Studies on the Syntheses of Heterocyclic Compounds. Part CDLXII.[1] Total Photolytic Syntheses of Aporphine [(±)-*N*-Methyl-laurotetanine, (±)-Cassythicine, and (±)-Pukateine], Proaporphine [(±)-Orientalinone], and Morphinandienone [(±)-Pallidine and (±)-Salutaridine] Alkaloids[2]

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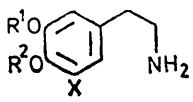
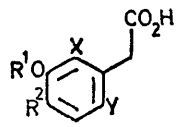
Total syntheses of some aporphine, proaporphine, and morphinandienone alkaloids by photolysis of phenolic bromoisoquinolines are described. The 8-bromo-1-(3-hydroxybenzyl)isoquinolines (34), (35), and (36) gave the aporphine alkaloids (±)-cassythicine (40), and (±)-pukateine (43), and (±)-*N*-methyl-laurotetanine (42), respectively. The 8-bromo-1-(4-hydroxybenzyl)isoquinoline (37) afforded the proaporphine alkaloid (±)-orientalinone (46). The 1-(2-bromobenzyl)-7-hydroxyisoquinoline (39) gave the morphinandienone alkaloid (±)-salutaridine (49). The photolysis of 8-bromo-1-(2-bromo-5-hydroxy-4-methoxybenzyl)-1,2,3,4-tetrahydro-7-hydroxy-6-methoxy-2-methylisoquinoline (38) gave an abnormal product, (±)-pallidine (48).

INTRAMOLECULAR coupling by phenolic oxidation[3] and by Pschorr reactions[4-6] of isoquinolines provides effective syntheses of aporphine, proaporphine, and morphinandienone alkaloids. However, these reactions have some disadvantages: for example coupling in the former method can occur both *ortho* and *para* to the phenolic hydroxy-group, leading to four possible products, and intermolecular coupling can also take place.[3] The latter method, in which coupling takes place only at the position occupied by an amino-group, gives many products by side reactions such as deamination, hydroxylation, *etc.*[7]

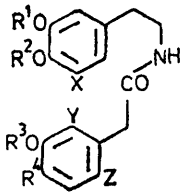
We have been looking for a simple and general synthetic method for the above types of alkaloid from



	R^1	R^2	X
(1)	CH_2		Br
(2)	Me	Me	Br
(3)	Me	CH_2Ph	Br
(4)	Me	CH_2Ph	H



	R^1	R^2	X	Y
(5)	CH_2Ph	OMe	H	H
(6)	CH_2Ph	H	H	H
(7)	Me	O·CH_2Ph	H	H
(8)	CH_2Ph	OMe	H	Br
(9)	CH_2Ph	OMe	Br	H



	R^1	R^2	R^3	R^4	X	Y	Z
(10)	CH_2		CH_2Ph	OMe	Br	H	H
(11)	CH_2		CH_2Ph	H	Br	H	H
(12)	Me	Me	CH_2Ph	OMe	Br	H	H
(13)	Me	CH_2Ph	Me	O·CH_2Ph	Br	H	H
(14)	Me	CH_2Ph	CH_2Ph	OMe	Br	H	Br
(15)	Me	CH_2Ph	CH_2Ph	OMe	H	Br	H

readily available starting materials. If the foregoing two reactions are considered to proceed through a radical mechanism, photolysis of phenolic bromoisoquinolines would be expected to be an effective method, because it is known to cause homolytic cleavage of a carbon–halogen bond.[8] We have studied this type of reaction, and here report total syntheses of a number of alkaloids.

The phenolic bromoisoquinolines (34)—(39) were synthesised by the usual method. 3-Benzyloxy-2-bromo-4-methoxyphenylacetic acid (9), required as an intermediate was obtained as follows. Bromination of 3-hydroxy-4-methoxybenzaldehyde, followed by benzylation, gave the *O*-benzyl-2-bromo-derivative, which was converted successively into the corresponding benzyl alcohol, chloride, and cyanide; finally the acid (9) was obtained by hydrolysis. Condensation of the phenethylamines (1)—(4) with the carboxylic acids (5)—(9) gave the corresponding amides (10)—(15). Bischler–Napieralski cyclisation of the amides (10)—(15) with phosphoryl chloride gave the 3,4-dihydroisoquinolines (16)—(21). Treatment of the dihydroisoquinolines (16)—(18), (20), and (21) with methyl iodide, followed by reduction of the methiodides (22)—(26) with sodium borohydride, gave the 1,2,3,4-tetrahydro-2-methylisoquinolines (27)—(31). Direct reduction of compound (19) with sodium borohydride, followed by reductive *N*-methylation of the 1,2,3,4-tetrahydroisoquinoline (32) with formalin and sodium borohydride, afforded the 2-methylisoquinoline (33). Debenzylation of the 1,2,3,4-tetrahydro-2-methylisoquinolines (27)—(31) and (33) with ethanolic hydrochloric acid afforded the phenolic bromoisoquinolines (34)—(39).

The isoquinoline (34) was irradiated through Pyrex with a 400 W mercury lamp in the presence of sodium hydroxide for 5 h to give (±)-cassythicine (40), an alkaloid from *Cassytha glabella*,[9] the structure of which was shown by comparison of its u.v. ($\lambda_{max.}$ 282 and 307 nm), i.r. ($\nu_{max.}$ 3500 cm^{-1}), and n.m.r. spectra [δ 7·62 p.p.m.

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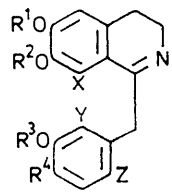
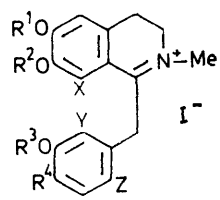
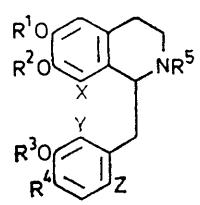
(s, 11-H)] with those of an authentic sample.[10] No formation of (±)-bulbocapnine (41), which would



	R^1	R^2	R^3	R^4	X	Y	Z
(16)	CH_2		CH_2Ph	OMe	Br	H	H
(17)	CH_2		CH_2Ph	H	Br	H	H
(18)	Me	Me	CH_2Ph	OMe	Br	H	H
(19)	Me	CH_2Ph	Me	O·CH_2Ph	Br	H	H
(20)	Me	CH_2Ph	CH_2Ph	OMe	Br	H	Br
(21)	Me	CH_2Ph	CH_2Ph	OMe	H	Br	H

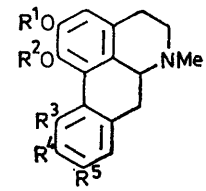


	R^1	R^2	R^3	R^4	X	Y	Z
(22)	CH_2		CH_2Ph	OMe	Br	H	H
(23)	CH_2		CH_2Ph	H	Br	H	H
(24)	Me	Me	CH_2Ph	OMe	Br	H	H
(25)	Me	CH_2Ph	CH_2Ph	OMe	Br	H	Br
(26)	Me	CH_2Ph	CH_2Ph	OMe	H	Br	H



	R^1	R^2	R^3	R^4	R^5	X	Y	Z
(27)	CH_2		CH_2Ph	OMe	Me	Br	H	H
(28)	CH_2		CH_2Ph	H	Me	Br	H	H
(29)	Me	Me	CH_2Ph	OMe	Me	Br	H	H
(30)	Me	CH_2Ph	CH_2Ph	OMe	Me	Br	H	Br
(31)	Me	CH_2Ph	CH_2Ph	OMe	Me	H	Br	H
(32)	Me	CH_2Ph	Me	O·CH_2Ph	H	Br	H	H
(33)	Me	CH_2Ph	Me	O·CH_2Ph	Me	Br	H	H
(34)	CH_2		H	OMe	Me	Br	H	H
(35)	CH_2		H	H	Me	Br	H	H
(36)	Me	Me	H	OMe	Me	Br	H	H
(37)	Me	Me	H	OH	Me	Br	H	H
(38)	Me	H	H	OMe	Me	Br	H	Br
(39)	Me	H	H	OMe	Me	H	Br	H

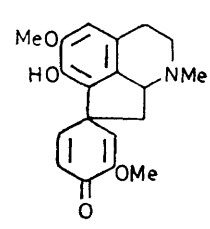
have resulted from coupling *ortho* to the hydroxy-group, was observed. Similarly, irradiation of compound (36) gave (±)-*N*-methyl-laurotetanine (42), an alkaloid from *Litsea cetrate*,[11] identified by its n.m.r. spectrum. In these reactions cyclisation occurs selectively *para* to the hydroxy-group.



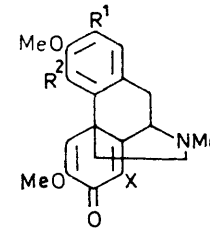
	R^1	R^2	R^3	R^4	R^5
(40)	CH_2		H	OMe	OH
(41)	CH_2		OH	OMe	H
(42)	Me	Me	H	OMe	OH
(43)	CH_2		OH	H	H
(44)	CH_2		H	H	OH
(45)	Me	H	H	OMe	OH

In contrast, irradiation of compound (35) afforded (±)-pukateine (43), by coupling *ortho* to the hydroxy-group. The spectroscopic data of the product were identical with those of natural material;[12,13] the u.v. spectrum showed absorption typical of a 1,2,11-trioxygenated aporphine system at 270 and 302 nm. Mecambroline (44), which would have been formed by coupling to the hydroxy-group, was not observed.

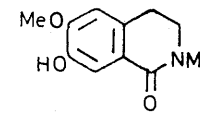
Irradiation through Pyrex of the 8-bromo-1-(4-hydroxybenzyl)isoquinoline derivative (37) with a 450 W mercury lamp gave (±)-orientalinone (46), identified from its spectroscopic data.[14] In this case, (±)-isoorientalinone,[15] a configurational isomer of (46), was not obtained in detectable amount (*cf.* refs. 16 and 17).



(46)



(47) R^1 = OH, R^2 = H, X = Br
(48) R^1 = OH, R^2 = X = H
(49) R^1 = X = H, R^2 = OH



(50)

Irradiation of the 2′,8-dibromoisoquinoline (38) was examined in the expectation that (±)-isoboldine (45) or the dienone (47) would be formed in moderate yield. However, the reaction gave only the abnormal product, (±)-pallidine (48), identified by comparison of spectroscopic data with those of an authentic sample.[18,19]

Finally, we synthesised salutaridine (49)[20] by this method; the reaction completes formal total syntheses

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[17] S. Ishiwata and K. Itakura, *Chem. and Pharm. Bull.* (*Japan*), 1970, **18**, 1224.
[18] T. Kametani, K. Fukumoto, A. Kozuka, H. Yagi, and M. Koizumi, *J. Chem. Soc.* (*C*), 1969, 2034.
[19] T. Kametani, M. Ihara, and T. Honda, *J. Chem. Soc.* (*C*), 1970, 1060.
[20] D. H. R. Barton, G. W. Kirby, W. Steglich, G. M. Thomas, A. R. Battersby, T. A. Dobson, and H. Ramuz, *J. Chem. Soc.*, 1965, 2423.

of morphine, sinomenine, *etc.*[20-23] Irradiation of compound (39) with a 400 W mercury lamp in the presence of sodium hydroxide and sodium iodide as usual gave (±)-salutaridine, identified by comparison (i.r., u.v., and mass spectra; R_F value) with an authentic sample,[23] along with 3-hydroxy-4-methoxybenzaldehyde and thalifoline (50). In the absence of sodium iodide, the 2'-bromoreticuline (39) gave only the latter two products.

Thus, we have developed a simple and general synthetic method for aporphine, proaporphine, and morphinandienone alkaloids, and have also accomplished formal total syntheses of morphine and related alkaloids.

EXPERIMENTAL

U.v. spectra were recorded with a Hitachi 124 spectrophotometer and i.r. spectra with a Hitachi EPI-S_2 spectrophotometer. N.m.r. spectra were determined with a Hitachi R-20 spectrometer (tetramethylsilane as an internal standard). Mass spectra were determined with a Hitachi RMU-7 spectrometer (80 eV).

3-*Benzyloxy*-2-*bromo*-4-*methoxyphenylacetic Acid* (9).—(a) 2-*Bromo*-3-*hydroxy*-4-*methoxybenzaldehyde*. Bromine (132 g) was added in portions to a solution of 3-hydroxy-4-methoxybenzaldehyde (125 g) in acetic acid (1 l) at room temperature. The mixture was stirred for 1 h at room temperature, water (1 l) was added, and the separated solid was collected to give the *bromo-aldehyde* (150 g) as prisms, m.p. 170° (from ethanol) (Found: C, 41·85; H, 3·3. $C_8H_7BrO_3$ requires C, 41·6; H, 3·05%), $\nu_{max.}$ ($CHCl_3$) 3500 (OH) and 1680 cm^{-1} (C=O).

(b) 3-*Benzyloxy*-2-*bromo*-4-*methoxybenzaldehyde*. A mixture of the foregoing bromo-aldehyde (100 g), benzyl chloride (60 g), potassium carbonate (70 g), and ethanol (2 l) was refluxed for 5 h. The solid was filtered off and crystallised from ethanol to give the O-*benzyl derivative* (120 g) as needles, m.p. 74° (Found: C, 56·2; H, 4·0. $C_{15}H_{13}BrO_3$ requires C, 56·1; H, 4·1%), $\nu_{max.}$ ($CHCl_3$) 1680 cm^{-1} (C=O), δ ($CDCl_3$) 3·84 (3H, s, OMe), 4·94 (2H, s, O·CH_2Ph), 6·80 and 7·58 (each 1H, d, *J* 8·5 Hz, ArH), 7·3br (5H, s, ArH), and 11·5 p.p.m. (1H, s, CHO).

(c) 3-*Benzyloxy*-2-*bromo*-4-*methoxybenzyl alcohol*. To a solution of the foregoing *O*-benzyl-2-bromo-compound (120 g) in methanol (1 l), sodium borohydride (30 g) was added in portions; the mixture was set aside for 1 h at room temperature. The solvent was distilled off and the residue was decomposed with water and extracted with chloroform. The extract was washed with water, dried (Na_2SO_4), and evaporated to give the *alcohol* (110 g) as needles, m.p. 56° (from benzene–hexane) (Found: C, 55·55; H, 4·75. $C_{15}H_{15}BrO_3$ requires C, 55·6; H, 5·0%), $\nu_{max.}$ ($CHCl_3$) 3400 cm^{-1} (OH), δ ($CDCl_3$) 3·69 (3H, s, OMe), 4·45br (2H, s, HO·CH_2), 4·85 (2H, s, O·CH_2Ph), 6·62 and 7·0 (each 1H, d, *J* 8·5 Hz, ArH), and 7·1—7·4 p.p.m. (5H, m, ArH).

(d) 3-*Benzyloxy*-2-*bromo*-4-*methoxybenzyl chloride*. To a solution of the foregoing alcohol (100 g) in dry benzene (700 ml), thionyl chloride (100 g) was added in portions. The mixture was stirred for 0·5 h, then refluxed for 0·5 h. The solvent was distilled off to give the chloride (101 g) as a viscous oil, which was used immediately without purification; δ ($CDCl_3$) 3·67 (OMe, 3H, s), 4·51 (2H, s, $ClCH_2$), 4·86 (2H, s, O·CH_2Ph), 6·6 and 7·0 (each 1H, d, *J* 8·5 Hz, ArH), and 7·0—7·45 p.p.m. (5H, m, ArH).

(e) 3-*Benzyloxy*-2-*bromo*-4-*methoxybenzyl cyanide*. A mixture of the foregoing chloride (101 g), sodium cyanide (60 g), sodium iodide (60 g), and ethyl methyl ketone (500 g) was refluxed with stirring for 5 h. After addition of water (500 ml), the mixture was extracted with ether. The extract was washed with water, dried (Na_2SO_4), and evaporated to give the *cyanide* (100 g) as a viscous oil, $\nu_{max.}$ ($CHCl_3$) 2250 cm^{-1} (C≡N), δ ($CDCl_3$) 3·64 (2H, s, CN·CH_2), 3·75 (3H, s, OMe), 4·90 (2H, s, O·CH_2Ph), 6·70 and 7·02 (each 1H, d, *J* 8·5 Hz, ArH), and 7·10—7·40 p.p.m. (5H, m, ArH).

(f) 3-*Benzyloxy*-2-*bromo*-4-*methoxyphenylacetic acid* (9). A mixture of the foregoing cyanide (100 g), aqueous 60% potassium hydroxide (300 ml), methanol (800 ml), and dioxan (600 ml) was refluxed for 15 h. The mixture was evaporated and the residue was acidified with 10% hydrochloric acid and extracted with ether. The extract was washed with water, dried (Na_2SO_4), and evaporated to give the *acid* (9) (65 g) as needles, m.p. 122° (from benzene) (Found: C, 53·8; H, 4·0. $C_{16}H_{15}BrO_4$ requires C, 54·0; H, 4·3%), $\nu_{max.}$ ($CHCl_3$) 1710 cm^{-1} (C=O), δ ($CDCl_3$) 3·65 (2H, s, CH_2·CO_2H), 3·7 (3H, s, OMe), 4·89 (2H, s, O·CH_2Ph), 6·62 and 6·78 (each 1H, d, *J* 8·5 Hz, ArH), and 7·1—7·4 p.p.m. (5H, m, ArH).

3-*Benzyloxy*-N-(5-*bromo*-3,4-*methylenedioxyphenethyl*)-4-*methoxyphenylacetamide* (10).—A mixture of 5-bromo-3,4-methylenedioxyphenethylamine (1) [24] (12·5 g) and 3-benzyloxy-4-methoxyphenylacetic acid (5) (14·0 g) was heated at 180° for 1 h. The mixture was extracted with benzene. The extract was washed with 10% hydrochloric acid, 10% sodium hydroxide, and then water, dried (Na_2SO_4), and evaporated. The residual solid was recrystallised from methanol–ether to give the *amide* (10) (9·3 g) as needles, m.p. 123·5—124·5° (Found: C, 60·65; H, 5·05; N, 2·85. $C_{25}H_{24}BrNO_5$ requires C, 60·75; H, 4·9; N, 2·85%), $\nu_{max.}$ ($CHCl_3$) 3400 (NH) and 1655 cm^{-1} (C=O), δ ($CDCl_3$) 3·35 (2H, s, CH_2·CO·NH), 3·82 (3H, s, OMe), 5·03 (2H, s, O·CH_2Ph), 5·88 (2H, s, O·CH_2·O), and 6·73—6·34 p.p.m. (5H, m, ArH).

3-*Benzyloxy*-N-(3-*bromo*-4,5-*methylenedioxyphenethyl*)-*acetamide* (11).—A mixture of 3-bromo-4,5-methylenedioxyphenethylamine (1) (9 g) and 3-benzyloxyphenylacetic acid (6) [25] (10·1 g) was heated at 180° for 1 h, and then at 190° for 45 min. The mixture was extracted with chloroform. After the usual work-up, the crude amide was chromatographed on silica gel with chloroform as eluant to afford the *amide* (11) (4·5 g) as needles, m.p. 123—124° (from ethanol) (Found: C, 61·5; H, 4·9; N, 3·1. $C_{24}H_{22}BrNO_4$ requires C, 61·55; H, 4·75; N, 3·0%), $\nu_{max.}$ ($CHCl_3$) 3400 (NH) and 1658 cm^{-1} (C=O), δ ($CDCl_3$) 2·60 (2H, t, *J* 7 Hz, PhCH_2·CH_2·NH), 3·35 (2H, t, *J* 7 Hz, CH_2·CH_2·NH·CO), 3·5 (2H, s, CH_2·CO·NH), 5·03 (2H, s, O·CH_2Ph), 5·93 (2H, s, O·CH_2·O), 7·25—6·45 (6H, m, ArH), and 7·38br p.p.m. (5H, s, ArH).

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[25] M. Tomita and Z. Niijima, *J. Pharm. Soc. Japan*, 1959, **79**, 1019.

3-*Benzyloxy*-N-(5-*bromo*-3,4-*dimethoxyphenethyl*)-4-*methoxyphenylacetamide* (12).—A mixture of 5-bromo-3,4-dimethoxyphenethylamine (2) (13·8 g) and 3-benzyloxy-4-methoxyphenylacetic acid (5) (13·1 g) was heated at 180° for 1 h, cooled, and extracted with benzene. The extract was washed with 10% sodium hydroxide, 10% hydrochloric acid, and water, and then dried (Na_2SO_4) and evaporated. The residual solid was chromatographed on silica gel (200 g) with chloroform as eluant to afford the *amide* (12) (16·1 g, 65·5%) as needles, m.p. 154—155·5° (from methanol–ether) (Found: C, 60·55; H, 5·9; N, 2·45. $C_{26}H_{28}BrNO_5$ requires C, 60·7; H, 5·45; N, 2·7%), $\nu_{max.}$ ($CHCl_3$) 1660 cm^{-1} (C=O), δ ($CDCl_3$) 3·40 (2H, s, CH_2·CO·NH), 3·86 (3H, s, OMe), 3·79 (6H, s, 2 × OMe), and 5·18 p.p.m. (2H, s, O·CH_2Ph).

4-*Benzyloxy*-N-(4-*benzyloxy*-5-*bromo*-3-*methoxyphenethyl*)-3-*methoxyphenylacetamide* (13).—A mixture of 4-benzyloxy-5-bromo-3-methoxyphenethylamine (3) (8·5 g) and 4-benzyloxy-3-methoxyphenylacetic acid (7) (6·8 g) was heated at 180° in a current of nitrogen for 3 h, cooled, and extracted with chloroform (150 ml). The extract was washed with 5% sodium hydrogen carbonate, 10% hydrochloric acid, and water, dried (Na_2SO_4), and evaporated. The resulting solid crystallised from benzene to give the *amide* (13) (9·5 g) as *needles*, m.p. 145·5—146° (Found: C, 65·6; H, 5·63; N, 2·25. $C_{32}H_{32}BrNO_5$ requires C, 65·7; H, 5·45; N, 2·35%), $\nu_{max.}$ ($CHCl_3$) 3380 (NH) and 1660 cm^{-1} (C=O), δ ($CDCl_3$) 3·69 and 3·75 (6H, each s, 2 × OMe), 4·89 (2H, s, O·CH_2Ph), 5·00 (2H, s, O·CH_2Ph), 6·79—6·38 (5H, m, ArH), and 7·21br p.p.m. (10H, s, ArH).

5-*Benzyloxy*-N-(4-*benzyloxy*-5-*bromo*-3-*methoxyphenethyl*)-2-*bromo*-4-*methoxyphenylacetamide* (14).—A mixture of the amine (3) (3·0 g) and the carboxylic acid (8) (3·1 g) was heated at 180—195° for 1·5 h, cooled, and extracted with chloroform. The extract was washed with 10% hydrochloric acid, 10% ammonia, and water, and dried (Na_2SO_4). Evaporation afforded the amide (14) (5·4 g) as a brown solid, which crystallised from chloroform–ethanol to afford *needles*, m.p. 157—157·5° (Found: C, 57·55; H, 4·6; N, 2·3. $C_{32}H_{31}Br_2NO_5$ requires C, 57·4; H, 4·65; N, 2·1%), $\nu_{max.}$ ($CHCl_3$) 3380 (NH) and 1660 cm^{-1} (C=O), δ ($CDCl_3$) 2·68 (2H, t, *J* 6·5 Hz, CH_2·CH_2·NH), 3·40 (2H, t, *J* 6·5 Hz, CH_2·NH·CO), 3·54 (2H, s, CH_2·CO·NH), 3·80 (3H, s, OMe), 3·86 (3H, s, OMe), 4·99 (2H, s, O·CH_2Ph), 5·10 (2H, s, O·CH_2Ph), 6·64 (1H, d, *J* 2 Hz, 2′-H), 6·84 (1H, s, 6-H), 6·88 (1H, d, *J* 2 Hz, 6′-H), 7·04 (1H, s, 3-H), and 7·39 p.p.m. (10H, s, ArH).

3-*Benzyloxy*-N-(4-*benzyloxy*-3-*methoxyphenethyl*)-2-*bromo*-4-*methoxyphenylacetamide* (15).—A mixture of the carboxylic acid (9) (40 g) and 4-benzyloxy-3-methoxyphenethylamine (4) (30 g) was heated at 190° for 2 h under a current of nitrogen. The product was cooled and recrystallised from benzene–ether to give the amide (15) (55 g) as *needles*, m.p. 125° (Found: C, 60·0; H, 5·65; N, 2·45. $C_{32}H_{32}BrNO_5$ requires C, 59·6; H, 5·45; N, 2·35%), $\nu_{max.}$ ($CHCl_3$) 1660 cm^{-1} (C=O), δ ($CDCl_3$) 2·6 (2H, t, *J* 6 Hz, N·CH_2·CH_2), 3·31 (2H, t, *J* 6 Hz, N·CH_2·CH_2), 3·52 (2H, s, CH_2·CO·NH), 3·75 (6H, s, 2 × OMe), 4·9 (2H, s, O·CH_2Ph), 4·95 (2H, s, O·CH_2Ph), 6·3—7·0 (5H, m, ArH), and 7·1—7·5 p.p.m. (10H, m, ArH).

1-(3-*Benzyloxy*-4-*methoxybenzyl*)-8-*bromo*-3,4-*dihydro*-6,7-*methylenedioxyisoquinoline* (16).—A mixture of the amide (10) (8·5 g), phosphoryl chloride (5 g), and dry benzene (50 ml) was refluxed for 1·5 h. The solvent was removed and the residue was washed with n-hexane to give the 3,4-dihydroisoquinoline (16) hydrochloride. This was made basic with 10% ammonia and the free isoquinoline was extracted with chloroform. The extract was washed with water, dried (Na_2SO_4), and evaporated to give a brownish oil (5·5 g), which was used without purification.

1-(3-*Benzyloxybenzyl*)-8-*bromo*-3,4-*dihydro*-6,7-*methylenedioxyisoquinoline* (17).—A mixture of the amide (11) (4·4 g), phosphoryl chloride (3·5 g), and dry benzene (58 ml) was refluxed for 3 h. Work-up as for compound (16) gave the isoquinoline (17) (4 g) as a pale brownish solid, which was used without purification.

1-(3-*Benzyloxy*-4-*methoxybenzyl*)-8-*bromo*-3,4-*dihydro*-6,7-*dimethoxyisoquinoline* (18).—A mixture of the amide (12) (7·5 g), phosphoryl chloride (6 g), and dry benzene (120 ml) was refluxed for 2 h. Work-up as for compound (16) gave the isoquinoline (18) (5 g) as a brownish oil, which was used without purification.

7-*Benzyloxy*-1-(3-*benzyloxy*-2-*bromo*-4-*methoxybenzyl*)-3,4-*dihydro*-6-*methoxyisoquinoline* (21).—A solution of the amide (15) (40 g) and phosphoryl chloride (40 g) in dry benzene (300 ml) was refluxed for 2 h and the solvent was distilled off. The residue was poured into an excess of n-hexane and the separated solid was recrystallised from methanol–ether to afford the 3,4-*dihydroisoquinoline* (21) *hydrochloride* (30 g) as needles, m.p. 221° (Found: C, 62·9; H, 5·45; N, 2·45. $C_{32}H_{30}BrNO_4$,HCl requires C, 63·0; H, 5·3; N, 2·3%).

1-(3-*Benzyloxy*-4-*methoxybenzyl*)-8-*bromo*-1,2,3,4-*tetrahydro*-2-*methyl*-6,7-*methylenedioxyisoquinoline* (27).—A mixture of 3,4-dihydroisoquinoline (16) (10 g), methanol (30 ml), and methyl iodide (30 ml) was refluxed for 3 h, then evaporated. Sodium borohydride (3 g) was added in small portions to a stirred solution of the residue in a mixture of methanol (100 ml) and chloroform (40 ml). Stirring was continued for 0·5 h at room temperature, then the mixture was refluxed for 0·5 h and evaporated. The residue was diluted with water and extracted with chloroform. The extract was washed with water, dried (Na_2SO_4), and evaporated to afford a syrup, which was chromatographed on silica gel (100 g). After elution with chloroform, elution with methanol–chloroform (1 : 99) afforded the tetrahydroisoquinoline (27) (5·1 g) as a pale brownish oil, δ ($CDCl_3$) 2·19 (3H, s, NMe), 3·80 (3H, s, OMe), 5·08 (2H, s, O·CH_2Ph), 5·85 (2H, s, O·CH_2·O), 6·40 (1H, s, 5-H), and 6·8—6·6 p.p.m. (3H, m, ArH), which was used without purification.

1-(3-*Benzyloxybenzyl*)-8-*bromo*-1,2,3,4-*tetrahydro*-2-*methyl*-6,7-*methylenedioxyisoquinoline* (28).—A mixture of the dihydroisoquinoline (17) (3·8 g), methyl iodide (15 ml), and methanol (32 ml) was refluxed for 3 h, then evaporated. To a stirred solution of the residue in a mixture of methanol (90 ml) and chloroform (10 ml), sodium borohydride (3 g) was added in small portions during 1 h. The mixture was refluxed for 0·5 h, then evaporated, and the residue was diluted with water (100 ml) and extracted with chloroform. The extract was washed with water, dried (Na_2SO_4), and evaporated. The residue (2·8 g) was chromatographed on silica gel (60 g). After elution with chloroform, elution with methanol–chloroform (1 : 99) left the tetrahydroisoquinoline (28) (1·7 g) as *needles*, m.p. 99—101·5° (from n-hexane–ether) (Found: C, 65·9; H, 5·65; N, 3·15. $C_{25}H_{24}BrNO_3$,0·33C_6H_{14} requires C, 65·5; H, 5·85; N, 2·85%), δ ($CDCl_3$) 2·26 (3H, s, NMe), 5·03 (2H, s, O·CH_2Ph),

5·92 (2H, s, O·CH_2·O), 6·49 (1H, s, 5-H), 7·1—6·6 (4H, m, ArH), and 7·38br p.p.m. (5H, s, ArH), *m/e* 465 (M^+) and 467 (M + 2, isotope peak).

1-(3-*Benzyloxy*-4-*methoxybenzyl*)-8-*bromo*-1,2,3,4-*tetrahydro*-6,7-*dimethoxy*-2-*methylisoquinoline* (29).—A mixture of the dihydroisoquinoline (18) (7·2 g), methyl iodide (20 ml), and methanol (50 ml) was heated under reflux for 3 h, then evaporated. The residue (24) was extracted with a mixture of methanol (100 ml) and chloroform (20 ml). To this solution sodium borohydride (4 g) was added in small portions with stirring at room temperature during 0·5 h. Stirring was continued for 0·5 h, then the mixture was refluxed for 0·5 h and the solvent was evaporated off. The residue was diluted with water and extracted with chloroform. The extract was washed with water, dried (Na_2SO_4), and evaporated to leave a brownish oil (7·0 g), which was chromatographed on silica gel (100 g) with chloroform as eluant (100 ml fractions). Evaporation of the fractions 3—10 gave a brownish oil (6 g), which was further chromatographed on silica gel (100 g) with the same eluant to give the tetrahydroisoquinoline (29) (3·0 g) as a pale brownish oil. This was purified by preparative thick-layer chromatography [benzene–ethyl acetate–methanol (6 : 3 : 1) as developing solvent] to give a *syrup*, R_F 0·50 (Found: C, 63·25; H, 5·85; N, 2·8. $C_{27}H_{30}BrNO_4$ requires C, 63·3; H, 5·95; N, 2·75%), $\nu_{max.}$ ($CHCl_3$) 2700 cm^{-1} (NMe), δ ($CDCl_3$) 2·23 (3H, s, NMe), 3·79 (3H, s, OMe), 3·81 (6H, s, 2 × OMe), 5·11 (2H, s, O·CH_2Ph), 6·56 (1H, s, 5-H), 6·9—6·7 (3H, m, ArH), and 7·4—7·28br p.p.m. (5H, s, ArH).

7-*Benzyloxy*-1-(4-*benzyloxy*-3-*methoxybenzyl*)-8-*bromo*-1,2,3,4-*tetrahydro*-6-*methoxyisoquinoline* (32).—A mixture of the amide (13) (9·5 g), dry acetonitrile (300 ml), and phosphoryl chloride (8·5 ml) was refluxed for 2 h, then evaporated. The residue was washed with n-hexane to give the 3,4-dihydroisoquinoline (19) hydrochloride (9·3 g), $\nu_{max.}$ ($CHCl_3$) 1640 cm^{-1} (C=$\overset{+}{N}$). To a stirred, cooled solution of the hydrochloride (9·3 g) in methanol (350 ml), sodium borohydride (7 g) was added in small portions during 1 h. Stirring was continued for 1 h at room temperature, then the mixture was refluxed for 0·5 h. The solvent was evaporated off and the residue was diluted with water and extracted with chloroform. The extract was washed with water, dried (K_2CO_3), and evaporated to leave a yellowish oil (9·0 g), which was chromatographed on silica gel (100 g) with chloroform as eluant to afford the 1,2,3,4-tetrahydroisoquinoline (32) (8·5 g) as a pale yellowish oil, $\nu_{max.}$ ($CHCl_3$) 3350 cm^{-1} (NH), δ ($CDCl_3$) 3·79 (3H, s, OMe), 3·82 (3H, s, OMe), 4·99 (2H, s, O·CH_2Ph), 5·08 (2H, s, O·CH_2Ph), 6·59 (1H, s, 5-H), 6·76br (3H, s, ArH), and 7·34br p.p.m. (10H, s, ArH).

7-*Benzyloxy*-1-(4-*benzyloxy*-3-*methoxybenzyl*)-8-*bromo*-1,2,3,4-*tetrahydro*-6-*methoxy*-2-*methylisoquinoline* (33).—A mixture of the isoquinoline (32) (8 g), methanol (350 ml), and 37% formalin (18 ml) was refluxed for 1 h, then cooled. Sodium borohydride (7 g) was added in small portions with stirring and cooling during 1 h. Stirring was continued for a further 1 h at room temperature, then the mixture was refluxed for 0·5 h. The solvent was distilled off and the residue was diluted with water and extracted with ether (5 × 50 ml). The extract was washed with water, dried (Na_2SO_4), and evaporated. The resulting syrup (8 g) was chromatographed on silica gel (100 g). Elution with methanol–chloroform (1 : 99) afforded the 2-methyl derivative (33) (7·5 g) as a pale yellowish syrup, which was used without further purification; δ ($CDCl_3$) 2·32 (3H, s, NMe), 3·77 (3H, s, OMe), 3·79 (3H, s, OMe), 4·97 (2H, s, O·CH_2Ph), 5·05 (2H, s, O·CH_2Ph), 6·55 (1H, s, 5-H), 6·75 (3H, s, ArH), and 7·30br p.p.m. (10H, s, ArH).

7-*Benzyloxy*-1-(5-*benzyloxy*-2-*bromo*-4-*methoxybenzyl*)-8-*bromo*-1,2,3,4-*tetrahydro*-6-*methoxy*-2-*methylisoquinoline* (30).—A mixture of the amide (14) (865 mg), phosphoryl chloride (1·1 ml), and dry benzene (20 ml) was refluxed for 2·5 h. The solvent was removed and the residue was washed with n-hexane, basified with 28% ammonia, and extracted with chloroform. The extract was washed with water, dried (Na_2SO_4), and evaporated to leave the 3,4-dihydroisoquinoline (20) as a dark brown gum (700 mg), to which were added methyl iodide (15 ml) and methanol (15 ml). The mixture was refluxed for 14 h; evaporation then left the methiodide (25) as a yellowish brown gum, to a solution of which in chloroform (5 ml) and methanol (10 ml) sodium borohydride (1·0 g) was added in small portions. Stirring was continued for 4 h, then the solvent was removed. The residue was diluted with water and extracted with chloroform. The extract was washed with water, dried (Na_2SO_4), and evaporated to leave a dark brown oil (650 mg), which was chromatographed on silica gel (15 g) with chloroform (25 ml fractions; monitored by n.m.r. spectrum) as eluant. Fractions 11—14 gave the 1,2,3,4-*tetrahydroisoquinoline* (30) (100 mg) as a yellow solid, which afforded plates, m.p. 150—151° (from ethanol) (Found: C, 59·5; H, 4·85; N, 2·52. $C_{33}H_{33}Br_2NO_4$ requires C, 59·4; H, 5·0; N, 2·1%), δ ($CDCl_3$) 2·27 (3H, s, NMe), 3·84 (6H, s, 2 × OMe), 3·98 (1H, t, *J* 6 Hz, 1-H), 4·98 (2H, s, O·CH_2Ph), 5·13 (2H, s, O·CH_2Ph), 6·63 (1H, s, 5-H), 6·98 (2H, s, 3′- and 6′-H), and 7·35 p.p.m. (10H, s, ArH), *m/e* 665 (M^+), 667 (M + 2), 669 (M + 4), 360 (M − 305), 362 (M − 305 + 2), and 269 (360 − CH_2Ph).

8-*Bromo*-1,2,3,4-*tetrahydro*-1-(3-*hydroxy*-4-*methoxybenzyl*)-2-*methyl*-6,7-*methylenedioxyisoquinoline* (34).—A solution of the tetrahydroisoquinoline (27) (4 g) in ethanol (30 ml) and concentrated hydrochloric acid (5 ml) was refluxed for 1 h. The solvent was removed and the residue was basified with 10% ammonia and extracted with chloroform. The extract was washed with water, dried (Na_2SO_4), and evaporated to yield the isoquinoline (34) (1·9 g) as *needles*, m.p. 137·5—138·5° (from methanol–ether) (Found: C, 56·15; H, 5·25; N, 3·55. $C_{19}H_{20}BrNO_4$ requires C, 56·15; H, 4·95; N, 3·45%), $\nu_{max.}$ ($CHCl_3$) 3510 (OH) and 2700 cm^{-1} (NMe).

8-*Bromo*-1,2,3,4-*tetrahydro*-1-(3-*hydroxybenzyl*)-2-*methyl*-6,7-*methylenedioxyisoquinoline* (35).—A mixture of the tetrahydroisoquinoline (28) (1·5 g), ethanol (15 ml), and concentrated hydrochloric acid (15 ml) was refluxed for 45 min. Work-up as for compound (34) gave the isoquinoline (35) (0·6 g) as *needles*, m.p. 195—201·5° (from methanol–ether) (Found: C, 57·1; H, 4·8; N, 3·7. $C_{18}H_{18}BrNO_3$ requires C, 57·45; H, 4·8; N, 3·75%), δ ($CDCl_3$) 2·33 (3H, s, NMe), 6·0 (2H, s, O·CH_2·O), and 7·15—6·45 p.p.m. (5H, m, ArH).

8-*Bromo*-1,2,3,4-*tetrahydro*-1-(3-*hydroxy*-4-*methoxybenzyl*)-6,7-*dimethoxy*-2-*methylisoquinoline* (36).—A mixture of the tetrahydroisoquinoline (29) (1·6 g), ethanol (16 ml), and concentrated hydrochloric acid (16 ml) was refluxed for 45 min. Work-up as for compound (34) gave the isoquinoline (36) as a brownish oil (1·3 g), which was purified by preparative thick-layer chromatography on silica gel [benzene–ethyl acetate–methanol (6 : 3 : 1)] to give a

syrup, R_F 0·44 (Found: C, 57·0; H, 5·85. $C_{20}H_{24}BrNO_4$ requires C, 56·85; H, 5·7%), $\nu_{max.}$ ($CHCl_3$) 3500 cm^{-1} (OH), δ ($CDCl_3$) 2·30 (3H, s, NMe), 3·81br (9H, s, 3 × OMe), 6·55 (1H, s, 5-H), and 6·85—6·68 p.p.m. (3H, m, ArH).

8-*Bromo*-1,2,3,4-*tetrahydro*-7-*hydroxy*-1-(4-*hydroxy*-3-*methoxybenzyl*)-6-*methoxy*-2-*methylisoquinoline* (37).—A mixture of the tetrahydroisoquinoline (33) (7 g), concentrated hydrochloric acid (70 ml), and ethanol (70 ml) was refluxed for 4 h. Work-up as for compound (34) gave a brownish oil (6 g); this was chromatographed on silica gel (100 g). Elution with methanol–chloroform (2 : 98) afforded the isoquinoline (37) (5 g) as a pale yellowish gum, which was used without further purification; $\nu_{max.}$ ($CHCl_3$) 3500 cm^{-1} (OH), δ ($CDCl_3$) 2·34 (3H, s, NMe), 3·84 (3H, s, OMe), 3·87 (3H, s, OMe), 6·55 (1H, s, 5-H), and 6·79 p.p.m. (3H, s, ArH).

8-*Bromo*-1-(2-*bromo*-5-*hydroxy*-4-*methoxybenzyl*)-1,2,3,4-*tetrahydro*-7-*hydroxy*-6-*methoxy*-2-*methylisoquinoline* (38).—A mixture of the tetrahydroisoquinoline (30) (1·4 g), ethanol (60 ml), acetone (80 ml), and concentrated hydrochloric acid (100 ml) was refluxed for 8 h. The solvent was removed and the residue was basified with 28% ammonia and extracted with chloroform. The extract was washed with water, dried (Na_2SO_4), and evaporated to give a dark brown oil (1·6 g), which was chromatographed on silica gel (15 g). After elution with chloroform and methanol–chloroform (1 : 99), elution with methanol–chloroform (5 : 95) gave the isoquinoline (38) (300 mg) as a pale brown solid, which crystallised from chloroform–ether–n-hexane as pale yellow *cubes*, m.p. 178—180° (Found: C, 47·15; H, 4·75; N, 2·85. $C_{19}H_{21}Br_2NO_4$ requires C, 46·85; H, 4·35; N, 2·9%), $\nu_{max.}$ 3500 cm^{-1} (OH), δ ($CDCl_3$) 2·38 (3H, s, NMe), 3·80 (3H, s, OMe), 3·87 (3H, s, OMe), 4·23 (1H, t, *J* 7 Hz, 1-H), 6·60 (1H, s, 5-H), 6·92 (1H, s, 6′-H), and 7·04 p.p.m. (1H, s, 3′-H), *m/e* 485 (M^+), 487 (M + 2), 489 (M + 4), 270 (M − 215), and 272 (M − 215 + 2).

1-(2-*Bromo*-3-*hydroxy*-4-*methoxybenzyl*)-1,2,3,4-*tetrahydro*-7-*hydroxy*-6-*methoxy*-2-*methylisoquinoline* (39).—A mixture of the 3,4-dihydroisoquinoline (21) [prepared from the hydrochloride (40 g)] and methyl iodide (50 ml) was set aside for 1 h at room temperature. The excess of methyl iodide was then distilled off and the residue was triturated with ether to give the *methiodide* (26) (34 g) as prisms, m.p. 183—185° (from benzene–ether) (Found: C, 55·75; H, 5·0; N, 2·2. $C_{32}H_{30}BrNO_4,CH_3I$ requires C, 55·4; H, 4·8; N, 1·95%).

To a solution of the methiodide (26) (34 g) in methanol (200 ml) and chloroform (200 ml), sodium borohydride (2 g) was added in portions; the mixture was then set aside for 1 h at room temperature. The solvent was distilled off and the residue was decomposed with water and extracted with chloroform. The extract was washed with water, dried (Na_2SO_4), and evaporated to give the 1,2,3,4-tetrahydro-2-methylisoquinoline (31) (28 g) as a viscous oil, δ ($CDCl_3$) 2·4 (3H, s, NMe), 2·5—3·5 (6H, m, 3 × CH_2), 3·7 (3H, s, OMe), 3·75 (3H, s, OMe), 4·7 (2H, s, O·CH_2Ph), 4·9 (2H, s, O·CH_2Ph), 6·0 and 6·46 (each 1H, s, ArH), 6·61 (2H, s, ArH), and 7·0—7·5 p.p.m. (10H, m, ArH).

A mixture of compound (31) (28 g), concentrated hydrochloric acid (200 ml), and ethanol (200 ml) was refluxed for 5 h. The solvent was evaporated off; the residue was diluted with water (50 ml), basified with 28% ammonia, and then extracted with chloroform. The extract was washed with water, dried (Na_2SO_4), and evaporated to give the 2′-*bromoreticuline* (39) as prisms, m.p. 194—195° (from methanol) (Found: C, 55·65; H, 5·4; N, 3·7. $C_{19}H_{22}BrNO_4$ requires C, 55·85; H, 5·45; N, 3·45%).

(±)-*Cassythicine* (40).—A stirred mixture of the isoquinoline (34) (1·5 g), sodium hydroxide (1·5 g), water (200 ml), and ethanol (800 ml) was irradiated with a Riko 400 W mercury lamp (Pyrex filter) at room temperature for 5 h. Most of the ethanol was evaporated off and the remaining aqueous solution was extracted with chloroform after addition of an excess of crystalline ammonium chloride. The extract was washed with water, dried (Na_2SO_4), and evaporated. The residue (1·2 g) was chromatographed on silica gel (35 g). After elution with chloroform, elution with methanol–chloroform (1 : 99) gave a brownish gum (0·2 g); this was chromatographed on neutral alumina (6 g) with chloroform as an eluant to yield (±)-*cassythicine* (40), which formed needles (24 mg), m.p. 128—129° (from methanol–ether) (lit.,[10] 116—122°) (Found: C, 69·75; H, 5·9; N, 4·25. $C_{19}H_{19}NO_4$ requires C, 70·15; H, 5·55; N, 4·35%), δ ($CDCl_3$) 2·53 (3H, s, NMe), 3·90 (3H, s, OMe), 5·90, 6·05 (2H, each d, *J* 1·5 Hz, O·CH_2·O), 6·48 (1H, s, 3-H), 6·77 (1H, s, 8-H), and 7·62 p.p.m. (1H, s, 11-H).

N-*Methyl-laurotetanine* (42).—A water-cooled mixture of the isoquinoline (36) (1·0 g), sodium hydroxide (1 g), water (900 ml), and ethanol (100 ml) was irradiated with a Riko 400 W mercury lamp (Pyrex filter) for 5 h. Crystalline ammonium chloride (5 g) was added and the mixture was extracted with chloroform. The extract was washed with water, dried (Na_2SO_4), and evaporated to leave a brownish oil (0·7 g), which was chromatographed on silica gel (20 g). After elution with chloroform, elution with methanol–chloroform (1 : 99) gave *N*-methyl-laurotetanine (42) (120 mg) as a pale yellowish solid, the *oxalate* of which crystallised from acetone–ether to afford needles, m.p. 199—202° (decomp.) [lit.,[26] 212° (decomp.)] (Found: C, 60·95; H, 6·25; N, 3·5. $C_{20}H_{23}NO_4,C_2H_2O_4$ requires C, 61·25; H, 5·85; N, 3·25%), $\nu_{max.}$ ($CHCl_3$) 3500 (OH) and 2700 cm^{-1} (NMe), δ ($CDCl_3$) 2·5 (3H, s, NMe), 3·62 (3H, s, OMe), 3·85 (6H, s, 2 × OMe), 6·59 and 6·77 (2H, each s, ArH), 8·02 p.p.m. (1H, s, 11-H), *m/e* 341 (M^+), 340 (M − 1), 326 (M − 15), 310 (M − 31), and 298 (M − 43), $\lambda_{max.}$ (MeOH) 304 and 282 nm.

(±)-*Pukateine* (43).—A water-cooled mixture of the isoquinoline (35) (0·6 g), ethanol (10 ml), sodium hydroxide (0·6 g), and water (1 l) was irradiated with a Riko 400 W mercury lamp (Pyrex filter) for 5 h. Excess of crystalline ammonium chloride was added and the mixture was extracted with chloroform. The extract was washed with water, dried (Na_2SO_4), and evaporated to give a brownish oil (0·4 g), which was chromatographed on silica gel. After elution with chloroform, elution with methanol–chloroform (1 : 99) yielded (±)-pukateine (43) as *needles* (20 mg), m.p. 213—215° (lit.,[12,13] 232—233°) (from methanol–ether) (Found: C, 72·85; H, 5·7; N, 4·65. $C_{18}H_{17}NO_3$ requires C, 73·1; H, 5·8; N, 4·75%), identical (spectroscopic data) with an authentic specimen; δ ($CDCl_3$) 2·53 (3H, s, NMe), 5·93, 6·10 (2H, each d, *J* 1·3 Hz, O·CH_2·O), 6·62 (1H, s, 3-H), and 7·35—6·8 p.p.m. (3H, m, ArH).

Photolysis of the Isoquinoline (37).—A stirred water-cooled, mixture of compound (37) (3 g), 10% sodium hydroxide (10 ml), ethanol (80 ml), and water (910 ml) was irradiated with a Hanovia 450 W mercury lamp

[26] I. Kikkawa, *J. Pharm. Soc. Japan*, 1959, **79**, 183.

(Pyrex filter) for 7 h. After removal of ethanol, an excess of crystalline ammonium chloride was added to the mixture, which was then extracted with chloroform. The extract was washed with water, dried (Na_2SO_4), and evaporated to leave a brownish oil (2·5 g), which was chromatographed on silica gel (75 g). Elution (100 ml fractions) with methanol–chloroform (1 : 99) afforded the isoquinoline (37) (0·5 g) (fractions 9—13) and elution with methanol–chloroform (2 : 98) (fractions 14—17) gave a brownish oil (530 mg), which showed dienone bands in its i.r. spectrum; this was rechromatographed on silicic acid (12 g) with methanol–chloroform (0·8 : 99·2) as eluant. Fractions 12—17 gave the dienone (250 mg), which was further chromatographed on neutral alumina (25 g) with benzene–chloroform (40 : 60) as eluant to give orientalinone (46) (210 mg). This crystallised from benzene to give *needles*, m.p. 233—235° (decomp.) [lit.,[14] 203° (decomp.); lit.,[27] 227—229° (decomp.)] (Found: C, 69·05; H, 6·65; N, 3·75. $C_{19}H_{21}NO_4,0·25H_2O$ requires C, 68·75; H, 6·55; N, 4·2%), $\nu_{max.}$ ($CHCl_3$) 3500 (OH), 1655, 1635, and 1610 cm^{-1} (dienone system), δ ($CDCl_3$) 2·39 (3H, s, NMe), 3·64 (3H, s, OMe), 3·80 (3H, s, OMe), 5·93 (1H, d, *J* 2·5 Hz, olefinic β-proton adjacent to methoxy-group), 6·38 (1H, d, *J* 9·5 Hz, olefinic α-proton), 6·58 (1H, s, ArH), and 6·85 p.p.m. (1H, dd, *J* 2·5 and 9·5 Hz, olefinic β-proton).

Photolysis of the Isoquinoline (38).—A mixture of compound (38) (250 mg), 1% sodium hydroxide solution (25 ml), and ethanol (5 ml) was diluted to 1 l with ethanol (100 ml) and water. The solution was irradiated for 6 h with a Hanovia 450 W mercury lamp (Pyrex filter) with stirring. Ethanol was removed and an excess of crystalline ammonium chloride was added to the remaining aqueous solution. The mixture was extracted with chloroform. The extract was washed with water and saturated sodium chloride solution, dried (Na_2SO_4), and evaporated to leave a dark brown gum (100 mg), which was chromatographed on silica gel (10 g). After elution (25 ml fractions) with chloroform (fractions 1—5), methanol–chloroform (1 : 99) (fractions 6—13), and methanol–chloroform (5 : 95) (fractions 14—16), elution with methanol–chloroform (5 : 95) (fractions 17—21) gave a brownish oil (10 mg), which showed dienone bands in the i.r. spectrum; this was purified by preparative t.l.c. on silica gel [methanol–chloroform (1 : 10) as eluant] to give (±)-pallidine (48) [18] (4 mg) identical (i.r. spectrum) with an authentic sample; *m/e* 327 (M^+).

Photolysis of 2′-Bromoreticuline (39).—A mixture of 2′-bromoreticuline (39) (3 g), sodium hydroxide (3 g), sodium iodide (3 g), ethanol (300 ml), and water (600 ml) was irradiated with a Riko 400 W mercury lamp (Pyrex filter) for 7 h at room temperature. An excess of ammonium chloride was then added and the mixture was extracted with chloroform. The extract was washed with water, dried (Na_2SO_4), and evaporated. The residue was chromatographed on silica gel (50 g). Initial elution with chloroform (800 ml) gave 3-hydroxy-4-methoxybenzaldehyde (50 mg), identical [i.r. spectrum ($CHCl_3$)] with an authentic sample. Further elution with chloroform (500 ml) gave thalifoline (50) (25 mg), m.p. 216—217° (lit.,[28] 216—217°), $\nu_{max.}$ ($CHCl_3$) 3500 (OH) and 1640 cm^{-1} (C=O), δ ($CDCl_3$) 2·88 (2H, t, *J* 7·5 Hz, N·CH_2·CH_2Ar), 3·10 (3H, s, NMe), 3·52 (2H, t, *J* 7·5 Hz, N·CH_2·CH_2Ar), 3·88 (3H, s, OMe), 6·57 (1H, s, 5-H), and 7·68 p.p.m. (1H, s, 8-H). Elution with chloroform–methanol (99 : 1; 1 l) then gave the starting material (39) (50 mg), and elution with methanol–chloroform (1 : 50; 500 ml) gave a cyclohexadienone fraction. The latter was again chromatographed on alumina [neutral (20 g)] with chloroform–benzene (1 : 4) as eluant. The initial eluate (100 ml) gave (±)-salutaridine (49) as a pale yellow syrup (23 mg, 1%), $\nu_{max.}$ ($CHCl_3$) 3560 (OH), 1671, 1644, and 1624 cm^{-1} (cyclohexadienone), *m/e* 327 (M^+), 312 (M − 15), 299 (M − 28), and 284, identical with an authentic sample (direct spectral comparison).

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