SECTION C
Organic Chemistry

Syntheses of a Proerythrinadienone by Phenolic Oxidation and a Morphinandienone System by a Photo-Pschorr Reaction †

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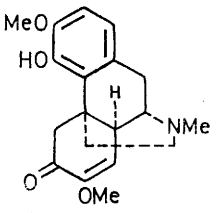
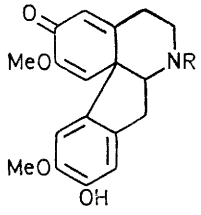
Phenolic oxidative coupling of ethyl 1,2,3,4-tetrahydro-6-hydroxy-1-(3-hydroxy-4-methoxybenzyl)-7-methoxyisoquinoline-2-carboxylate (2c) with potassium ferricyanide afforded the indenoisoquinoline (3c), which rearranged on treatment with acid. Spectral data, and methylation of the rearrangement product and comparison with the dienone (22) obtained from the diazotisation of the aminobenzylisoquinoline (15), followed by photolysis, excluded the morphinan structure (12), and confirmed the dibenz[*d,f*]indole structure (13).

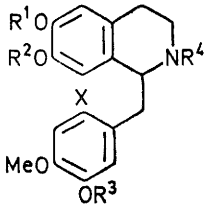
SINOMENINE, an alkaloid isolated from *Sinomenium acutum*, was assigned structure (1) by Goto and his co-workers.[1] For the synthesis of sinomenine, a dienone



(1)



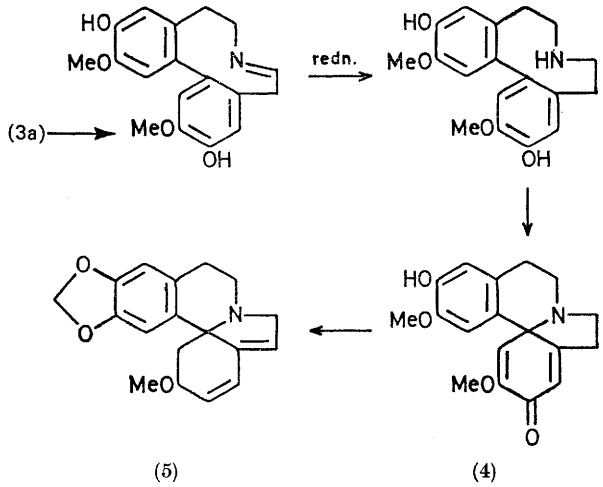
(3a) R = H
(3b) R = Me
(3c) R = CO_2Et



(2a) $R^1 = R^3 = R^4 = X = H$, $R^2 = Me$
(2b) $R^1 = R^3 = X = H$, $R^2 = R^4 = Me$
(2c) $R^1 = R^3 = X = H$, $R^2 = Me$, $R^4 = CO_2Et$
(9) $R^1 = R^3 = CH_2Ph$, $R^2 = Me$, $R^4 = X = H$
(10) $R^1 = R^3 = CH_2Ph$, $R^2 = Me = R^4 CO_2Et$, $X = H$
(15) $R^1 = R^3 = Me$, $R^2 = CH_2Ph$, $R^4 = CO_2Et$, $X = NH_2$
(17) $R^1 = R^3 = Me$, $R^2 = CH_2Ph$, $R^4 = X = H$
(18) $R^1 = R^3 = Me$, $R^2 = CH_2Ph$, $R^4 = H$, $X = NO_2$
(19) $R^1 = R^3 = Me$, $R^2 = CH_2Ph$, $R^4 = CO_2Et$, $X = NO_2$
(21) $R^1 = R^3 = Me$, $R^2 = CH_2Ph$, $R^4 = CO_2Et$, $X = OH$

of type (3) was thought to be a useful model intermediate. The new biogenetic theory of the erythrina alkaloids proposed by Barton [2] suggests that the dienone (3a) derived from norprotosinomenine (2a) by phenolic oxidation, would be converted into erythraline (5) through the erythrinadienone (4).[2,3]

A dienone of type (6) was also suggested by Battersby [4] as a precursor of hasubanonine (7). We have been investigating biogenetic-type syntheses of these alkaloids,[5] and now report the synthesis of the dienone-type compound (3c), named tentatively as proerythrinadienone.



(5) (4)

At first, the diphenolic isoquinolines (2a) and (2b) were prepared and were subjected to the oxidative process. Since both the isoquinolines were insoluble in chloroform, iron(III) chloride hexahydrate was used as oxidising agent in aqueous media; in both cases, the starting

† Preliminary communication, T. Kametani, R. Charubala, M. Ihara, M. Koizumi, and K. Fukumoto, *Chem. Comm.*, 1971, 289; this paper forms part CDXX of Studies on the Syntheses of Heterocyclic Compounds (Part CDXIX, T. Kametani, S. Shibuya, and T. Kohno, *J. Pharm. Soc. Japan*, 1971, **91**, 818).

[1] K. Goto, 'Sinomenine,' Kitasato Institute, Tokyo, 1964; T. Kametani, 'The Chemistry of the Isoquinoline Alkaloids,' Hirokawa Inc., Tokyo, 1968, and Elsevier, Amsterdam, 1968, pp. 149, 251.

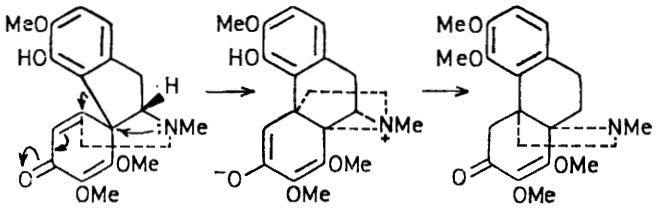
[2] D. H. R. Barton, R. James, G. W. Kirby, and D. A. Widdowson, *Chem. Comm.*, 1967, 266; D. H. R. Barton, R. James, G. W. Kirby, D. W. Turner, and D. A. Widdowson, *J. Chem. Soc.*, (*C*) 1968, 1529.

[3] D. H. R. Barton, R. B. Boar, and D. A. Widdowson, *J. Chem. Soc.* (*C*), 1970, 1213.

[4] A. R. Battersby, 'Oxidative Coupling of Phenols,' ed. W. I. Taylor and A. R. Battersby, Dekker, New York, 1967, p. 117.

[5] T. Kametani, K. Fukumoto, M. Kawatsu, and M. Fujihara, *J. Chem. Soc.* (*C*), 1970, 922.

material was recovered.[6] Therefore the oxidation of the diphenolic *N*-ethoxycarbonylisoquinoline (2c), which was synthesised as follows, was carried out.



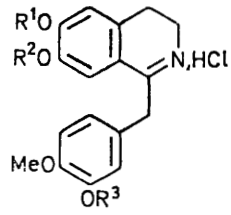
(6) (7)

The hydrochloride of the dihydroisoquinoline [7] (8) was reduced with sodium borohydride to give the tetrahydroisoquinoline (9), which was ethoxycarbonylated with ethyl chloroformate and triethylamine in chloroform. The product (10) was debenzylated with ethanolic hydrochloric acid to give the 2-ethoxycarbonylnorprotosinomenine (2c), which dissolved readily in chloroform. Oxidation was tried under various conditions; the best reagent was a two-phase system of chloroform and aqueous potassium ferricyanide, with ammonium acetate and ammonia. At pH 9·2 this afforded the dienone (3c), in 2% yield. The molecular formula was confirmed by the mass spectrum (M^+ 385·1550), and the i.r. and u.v. spectra were as expected for a cross-conjugated α-methoxycyclohexadienone system. The n.m.r. spectrum ($CDCl_3$) revealed two aromatic and two olefinic protons (singlets at τ 3·18, 3·69, 3·76, and 4·29), two *O*-methyl groups (6·21 and 6·39) and an ethyl ester function (8·76 and 5·87).

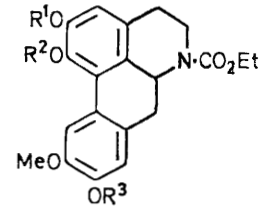
Treatment of compound (3c) with concentrated sulphuric acid at room temperature for 1 h in a current of nitrogen, gave a rearrangement product in 60% yield, for which three possible structures [(11)—(13)] were considered. Structure (13) was assigned on the basis of the following evidence. High resolution mass spectrometry verified the molecular formula (M^+ 371·1412). The n.m.r. spectrum showed two aromatic and two olefinic protons (singlets at τ 3·00, 3·25, 3·37, and 3·71), an aromatic methoxy-group (τ 6·05), and the ethyl group (τ 8·68 and 5·78). The i.r. and u.v. [$\lambda_{max.}$ (MeOH) 355, 290, and 265 nm (log ε 3·84, 3·76, and 3·72)] [8,9] spectra were in full agreement with the assignment.

To confirm structure (13), the compound was methylated with diazomethane and the product (14) was compared with the dienone (22) obtained by diazotisation of the aminoisoquinoline (15) followed by photolysis. Compound (15) was synthesised as follows. The dihydroisoquinoline (16) [10] was reduced with sodium borohydride to yield the tetrahydroisoquinoline (17). Nitration of compound (17) with concentrated nitric acid in glacial acetic acid afforded the 2′-nitroisoquinoline (18), which was ethoxycarbonylated to give the ester (19). This was then reduced with zinc, acetic acid, and concentrated hydrochloric acid.

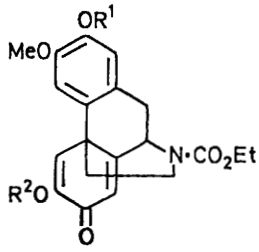
Diazotisation of compound (15), followed by irradiation of the resulting diazonium salt (15a) gave three compounds, which were separated and purified by silica gel column chromatography.



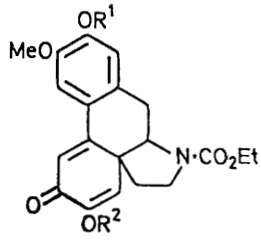
(8) $R^1 = R^3 = CH_2Ph$, $R^2 = Me$
(16) $R^1 = R^3 = Me$, $R^2 = CH_2Ph$



(11) $R^1 = R^3 = H$, $R^2 = Me$
(20) $R^1 = R^3 = Me$, $R^2 = CH_2Ph$



(12) $R^1 = R^2 = H$
(22) $R^1 = R^2 = Me$



(13) $R^1 = R^2 = H$
(14) $R^1 = R^2 = Me$

The first compound was the aporphine (20), obtained in 25% yield, and identified by spectra and microanalysis. The second was the benzylisoquinoline (21). The third compound (22), $C_{22}H_{25}NO_6$, was shown to contain an α-alkoxylated cross-conjugated cyclohexadienone system by the i.r. and u.v. spectral data. The n.m.r. spectrum ($CDCl_3$) revealed the expected signals for two olefinic and two aromatic protons (τ 3·69, 3·45, and 3·20), an *N*-ethoxycarbonyl group, and three *O*-methyl groups.

Comparison of the two dienones (22) and (14) (spectral data and t.l.c.) showed that they were different, thus eliminating structure (12) for the dienone obtained by the treatment of compound (3c) with sulphuric acid.

EXPERIMENTAL

I.r. spectra were measured with a Hitachi EPI-3 recording spectrophotometer, u.v. spectra with a Hitachi EPS-3 recording spectrophotometer, and n.m.r. spectra with a Hitachi R-20 spectrometer with tetramethylsilane as an internal standard. Mass spectra were taken with an Hitachi RMU-7 spectrometer.

6-Benzyloxy-1-(3-benzyloxy-4-methoxybenzyl)-1,2,3,4-tetrahydro-7-methoxyisoquinoline (9).—To a cooled mixture of the dihydroisoquinoline hydrochloride (8) (20 g), methanol (2 l), and water (100 ml), sodium borohydride (14 g) was added in portions with stirring. The mixture was stirred at room temperature for 10 min. After refluxing for 1 h, removal of the solvent left a residue, which was treated with water and extracted with chloroform. The extract

[6] T. Kametani and S. Shibuya, *J. Pharm. Soc. Japan*, 1968, **88**, 583.
[7] R. Robinson and S. Sugasawa, *J. Chem. Soc.*, 1931, 3163.
[8] K. L. Stuart, C. Chambers, and D. Byfield, *J. Chem. Soc.* (*C*), 1969, 1681.
[9] A. R. Battersby, A. K. Bhatnagai, P. Hackett, C. W. Thornber, and J. Staunton, *Chem. Comm.*, 1968, 1214.
[10] M. Shamma and W. A. Slusarchyk, *Tetrahedron*, 1967, 2563.

was washed with water, dried (Na_2SO_4), and evaporated to give a pale yellow oil (12 g). Recrystallisation of the *hydrochloride* of compound (9) from methanol afforded prisms, m.p. 206—208° (Found: C, 72·1; H, 6·1; N, 2·9. $C_{32}H_{33}NO_4$,HCl requires C, 72·2; H, 6·1; N, 2·6%).

Ethyl 6-*Benzyloxy*-1-(3-*benzyloxy*-4-*methoxybenzyl*)-1,2,3,4-*tetrahydro*-7-*methoxyisoquinoline*-2-*carboxylate* (10).—To a solution of compound (9) (14 g) and triethylamine (12 g) in chloroform (100 ml), ethyl chloroformate (12 g) was added dropwise with stirring at 10°. The mixture was stirred at room temperature for 3 h, washed with water, and dried (Na_2SO_4). Evaporation gave the isoquinoline derivative (10) (12 g), which formed *needles* (11 g), m.p. 138—140° (from benzene–hexane) (Found: C, 74·0; H, 6·5; N, 2·9. $C_{35}H_{37}NO_6$ requires C, 74·1; H, 6·6; N, 2·5%), $\nu_{max.}$ ($CHCl_3$) 1680 cm^{-1} (N·CO_2Et).

Ethyl 1,2,3,4-*Tetrahydro*-6-*hydroxy*-1-(3-*hydroxy*-4-*methoxybenzyl*)-7-*methoxyisoquinoline*-2-*carboxylate* (N-*Ethoxycarbonylnorprotosinomenine*) (2c).—A mixture of the isoquinoline (10) (10 g), ethanol (800 ml), and concentrated hydrochloric acid (340 ml) was refluxed for 5 h. The ethanol was then distilled off and the residue was extracted with chloroform. The extract was washed with 10% ammonia and water, dried (Na_2SO_4), and evaporated to give a gum, crystallisation of which from benzene–hexane afforded the *diphenol* (2c) (5 g) as prisms, m.p. 148—150° (Found: C, 65·5; H, 6·5; N, 3·9. $C_{21}H_{25}NO_6$ requires C, 65·1; H, 6·5; N, 3·6%), $\nu_{max.}$ ($CHCl_3$) 3400 (OH) and 1680 cm^{-1} (N·CO_2Et).

Phenolic Oxidation of the Diphenol (2c).—To a mixture of compound (2c) (2 g), chloroform (200 ml), and aqueous ammonium acetate (8%; 250 ml), under nitrogen, at room temperature, potassium ferricyanide solution [5·75 g in water (187·5 ml)] was added dropwise during 30 min, with vigorous stirring. Stirring was continued for a further 1 h, after which concentrated ammonia (12 ml) was added in portions until pH 9·2 was reached. The organic layer was separated and the aqueous layer was extracted several times with chloroform. The combined extracts were washed with water, dried (Na_2SO_4), and evaporated to give a gum (0·9 g). This was chromatographed on silica gel (50 g) with chloroform (each fraction 150 ml; fractions 1—25), chloroform–methanol (99 : 1 v/v; 26—35) and chloroform–methanol (98 : 2 v/v; 36—50) as eluants (t.l.c. and i.r., and u.v. spectral control).

Fractions 16—23 gave a crude dienone (3c) (100 mg), which was rechromatographed on alumina (2 g) with benzene and benzene–chloroform as eluants. Elution with benzene–chloroform (90 : 10 v/v) gave a viscous syrup (40 mg) which crystallised from chloroform–hexane to give a *powder*, m.p. 144—146° (Found: C, 62·45; H, 6·75. $C_{21}H_{23}NO_6$,H_2O requires C, 62·5; H, 6·25%), $\nu_{max.}$ ($CHCl_3$ 1675 (N·CO_2Et), 1660, 1639, and 1615 cm^{-1} (cyclohexadienone), $\lambda_{max.}$ (MeOH) 287 and 240 nm (log ε 3·88 and 4·23), τ ($CDCl_3$) 8·76 (3H, t, *J* 7 Hz, N·CO_2·CH_2·CH_3), 6·39 (3H, s, OMe), 6·21 (3H, s, OMe), 5·87 (2H, q, *J* 7 Hz, N·CO_2·CH_2·CH_3), and 4·29, 3·76, 3·69, and 3·18 (4H, each s, 2 olefinic and 2 aromatic protons), *m/e* 385·1550 (M^+) (Calc. for $C_{21}H_{23}NO_6$: 385·1525), 370 (M^+ — Me), 357 (M^+ — CO), and 340 (M^+ — OEt).

Rearrangement of the Dienone.—A mixture of compound (3c) (20 mg) and concentrated sulphuric acid (1 ml) was stirred under nitrogen at room temperature for 1 h. The resulting reddish solution was poured on ice and basified with a mixture of sodium hydroxide (15%; 5 ml) and N-sodium hydrogen carbonate (25 ml) to pH 8·0. The resulting mixture was then extracted with chloroform, and the combined extracts were washed with N-sodium hydrogen carbonate solution, dried (Na_2SO_4), and evaporated. The residue (20 mg) was chromatographed on silica gel (2 g), with chloroform as eluant. Fractions 7—13 (each fraction 25 ml) gave material tentatively identified as ethyl 5,6,7a,8-tetrahydro-3,10-dihydroxy-11-methoxy-2-oxo-2*H*,7*H*-dibenz[*d*,*f*]indole-7-carboxylate (13), a pale yellow viscous syrup, $\nu_{max.}$ ($CHCl_3$) 1685 (N·CO_2Et), and 1635 and 1620sh cm^{-1} (enone), $\lambda_{max.}$ (MeOH) 355, 290, and 265 nm (log ε 3·72, 3·76, and 3·84), τ ($CDCl_3$) 8·68 (3H, q, *J* 7 Hz, N·CO_2·CH_2·CH_3), 6·05 (3H, s, OMe), 5·78 (2H, q, N·CO_2·CH_2·CH_3), and 3·71, 3·37, 3·25 and 3·00 (4H, each s, 2 olefinic and 2 aromatic proteins), *m/e* 371·1412 (M^+) (Calc. for $C_{20}H_{21}NO_6$: 371·1368), 342 (M^+ — H — CO), 314 (M^+ — H — 2CO).

Methylation of the Dibenzindole (13).—To an excess of diazomethane in ether (200 ml) was added a solution of compound (13) (20 mg) in methanol (8 ml) and the mixture was set aside at room temperature for 4 days. Evaporation left a yellow syrup (10 mg), which was chromatographed on alumina (2 g) with benzene and benzene–chloroform as eluants. Elution with benzene–chloroform (95 : 5 v/v) gave the trimethyl ether (14) (1 mg) as a pale yellow syrup, $\nu_{max.}$ 1650, 1630, and 1591 cm^{-1} (cyclohexadienone), $\lambda_{max.}$ (MeOH) 355, 288, and 265 nm (log ε 3·69, 3·77, and 3·82), τ ($CDCl_3$) 6·28 (3H, s, OMe) and 6·10 (6H, s, 2 × OMe), *m/e* 399·1725 (M^+) (Calc. for $C_{22}H_{25}NO_6$: 399·1680), 384 (M^+ — 15), 382 (M^+ — 17), 370 (M^+ — 29), 354 (M^+ — 45), 326 (M^+ — 73).

7-*Benzyloxy*-1-(4,5-*dimethoxybenzyl*)-1,2,3,4-*tetrahydro*-6-*methoxyisoquinoline* (17).—To a cooled mixture of the dihydroisoquinoline hydrochloride (16) (15 g), methanol (600 ml), and water (50 ml), sodium borohydride (10 g) was added in portions with stirring, and stirring was continued for 10 min at room temperature. After refluxing for 1 h, solvent was removed *in vacuo*, and the residue was taken up in water and extracted with chloroform. After being washed with water, the dried (Na_2SO_4) chloroform extract was evaporated to leave the tetrahydroisoquinoline (17) as an oil (13 g). Crystallisation of the *hydrochloride* from methanol afforded prisms, m.p. 215—217° (Found: C, 68·1; H, 6·3; N, 3·4. $C_{26}H_{29}NO_4$,HCl requires C, 68·5; H, 6·6; N, 3·1%).

7-*Benzyloxy*-1-(4,5-*dimethoxy*-2-*nitrobenzyl*)-1,2,3,4-*tetrahydro*-6-*methoxyisoquinoline* (18).—To a cooled solution of compound (17) (50 g) in glacial acetic acid (350 ml), concentrated nitric acid (85 ml) was added in five portions, the temperature being maintained between 8—10°. The reddish mixture was then poured on ice, and a yellow solid was filtered off, dried, and recrystallised from methanol to give the *nitrate* of (18) (35 g) as yellow fluffy needles, m.p. 210—211° (Found: C, 58·9; H, 5·6; N, 7·9. $C_{26}H_{28}N_2O_6$,HNO_3 requires C, 59·2; H, 5·5; N, 8·0%), $\nu_{max.}$ ($CHCl_3$) 1325 cm^{-1} (NO_2).

Ethyl 7-*Benzyloxy*-1-(4,5-*dimethoxy*-2-*nitrobenzyl*)-1,2,3,4-*tetrahydro*-6-*methoxy isoquinoline*-2-*carboxylate* (19).—The foregoing salt of compound (18) (10 g) was basified with ammonia and the mixture was extracted with chloroform. The dried (Na_2SO_4) extract was evaporated to yield a brown oil (8 g). To a cooled solution of the oil and triethylamine (5 g) in chloroform (300 ml), ethyl chloroformate (5 g) was added dropwise with stirring. The mixture was stirred at room temperature for 2 h, and the solvent layer was washed with water, dried (Na_2SO_4), and evaporated to give

a yellow solid, which (from chloroform–hexane) yielded the *ester* (19) (7 g) as pale yellow needles, m.p. 125—127° (Found: C, 64·9; H, 6·0; N, 5·2. $C_{29}H_{32}N_2O_8$ requires C, 64·6; H, 5·8; N, 5·2%), $\nu_{max.}$ ($CHCl_3$) 1675 cm^{-1} (N·CO_2Et).

Ethyl 1-(2-*Amino*-4,5-*dimethoxybenzyl*)-7-*benzyloxy*-1,2,3,4-*tetrahydro*-6-*methoxyisoquinoline*-2-*carboxylate* (15).—Within 1 h at a temperature below 5°, zinc powder (50 g) was added in small portions to a stirred mixture of compound (19) (10 g), concentrated hydrochloric acid (120 ml), glacial acetic acid (440 ml), and water (80 ml). Stirring was continued at the same temperature for 5 h. Zinc was filtered off and the filtrate was basified with concentrated ammonia and extracted with chloroform. The extract was washed with saturated sodium chloride solution, dried (Na_2SO_4), and distilled to leave the aminoisoquinoline (15) (7·5 g) as a brown viscous syrup, which crystallised from benzene–hexane to give fluffy *needles*, m.p. 115—117° (Found: C, 68·8; H, 6·8; N, 5·5. $C_{29}H_{34}N_2O_6$ requires C, 68·4; H, 6·6; N, 5·5%).

Photolysis of the Diazonium Salt of the Amine (15).—To a stirred solution of the aminoisoquinoline (15) (2 g) in glacial acetic acid (25 ml) and N-sulphuric acid (200 ml), a solution of sodium nitrite (0·272 g) in water (4 ml) was added dropwise at 5° within 20 min, and stirring was continued at 5° for 1 h. After decomposition of the excess of nitrous acid with urea, followed by dilution to 1 l with water, the mixture was irradiated with a Hanovia 450 W mercury lamp (Pyrex filter at 5—10° for 4 h). The reaction mixture was then basified with concentrated ammonia and extracted with chloroform. The extract was washed with water, dried (Na_2SO_4), and evaporated to afford a dark brown gum (2·5 g), which was chromatographed on silica gel (60 g) with benzene (each fraction 200 ml, fractions 1—8) and benzene–chloroform [90 : 10 v/v (fractions 9—18); 70 : 30 (fractions 19—28), 50 : 50 (fractions 29—49); 25 : 75 (fractions 50—57) and 5 : 95 (fractions 58—88)] as eluants (t.l.c. and i.r. and u.v. spectral control). Fractions 29—32 gave the aporphine (20) as a yellowish viscous syrup (50 mg), which formed *prisms*, m.p. 144—146° (from chloroform–hexane) (Found: C, 71·0; H, 6·6; N, 2·9. $C_{29}H_{31}NO_6$ requires C, 71·1; H, 6·4; N, 2·9%), $\lambda_{max.}$ (MeOH) 303 and 283 nm (log ε 4·11 and 4·10), τ ($CDCl_3$) 8·76 (3H, t, *J* 7 Hz, N·CO_2·CH_2·CH_3), 6·50 (3H, s, OMe), 6·10 (6H, s, 2 × OMe), 5·75 (2H, q, *J* 7 Hz, N·CO_2·CH_2·CH_3), 5·05 and 5·50 (each 1H, each d, *J* 11 Hz, O·CH_2Ph), 3·40 (1H, s, 3-H), 3·29 (1H, s, 8-H), 2·70 (5H, s, O·CH_2·C_6H_5), and 1·97 (1H, s, 11-H).

Fractions 39—45 gave ethyl 6-benzyloxy-1,2,3,4-tetrahydro-1-(2-hydroxy-4,5-dimethoxybenzyl)-7-methoxyisoquinoline-2-carboxylate (21) (250 mg) as a pale brown solid, which formed *needles*, m.p. 148—150° (from methanol–ether) (Found: C, 68·2; H, 6·1; N, 3·0. $C_{29}H_{33}NO_7$ requires C, 68·6; H, 6·6; N, 2·8%), $\nu_{max.}$ ($CHCl_3$) 3500 and 3300 (OH), and 1660 cm^{-1} (N·CO_2Et), $\lambda_{max.}$ (MeOH), 280 nm, τ ($CDCl_3$) 8·72 (3H, t, *J* 7 Hz, N·CO_2·CH_2·CH_3), 6·38 (3H, s, OMe), 6·18 (6H, s, 2 × OMe), 5·88 (2H, q, *J* 7 Hz, N·CO_2·CH_2·CH_3), 5·20 (2H, s, O·CH_2Ph), 3·85, 3·45, and 3·35 (4H, 3s, Ar-H), and 2·79 (5H, s, O·CH_2·C_6H_5). The *O*-acetyl derivative was a pale brown syrup, $\nu_{max.}$ ($CHCl_3$) 1750 (O–Ac) and 1660 cm^{-1} (N·CO_2Et), τ ($CDCl_3$) 7·73 (3H, s, Ac).

Fractions 59—75 afforded the crude morphinandienone (22) (400 mg) as a brown syrup, which was rechromatographed on silica gel (25 g) with benzene and benzene–chloroform. Elution with chloroform–benzene (9 : 1) gave the dienone as a pale yellow syrup (97 mg), which was again chromatographed on alumina. Elution with benzene–chloroform (9 : 1) gave the dienone (50 mg), which was finally purified by preparative t.l.c. on silica gel in benzene–ethyl acetate–methanol (5 : 4 : 1). The portion of R_F 0·35 was extracted with chloroform–methanol (98 : 2 v/v) to give a pale brown solid, which gave compound (22) (30 mg) as a *powder*, m.p. 78—81° (from chloroform–hexane) (Found: C, 66·2; H, 6·6. $C_{22}H_{25}NO_6$ requires C, 66·2; H, 6·3%), $\nu_{max.}$ ($CHCl_3$) 1670, 1643, and 1620 cm^{-1}, $\lambda_{max.}$ (MeOH) 283 and 233 nm (log ε 3·8 and 4·2), τ ($CDCl_3$) 8·75 (3H, t, *J* 7 Hz, N·CO_2·CH_2·CH_3), 6·23 (3H, s, OMe), 6·19 (3H, s, OMe), 6·13 (3H, s, OMe), 5·90 (2H, q, *J* 7 Hz, N·CO_2·CH_2·CH_3), and 3·69 (2H), 3·45 (1H), and 3·20 (1H) (each s, 2 olefinic and 2 aromatic protons).

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