Photocyclisation of Enamides. Part 17.[1] Total Synthesis of (±)-Corynoline, (±)-12-Hydroxycorynoline, and (±)-11-Epicorynoline [2]

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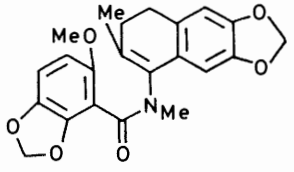
Photocyclisation of the enamide (1) followed by stereoselective functionalisation of the *cis*-lactam (4c) completed the first total synthesis of the alkaloids, (±)-corynoline (7e), (±)-12-hydroxycorynoline (7d), and (±)-11-epicorynoline (7c). Participation of the basic nitrogen in the oxidation with peracid was also suggested.

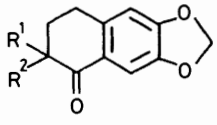
PREVIOUSLY,[3] we have developed a stereoselective synthetic route toward hexahydro-10b-methylbenzo[*c*]-phenanthridine alkaloids,[4] corynoline, and related alkaloids, by preparing basic structures of these alkaloids. As an extension of our work [5a,b] on the synthetic study of benzo[*c*]phenanthridine alkaloids, we now report the first total synthesis of (±)-corynoline, (±)-12-hydroxycorynoline, and (±)-11-epicorynoline by employing the enamide photocyclisation and the stereoselective introduction of hydroxy-groups. Synthetic studies of corynoline and related alkaloids have been limited to the synthesis of an analogue of corynoline by Onda *et al.*[6]

RESULTS AND DISCUSSION

In order to synthesise the enamide (1), which is an essential starting material for the photochemical synthesis of the hexahydro-10b-methylbenzo[*c*]phenanthridine skeleton, we first tried to prepare the 2-methyl-1-tetralone (2a) from piperonal by the method reported by Tani *et al.*[7]



(1)



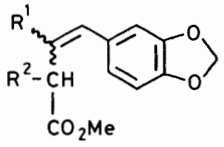
(2)

a ; R^1 = Me , R^2 = H

b ; R^1 = R^2 = H

c ; R^1 = CO_2Me , R^2 = H

d ; R^1 = CO_2Me, R^2 = Me



(3)

a ; R^1 = Me , R^2 = H

b ; R^1 = H , R^2 = Me

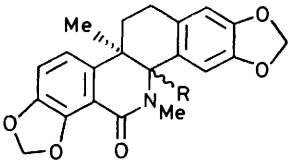
Treatment of piperonal with disodium methylsuccinate followed by esterification gave the ester (3a) in 41% yield, which showed the n.m.r. signals for an olefinic proton at δ 6.30 as a multiplet and for a vinylic methyl group at 1.92 as a doublet. These spectral data clearly showed that the structure of the product should be depicted not by the formula (3b) but (3a) and that the Perkin reaction of piperonal with methylsuccinate has actually occurred at the C-2 position. Furthermore, the 1-tetralone prepared from the ester (3a) by Tani's method [7] was not identical (i.r., n.m.r., t.l.c., and m.p.) with authentic 2-methyl-1-tetralone (2a), which was independently synthesised from the corresponding 1-tetralone (2b) by the following sequence of reactions.

Following the procedure given by Bachmann *et al.*,[8] reaction of the 1-tetralone (2b) with dimethyl oxalate, followed by decarbonylation, gave the keto-ester (2c) which was then methylated with methyl iodide and successively decarboxylated upon hydrolysis to afford the 2-methyl-1-tetralone (2a) in 68% overall yield from (2b).

Since all the hexahydrobenzo[*c*]phenanthridine alkaloids [4] so far isolated possess a common 8,9-disubstituted skeleton, in order to synthesise this type of the alkaloids by enamide photocyclisation, it was necessary to prevent cyclisation at the point of attachment of a methylenedioxy-group.[5b,c] The enamide (1) was therefore prepared from the tetralone (2a) and 6-methoxy-2,3-methylenedioxybenzoyl chloride in 66% yield as reported previously.[5b] The enamide (1) exhibited an intricate n.m.r. spectrum at room temperature and even at higher temperature (165 °C), suggesting the existence of rotational isomers, as occurs with an analogous enamide.[9]

Irradiation of a methanolic 0.003M solution of the enamide (1) with a high-pressure mercury lamp at room temperature for 16 h yielded a homogeneous product (4a) in 20% yield, which showed i.r. absorption at 1 645 cm^{-1} (lactam carbonyl) and n.m.r. signals at δ 6.98 (br s, 4-H), 6.80 (s, 9- and 10-H), 6.48 (s, 1-H), 3.05 (s, NMe and OMe), and 1.28 (s, 10b-Me). This spectroscopic evidence confirmed that the photoproduct (4a) did not have the methoxy-group on the benzene ring but at C-4b, as a result of specific migration,[5b] though its configuration was still undetermined. In order to remove the 4b-methoxy-group, the lactam (4a) was hydrogenated over 40% palladium–charcoal under a hydrogen atmosphere (2.5 atm.) to give a mixture of the *trans*-(4b) and the *cis*-lactams (4c) in 60 and 21% yields respectively. However, reduction of the lactam (4a) with sodium borohydride in the presence of boron trifluoride etherate [10] gave only the *cis*-lactam (4c) in

70% yield, which constitutes a common basic skeleton of hexahydrobenzo[*c*]phenanthridine alkaloids.[4] The stereochemistry of the *trans*- and *cis*-lactams (4b and c) was deduced by comparing their n.m.r. spectra with those of the basic structures of the alkaloids, whose stereochemistry has been already established.[3] In the case of the *cis*-lactam (4c), the signals for the 10b- and



(4)

a; R = OMe

b; R = β-H

c; R = α-H

N-methyl protons appeared at lower field, and signals for the 4b-proton at higher field, than those of the *trans*-lactam (4b).

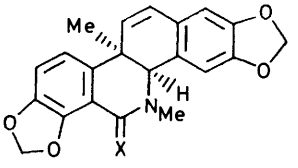
The *cis*-lactam (4c) was dehydrogenated with dichlorodicyanobenzoquinone in chloroform to give the 11,12-dehydrolactam (5a) in 28% yield, which was shown to have a double bond at C-11 from the n.m.r. signals at δ 6.40 and 6.08 (each d, *J* 10 Hz). Reduction of the dehydrolactam (5a) with lithium aluminium hydride afforded the corresponding amine (5b), identical with deoxycorynoline which had already been obtained from corynoline by Takao *et al.*[11]

Next, the introduction of hydroxy-groups at C-11 of the lactam (5a) and the amine (5b) was undertaken in order to synthesise natural alkaloids, employing stereoselective oxidation with peracid [3] on lactam and amine as described. Oxidation of the 11,12-dehydrolactam (5a) with performic acid followed by treatment with alkali furnished a mixture of two glycols (6a and b) in 40 and 20% yields respectively, which were separated by chromatography, and then reduced with lithium aluminium hydride to give the corresponding amines (7a and b) in good yields. The amine (7a) exhibited i.r. absorption at 3 550 and 3 400 cm^{-1} (2 × OH) and n.m.r. signals at δ 4.72 and 4.44 (each d, *J* 5 Hz, 11- and 12-H), and readily formed the corresponding acetonide. On the other hand, the amine (7b) failed to form an acetonide and showed n.m.r. signals at δ 4.36 and 4.32 (each d, *J* 7.5 Hz, 11- and 12-H). These data and the following reaction suggested that the amine (7a) has the 11α,12α-glycol structure, while (7b) has the 11α,12β-configuration.

Hydrogenolysis of either the 11α,12α-glycol (7a) or the 11α,12β-glycol (7b) over 40% palladium–charcoal yielded (±)-11-epicorynoline (7c) in 53% yield, which was identical with the natural alkaloid [12] on comparison of their i.r. and n.m.r. spectra.

Treatment of deoxycorynoline (5b) with performic acid followed by alkali furnished stereoselectively (±)-12-hydroxycorynoline (7d) in 91% yield, which was identical with the natural alkaloid [12a, 13] upon comparison of their i.r., n.m.r., and mass spectra, and R_F values.

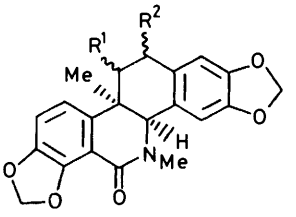
Hydrogenolysis of (±)-12-hydroxycorynoline (7d) over 40% palladium–charcoal as in the case of (7a and b) afforded (±)-corynoline (7e) along with the epimeric glycol (7f) in 35 and 17% yields respectively, the former



(5)

a; X = O

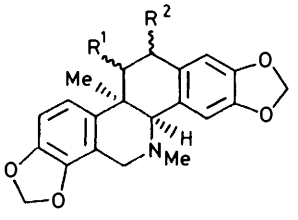
b; X = H_2



(6)

a; R^1 = α-OH, R^2 = α-OH

b; R^1 = α-OH, R^2 = β-OH



(7)

a; R^1 = α-OH, R^2 = α-OH

b; R^1 = α-OH, R^2 = β-OH

c; R^1 = α-OH, R^2 = H

d; R^1 = β-OH, R^2 = α-OH

e; R^1 = β-OH, R^2 = H

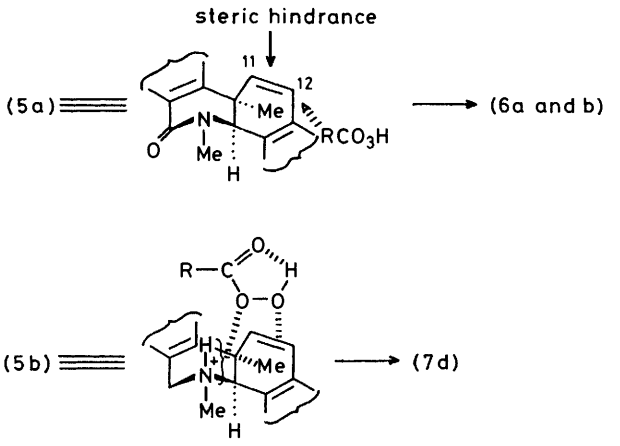
f; R^1 = β-OH, R^2 = β-OH

g; R^1 = β-OH, R^2 = OAc

of which was identical with the natural alkaloid [14] upon comparison of their i.r., n.m.r., and mass spectra, and R_F values. The epimeric glycol (7f) was also obtained by treatment of (7d) with 10% hydrochloric acid containing a small amount of perchloric acid under stirring at room temperature and showed i.r. absorption at 3 500 cm^{-1} (2 × OH) and n.m.r. peaks at δ 4.59 (d, *J* 5 Hz, 12-H), 3.90 (dd, *J* 5 and 2 Hz, 11-H), and 3.28 (d, *J* 2 Hz, 4b-H), which suggested that (7f) has the 11β,12β-glycol configuration. Thus, we had succeeded in preparing all the possible epimers of 11,12-dihydroxyamines (7a, b, d, and f), which enabled us to determine the stereochemistry of these compounds unambiguously. Since corynoline had already been converted into 6-oxocorynoline,[12a] corynoloxine,[15] and acetylcorynoline,[14] the present work formally completes the synthesis of all the *cis*-alkaloids of the corynoline group.

Finally, in order to explain the marked difference

observed in the behaviour of the lactam (5a) and the amine (5b) toward peracid, we carried out oxidation of the amine (5b) with peracetic acid. The product was 12-acetoxy-11β-hydroxyamine (7g) in 73% yield, which showed n.m.r. signals at δ 6.23 (s-like, 12-H), 3.88 (s-like, 11-H), 3.37 (s-like, 4b-H), and 2.13 (s, OAc), which therefore confirmed the presence of a β-hydroxy-group at C-11 and an acetoxy-group at C-12. The fact that 12-acetoxy-11β-hydroxyamine (7g) was obtained from (7b) suggested the occurrence of a β-epoxide as a primary intermediate in the oxidation of the amine (5b) with peracid. From the result obtained previously [3] and the data reported here, the reaction mechanism shown in the Scheme for the oxidation of the lactam and the amine can be proposed. Peracid attacks the double bond of



SCHEME

the lactam (5a) from the less hindered α-side, thus affording α-epoxide [3] or the 11α-hydroxylactam (6a and b). On the other hand, interaction between an ammonium salt and an oxidising agent would make the attack of performic acid from the more hindered β-side possible in the case of the amine (5b) as in the case of oxidation of allylic alcohol.[16]

EXPERIMENTAL

^{1}H N.m.r. spectra were measured with Varian A-60D, NEVA-21 (90 MHz), and JEOL PMX-60 instruments for solutions in deuteriochloroform unless otherwise stated (tetramethylsilane as internal reference), i.r. spectra for solutions in chloroform, and mass spectra with JEOL JMS-OlSG machine. M.p.s were determined with a Kofler-type hot-stage apparatus. The extracts from the reaction mixtures were dried over anhydrous sodium sulphate. The photochemical reactions were carried out by irradiation at room temperature with a high-pressure (300 W) mercury lamp (Eikosha PIH 300).

Methyl 3-*Methyl*-4-(3,4-*methylenedioxyphenyl*)*but*-3-*enoate* (3a).—Following the procedure given by Tani *et al.*[7] the reaction of piperonal and disodium methylsuccinate, followed by esterification, gave the ester (3a), b.p. 155—180 °C (bath temp.) at 5 mmHg (lit.,[7] 160—180 °C at 7 mmHg); $\nu_{max.}$ 1 730 cm^{-1}, δ 6.77 (3 H, s-like, aromatic H), 6.30 (1 H, m, olefinic H), 5.93 (2 H, s, OCH_2O), 3.72 (3 H, s, OMe), 3.15 (2 H, s, CH_2CO_2Me), and 1.92 (3 H, d, *J* 3 Hz, CMe). Following ref. 7 this ester (3a) was converted to 3,4-*dihydro*-3-*methyl*-6,7-*methylenedioxynaphthalen*-1(2H)-*one*, m.p. 91.5—93 °C (from methanol) (lit.,[7] 82—83 °C), identical (i.r. spectra and R_F values) with an authentic sample.

3,4-*Dihydro*-2-*methyl*-6,7-*methylenedioxynaphthalen*-1(2H)-*one* (2a).—Following the procedure given by Bachmann *et al.*[8] the reaction of the 1-tetralone [5b] (2b) and dimethyl oxalate, followed by decarbonylation, gave the keto-ester (2c) in 96% yield, which was methylated and decarboxylated to afford the 2-methyl-1-tetralone (2a) in 70% yield, m.p. 67.5—69.5 °C (from n-hexane); $\nu_{max.}$ 1 665 (CO) cm^{-1}; δ 7.47 (1 H, s, 8-H), 6.63 (1 H, s, 5-H), 5.98 (2 H, s, OCH_2O), and 1.25 (3 H, d, *J* 6.5 Hz, CMe) (Found: C, 70.9; H, 5.95. $C_{12}H_{12}O_3$ requires C, 70.55; H, 5.9%). This tetralone (2a) was not identical with 3-methyl-1-tetralone which was prepared from (3a).

N-(3,4-*Dihydro*-2-*methyl*-6,7-*methylenedioxy*-1-*naphthyl*)-6-*methoxy*-N-*methyl*-2,3-*methylenedioxybenzamide* (1).—Anhydrous methylamine gas was bubbled into a solution of the tetralone (2a) (11 g) in anhydrous chloroform (50 ml) under ice-cooling for 30 min. This mixture was added dropwise to an ice-cooled solution of titanium tetrachloride (6 ml) in anhydrous chloroform (20 ml) with stirring. After refluxing for 1 h, the solvent was evaporated to dryness *in vacuo*, and the residue dissolved in anhydrous benzene (100 ml) and filtered. Triethylamine (13 g) was added to the filtrate, then a solution of 6-methoxy-2,3-methylenedioxybenzoyl chloride (13 g) in anhydrous benzene (50 ml) was added dropwise to the reaction mixture, which was then heated under reflux for 2 h and filtered to remove triethylamine hydrochloride. The filtrate was evaporated to give a solid which was recrystallised from ethanol to afford the crystalline enamide (1) (14 g, 66%), m.p. 186—187.5 °C; $\nu_{max.}$ 1 630 (NCO) cm^{-1} (Found: C, 67.45; H, 5.4; N, 3.75. $C_{22}H_{21}NO_6$ requires C, 66.8; H, 5.35; N, 3.55%). The n.m.r. spectrum of the enamide (1) was complex at room temperature, and even at 165 °C, in [$^2H_6$]dimethyl sulphoxide.[9]

4b,10b,11,12-*Tetrahydro*-4b-*methoxy*-5,10b-*dimethyl*-2,3;7,8-*bis*(*methylenedioxy*)*benzo*[c]*phenanthridin*-6(5H)-*one* (4a).—A methanolic 0.003M-solution of the enamide (1) (2 g) was irradiated for 16 h, then evaporated and the resulting residue was chromatographed on alumina. Elution with benzene–chloroform gave a solid which was recrystallised from ethanol to give the lactam (4a) (400 mg, 20%) as colourless crystals, m.p. 128—130 °C; $\nu_{max.}$ 1 645 (NCO) cm^{-1}, δ 6.98 (1 H, br s, 4-H), 6.80 (2 H, s, 9- and 10-H), 6.48 (1 H, s, 1-H), 6.07 (2 H, m, OCH_2O), 5.88 (2 H, s, OCH_2O), 3.05 (6 H, s, NMe and OMe), and 1.28 (3 H, s, CMe) (Found: C, 66.05; H, 5.9; N, 3.05. $C_{22}H_{21}NO_6 \cdot 0.5$-EtOH requires C, 66.0; H, 5.8; N, 3.35%).

Conversion of the 4b-*Methoxylactam* (4a) *into the* cis-*Lactam* (4c).—(a) *Using palladium–charcoal.* A solution of the lactam (4a) (1 g) in methanol (200 ml) was shaken over 40% palladium–charcoal (500 mg) under a hydrogen atmosphere (2.5 atm) at 50 °C for 2 h. The catalyst was filtered off and the filtrate was evaporated. Purification of the residue by preparative t.l.c. on silica gel afforded trans-4b,10b,11,12-*tetrahydro*-5,10b-*dimethyl*-2,3;7,8-*bis*(*methylenedioxy*)*benzo*[c]*phenanthridin*-6(5H)-*one* (4b) (550 mg, 60%) as crystals, m.p. 206—208 °C (from methanol); $\nu_{max.}$ 1 645 (NCO) cm^{-1}; δ 4.90 (1 H, s, 4b-H), 3.10 (3 H, s, NMe), and 1.07 (3 H, s, CMe) (Found: C, 68.45; H, 5.3; N, 3.85. $C_{21}H_{19}NO_5$ requires C, 69.0;

H, 5.25; N, 3.8%), and cis-4b,10b,11,12-*tetrahydro*-5,10b-*dimethyl*-2,3;7,8-*bis*(*methylenedioxy*)*benzo*[c]*phenanthridin*-6[5H]-*one* (4c) (200 mg, 21%) as crystals, m.p. 295.5—296.5 °C (from methanol); $\nu_{max.}$ 1 640 (NCO) cm^{-1}; δ 4.17 (1 H, s, 4b-H), 3.40 (3 H, s, NMe), and 1.33 (3 H, s, CMe) (Found: C, 69.15; H, 5.4; N, 3.85. $C_{21}H_{19}NO_5$ requires C, 69.05; H, 5.25; N, 3.85%).

(b) *Using sodium borohydride in the presence of boron trifluoride etherate complex.* To a solution of the lactam (4a) (1 g) in anhydrous tetrahydrofuran (50 ml), sodium borohydride (250 mg) and then boron trifluoride–ether (700 mg) were added dropwise with stirring, and the reaction mixture was left to stand at room temperature for 30 min. The solvent was removed at room temperature, water was added to the residue, and the resulting mixture was extracted with chloroform. The extract was washed with water, dried, and evaporated to give a solid, which was recrystallised from methanol to afford the *cis*-lactam (4c) (650 mg, 70%) as crystals, m.p. 295—296 °C, identical (i.r., and R_F values) with the sample obtained in (a).

cis-4b,10b-*Dihydro*-5,10b-*dimethyl*-2,3;7,8-*bis*(*methylenedioxy*)*benzo*[c]*phenanthridin*-6(5H)-*one* (5a).—A solution of the lactam (4c) (200 mg) and dichlorodicyanobenzoquinone (220 mg) in anhydrous chloroform (6 ml) was stirred at 4 °C for 24 h. The solution, diluted with chloroform, was washed with 10% sodium hydroxide and water, dried, and evaporated. Purification of the residue by preparative t.l.c. afforded the starting lactam (4c) (85 mg) and 11,12-dehydrolactam (5a) (56 mg, 28%) as crystals, m.p. 283—284 °C (from methanol); $\nu_{max.}$ 1 655 (NCO) cm^{-1}, δ 6.68 and 6.58 (2 H, AB q, *J* 8.5 Hz, 9- and 10-H), 6.62 and 6.50 (each 1 H, s, 1- and 4-H), 6.40 and 6.08 (2 H, AB q, *J* 10 Hz, 11- and 12-H), 6.02 (2 H, m, OCH_2O), 5.85 (2 H, s, OCH_2O), 4.37 (1 H, s, 4b-H), 3.37 (3 H, s, NMe), and 1.47 (3 H, s, CMe); *m/e* 363 (M^+) (Found: C, 68.15; H, 4.95; N, 3.75. $C_{21}H_{17}NO_5 \cdot \frac{1}{3}H_2O$ requires C, 68.3; H, 4.8; N, 3.8%).

Oxidation of the 11,12-*Dehydrolactam* (5a) *with Performic Acid.*—To a solution of the lactam (5a) (100 mg) in 85% formic acid (5 ml), performic acid [prepared from 85% formic acid (5 ml) and 30% hydrogen peroxide (0.6 ml)] was added dropwise at room temperature with stirring. After stirring for 1 h, 10% sodium thiosulphate solution was added and the solution was reduced to small volume. To the residue, methanol (10 ml) and 20% sodium hydroxide was added to make the solution alkaline. After refluxing for 2 h and evaporating off methanol, the resulting residue was extracted with chloroform. The extract was washed with water, dried, and evaporated to give the crude product. Purification by preparative t.l.c. afforded 4bα,10b,11,12-*tetrahydro*-11α,12α-*dihydroxy*-5,10bα-*dimethyl*-2,3;7,8-*bis*(*methylenedioxy*)*benzo*[c]*phenanthridin*-6(5H)-*one* (6a) (44 mg, 40%) as crystals, m.p. 282—283 °C (from methanol); $\nu_{max.}$ 3 600—3 200 (OH) and 1 640 (NCO) cm^{-1} (Found: C, 62.55; H, 4.85; N, 3.5. $C_{21}H_{19}NO_7 \cdot \frac{1}{3}H_2O$ requires C, 62.5; H, 4.85; N, 3.45%), and 4bα,10b,11,12-*tetrahydro*-11α,12β-*dihydroxy*-5,10bα-*dimethyl*-2,3;7,8-*bis*(*methylenedioxy*)*benzo*[c]*phenanthridin*-6(5H)-*one* (6b) (22 mg, 20%) as crystals, m.p. 274.5—275.5 °C (from methanol); $\nu_{max.}$ (Nujol) 3 550 and 3 350 (OH), and 1 645 (NCO) cm^{-1} (Found: C, 60.9; H, 5.15; N, 3.15. $C_{21}H_{19}NO_7 \cdot H_2O$ requires C, 60.7; H, 5.1; N, 3.35%).

4bα,5,6,10b,11,12-*Hexahydro*-5,10bα-*dimethyl*-2,3;7,8-*bis*(*methylenedioxy*)*benzo*[c]*phenanthridine*-11α,12α-*diol* (7a).—Reduction of the lactam (6a) (30 mg) with lithium aluminium hydride in the usual way afforded the 11α,12α-glycolamine (7a) (25 mg, 83%) as a yellow oil, $\nu_{max.}$ 3 550 and 3 400 (OH) cm^{-1}; δ 6.98 and 6.72 (each 1 H, s, 1- and 4-H), 6.85 and 6.82 (2 H, AB q, *J* 8 Hz, 9- and 10 H), 5.92 (4 H, s-like, 2 × OCH_2O), 4.72 (1 H, d, *J* 5 Hz, 12-H), 4.44 (1 H, d, *J* 5 Hz, 11-H), 3.83 and 3.43 (2 H, AB q, *J* 16 Hz, 6-H_2), 3.48 (1 H, s, 4b-H), 2.40 (3 H, s, NMe), and 1.33 (3 H, s, CMe) (Found: M^+, 383.136. $C_{21}H_{21}NO_6$ requires *M*, 383.137).

Treatment of the amine (7a) (20 mg) in acetone (2 ml) containing two drops of 70% perchloric acid gave the acetonide (20 mg, 93%), m.p. 210—212 °C (from ether–methanol); the i.r. spectrum showed no hydroxy-group; δ 7.04 and 6.78 (each 1 H, s, 1- and 4-H), 6.99 and 6.77 (2 H, AB q, *J* 8 Hz, 9- and 10-H), 5.97 (4 H, s-like, 2 × OCH_2O), 5.19 (1 H, d, *J* 8 Hz, 12-H), 4.77 (1 H, d, *J* 8 Hz, 11-H), 4.06 and 3.41 (2 H, AB q, *J* 16 Hz, 6-H_2), 3.13 (1 H, s, 4b-H), 2.07 (3 H, s, NMe), 1.49 and 1.38 (each 3 H, s, CMe_2), and 1.00 (3 H, s, 10b-Me) (Found: M^+, 423.168. $C_{24}H_{25}NO_6$ requires *M*, 423.168).

4bα,5,6,10b,11,12-*Hexahydro*-5,10bα-*dimethyl*-2,3;7,8-*bis*(*methylenedioxy*)*benzo*[c]*phenanthridine*-11α,12β-*diol* (7b).—Treated as for (7a), the lactam (6b) was reduced to give the corresponding 11α,12β-glycolamine (7b) (78%) as crystals, m.p. 218—221 °C (decomp.) (from methanol), $\nu_{max.}$ (Nujol) 3 300 (OH) cm^{-1}; δ 7.04 and 6.71 (each 1 H, s, 1- and 4-H), 6.97 and 6.77 (2 H, AB q, *J* 8 Hz, 9- and 10-H), 5.97 (4 H, s, 2 × OCH_2O), 4.36 (1 H, d, *J* 7.5 Hz, 12-H), 4.32 (1 H, d, *J* 7.5 Hz, 11-H), 4.04 and 3.44 (2 H, AB q, *J* 15 Hz, 6-H_2), 3.11 (1 H, s, 4b-H), 2.08 (3 H, s, NMe), and 1.07 (3 H, s, CMe) (Found: M^+, 383.136. $C_{21}H_{21}NO_6$ requires *M*, 383.137). This amine (7b) did not form an acetonide.

(±)-11-*Epicorynoline* (7c).—A solution of either *cis*-glycol (7a) (20 mg) or *trans*-glycol (7b) (20 mg) in 10% hydrochloric acid (5 ml) containing one drop of 70% perchloric acid was hydrogenated over 40% palladium–charcoal (15 mg) under a hydrogen atmosphere (5 atm) at 50 °C for 24 h. The catalyst was filtered off and the filtrate was neutralised by adding potassium carbonate and then extracted with chloroform. The extract was washed with water, dried, and evaporated to give a glassy solid. Purification by preparative t.l.c. on silica gel in each case afforded a homogeneous amine (7c) (10 mg, 53%) as crystals, m.p. 182.5—183 °C (from methanol) (lit.,[12] 183—184 °C), identical (i.r., and n.m.r. spectra) with natural 11-epicorynoline [12] (Found: M^+, 367.142. $C_{12}H_{21}NO_5$ requires *M*, 367.142).

Deoxycorynoline (5b).—By the procedure given for (7a and b), reduction of the lactam (5a) (56 mg) with an excess of lithium aluminium hydride gave the amine (5b) (30 mg, 56%) as crystals, m.p. 144.5—145 °C (from ether–methanol) (lit.[11] 157—158 °C), identical (i.r. spectra and R_F values) with authentic deoxycorynoline which had been prepared from corynoline by Takao *et al.*[11] (Found: M^+, 349.132. $C_{21}H_{19}NO_4$ requires *M*, 349.131).

(±)-12-*Hydroxycorynoline* (7d).—By the procedure given for (6a and b), oxidation of the amine (5b) (30 mg) with performic acid and purification of the crude product by preparative t.l.c. on silica gel gave the glycol (7d) (33 mg, 91%) as crystals, m.p. 238—240 °C (from methanol–chloroform) (lit.,[12a] 245—246.5 °C), identical (i.r., n.m.r., and mass spectra, and R_F values) with natural 12-hydroxycorynoline [13] (Found: M^+, 383.135. $C_{21}N_{21}NO_6$ requires *M*, 383.137).

Hydrogenolysis of (±)-12-*Hydroxycorynoline* (7d).—By the procedure given for (7c), hydrogenolysis of (±)-12-hydroxycorynoline (7d) (30 mg) over 40% palladium–charcoal and purification of the crude product by preparative t.l.c. on silica gel afforded two products. The first product with high R_F is (±)-corynoline (7e) (10 mg, 35%) as crystals, m.p. 218—220 °C (from ether–methanol) (lit.,[14] 216—217 °C), identical (i.r. and mass spectra, and R_F values) with natural corynoline [14] (Found: M^+, 367.141. $C_{21}H_{21}NO_5$ requires M, 367.142). The second product with lower R_F is 4bα,5,6,10b,11,12-*hexahydro*-5,10bα-*dimethyl*-2,3;7,8-*bis*(*methylenedioxy*)*benzo*[c]*phenanthridine*-11β,12β-*diol* (7f) (5 mg, 17%) as crystals, m.p. 219—221 °C (from methanol) (lit.,[12a] 246.5—247.5 °C); $\nu_{max.}$ 3 500 (OH) cm^{-1}; δ 7.22 and 6.61 (each 1 H, s, 1- and 4-H), 6.92 and 6.80 (2 H, AB q, J 9 Hz, 9- and 10-H), 5.97 (4 H, s-like, 2 × OCH_2O), 4.59 (1 H, d, J 5 Hz, 12-H), 4.07 and 3.47 (2 H, AB q, J 15 Hz, 6-H_2), 3.90 (1 H, dd, J 5 and 2 Hz, 11-H), 3.28 (1 H, d, J 2 Hz, 4b-H), 2.18 (3 H, s, NMe), and 1.18 (3 H, s, CMe) (Found: C, 65.4; H, 5.45; N, 3.55%; M^+, 383.138. $C_{21}H_{21}NO_6$ requires C, 65.8; H, 5.5; N, 3.7%; M, 383.137).

12-*Acetoxy*-4bα,5,6,10b,11,12-*hexahydro*-5,10bα-*dimethyl*-2,3;7,8-bis(*methylenedioxy*)*benzo*[c]*phenanthridin*-11β-*ol* (7g).—To a solution of the amine (5b) (30 mg) in acetic acid (2 ml), peracetic acid (2 ml) [prepared from acetic anhydride (22 g) and 30% hydrogen peroxide (5 g)] was added dropwise at room temperature with stirring. After standing for 1 h, aqueous potassium carbonate solution was added and the mixture was extracted with chloroform. The extract was washed with water, dried, and evaporated to give a residue, which was purified by preparative t.l.c. on silica gel to afford (7g) as a yellow oil (27 mg, 73%); $\nu_{max.}$ 1 740 (OAc) cm^{-1}; δ 7.00 and 6.83 (2 H, AB q, J 8 Hz, 9- and 10-H), 6.93 and 6.73 (each 1 H, s, 1- and 4-H), 6.23 (1 H, s-like, 12-H), 6.07 (4 H, s-like, 2 × OCH_2O), 4.07 and 3.53 (2 H, AB q, J 16 Hz, 6-H_2), 3.88 (1 H, s-like, 11-H), 3.37 (1 H, s-like, 4b-H), 2.20 (3 H, s, NMe), 2.13 (3 H, s, COMe), and 1.33 (3 H, s, CMe); this thus established the presence of an acetoxy-group at the 12-position by comparison with the n.m.r. spectra of known related 12-acetoxy-compounds [6,12a,14,17] (Found: M^+, 425.147. $C_{23}H_{23}NO_7$ requires M, 425.148).

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