H, singlet, 3′-O*H*), 8·82 (1H, singlet, 7-O*H*), 6·81 (1H, singlet, 5-*H*), 6·26 (2H, broad singlet, 8- and 6′-H), 5·88 (1H, singlet 2′-*H*), 4·73 (1H, multiplet, 1-*H*), 3·77, 3·72 (6H, two singlets, 6- and 4′-OCH_3), 3·68 (3H, singlet, 5′-OCH_3), and 3·33 p.p.m. (6H, singlet $^+NMe_2$).

3-*Hydroxy*-4,5-*dimethoxybenzaldehyde* (XVII).—A mixture of 3-benzyloxy-4,5-dimethoxybenzaldehyde (Vf) [4] (600 mg.), ethanol (2 ml.), and concentrated hydrochloric acid (2 ml.) was refluxed for 2 hr., and the ethanol was distilled off. The resultant acidic solution was made basic with 10% sodium hydroxide solution and washed with ether. The preceding alkaline aqueous solution was acidified with concentrated hydrochloric acid and extracted with chloroform. The extract was dried (K_2CO_3) and evaporated to give a reddish-brown oil, whose purification by column chromatography on silicic acid (5·0 g.) using chloroform as eluent afforded a colourless oil (110 mg.). Recrystallisation from n-hexane afforded the *aldehyde* (XVII) as colourless prisms, m. p. 58—59·5° (Found: C, 59·8; H, 5·85. $C_9H_{10}O_4$ requires C, 59·35; H, 5·55%), $\nu_{max.}$ ($CHCl_3$) 3450 (OH), 2830 (CHO), 1695 (C=O), and 840 cm.$^{-1}$ (1,2,3,5-tetrasubstituted benzene), δ ($CDCl_3$) 9·85 (1H, singlet, aldehyde C*H*O), 7·12 (1H, doublet, J = 2·5 c./sec., 6-*H*), 7·06 (1H, doublet, J = 2·5 c./sec., 2-*H*), 6·10 (1H, multiplet, O*H*), 3·98 (3H, singlet, 4-OCH_3), 3·90 (3H, singlet, 5-OCH_3), t.l.c. R_F 0·78 [Wakogel B-5; chloroform–acetone–methanol (150 : 40 : 1); the spot was detected by iodine vapour].

Oxidation of (III) *with Ferric Chloride*.—To a solution of (III) (1·0 g.) in dry ether (100 ml.) was added a solution of hydrogen chloride gas in dry ether to give the hydrochloride of (III), which was washed with methanol–ether. To a solution of the above salt in water (150 ml.) was added dropwise a solution of ferric chloride hexahydrate (27 g.) in water (50 ml.), and the mixture was heated with stirring at 60—80° for 48 hr. After cooling, the dark green reaction mixture was made basic with ammonia and extracted with chloroform. The solvent was dried (K_2CO_3) and distilled to give a dark reddish-brown oil (148 mg.), which was purified by column chromatography on silicic acid (15·0 g.). Removal of the first chloroform eluate afforded colourless crystals (17 mg., 3·3%), which was identical with an authentic sample of (XVII) (mixed m. p., i.r., n.m.r., u.v., and t.l.c.). Secondly, removal of the chloroform–methanol (97 : 3) eluate afforded a pale yellow solid, whose recrystallisation from methanol–ether–n-hexane gave 2a,3,4,5-*tetrahydro*-2,8-*dihydroxy*-7-*methoxy*-3-*methyl*-2H-*cyclopent*[ij]*isoquinolin*-1-*one* (XVIII) (7 mg., 1·1%) as colourless fine needles,* m. p. 260° (decomp.) (Found: C, 55·85; H, 7·15. $C_{13}H_{15}NO_4,CH_3OH,H_2O$ requires C, 56·15; H, 7·05%), $\nu_{max.}$ ($CHCl_3$) 3610 (H_2O or CH_3OH, weak), 3350—3100 (OH, hydrogen bonding with nitrogen), 2795 (N-CH_3), 2750—2550 (OH chelated with C=O), and 1635 cm.$^{-1}$ (chelated C=O), δ ($CDCl_3$), 12·80 (1H, broad singlet, 8-O*H*), 6·81 (1H, singlet, 6-*H*), 3·87 (3H, singlet, 7-OCH_3), 3·25 (1H, multiplet, 2-O*H*), and 2·51 (3H, singlet, N-CH_3), $\lambda_{max.}$ ($CHCl_3$) 232, 273, and 358 mμ; $\lambda_{max.}$ (dioxan) 232, 273, and 358 mμ; $\lambda_{max.}$ (MeOH) 231, 273, and 364; $\lambda_{max.}$ (0·1N-NaOH–dioxan) 233, 273, and 374 mμ. Mass spectrum (*m/e*): 249 (M^+), 248, 247, 231, 219, 218, 204, 191 (base peak), 190, 176, 162, and 123·5 (M-2^{++}). T.l.c., R_F 0·57 [Wakogel B-5, 0·5 mm., activated at 120° for 4 hr.; chloroform–acetone–methanol (50 : 40 : 1); the spot was detected by iodine vapour].

2,8-*Diacetoxy*-2a,3,4,5-*tetrahydro*-7-*methoxy*-3-*methyl*-2H-*cyclopent*[ij]*isoquinolin*-1-*one* (XIX).—A mixture of the above diol (XVIII) (3 mg.), acetic anhydride (0·5 ml.), and pyridine (one drop) was heated on a water-bath for 2 hr., and the mixture was made basic with 10% sodium hydrogen carbonate solution. The resultant alkaline solution was extracted with benzene. The extract was washed with water, dried (Na_2SO_4), and evaporated to give the diacetate (XIX) as a colourless oil, $\nu_{max.}$ ($CHCl_3$) 2795 (N-CH_3), 1755 ($COCH_3$), and 1685 cm.$^{-1}$ (non-chelated C=O), δ ($CDCl_3$) 6·90 (1H, singlet, 6-*H*), 3·81 (3H, singlet, 7-OCH_3), 2·48 (3H, singlet, N-CH_3), and 2·36 p.p.m. (6H, broad singlet, 2COCH_3), t.l.c. R_F 0·62 [under the same conditions as (XVIII)].

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* Since this compound was labile, it was dried on P_2O_5 at room temperature for 24 hr. under reduced pressure.