Photocyclisation of Enamides. Part 21.[1] Synthesis of Benzo[*a*]quinolizines Related to the Alkaloids Emetine[2] and Flavopereirine[2]

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Acylation of 3,4-dihydro-1-methylisoquinoline with substituted acryloyl chlorides followed by irradiation of the resulting enamides provides a useful synthetic route to the benzo[*a*]quinolizines (**4**), (**8a—d**), and (**9a**) and (**9b**), and has been applied to a new total synthesis of flavopereirine (**14**).

Cyclic imines such as 3,4-dihydro-1-methylisoquinoline (**1**) and harmalane (**10**) have been successfully employed as the starting compounds for the syntheses of some alkaloids and related heterocyclic compounds *via* enamide cyclisation; for example, the photocyclisation of enamides of the *N*-aroylenamine type has been used for the preparation of protoberberine[3] and indole alkaloids.[4] We have now investigated the photocyclisation of enamides of the *N*-acryloylenamine type which can be readily prepared by the acylation of the cyclic imines with acryloyl chlorides, and have thus established new routes to benzo[*a*]- and indolo[2,3-*a*]-quinolizines which have been used in the synthesis of two alkaloids, emetine and flavopereirine.

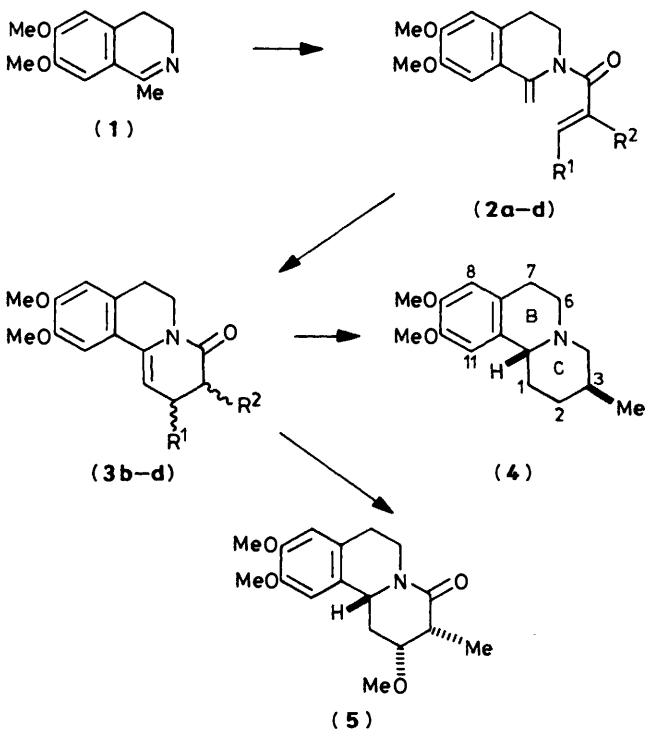
Synthesis of Benzo[a]*quinolizines.*—Benzo[*a*]quinolizine is an important basic structure which commonly appears in natural alkaloids such as emetine,[5] a representative alkaloid of the Ipecacuanha species which has potent clinical activity. Kametani *et al.*[6] investigated the irradiation of the enamide (**2a**) in the hope of finding a new route for the preparation of benzo[*a*]quinolizines; however, the desired photocyclisation did not take place. Later[7] they succeeded in synthesising emetine by a different route, also using the 3,4-dihydro-1-methylisoquinoline (**1**).

We have already reported[1] that the photocyclisation of enamides of the α,β-unsaturated acylanilide type is affected by the presence of a substituent at the α-position in the acyl moiety. Taking into account this substituent effect and the fact that Ipecac alkaloids such as emetine have the 3-substituted benzo[*a*]quinolizine structure as a common skeleton, we first investigated the photocyclisation of the enamide (**2b**) of the 2-methacryloylenamine type. Treatment of the 3,4-dihydro-1-methylisoquinoline (**1**) with 2-methacryloyl chloride in the presence of triethylamine in benzene solution afforded the unstable enamide (**2b**) quantitatively ($\nu_{max.}$ 1 610 cm^{-1}).

Irradiation of the crude enamide (**2b**), in benzene solution, with a low-pressure mercury lamp at room temperature for several hours afforded the unstable product (**3b**). The structure of the product (**3b**) was deduced from its n.m.r. spectrum which showed a signal at δ 0.92 (d, *J* 6 Hz, 3-Me) and an olefinic proton signal at δ 5.08 (br t); it was further confirmed by conversion into the known[8] hydrobenzo[*a*]quinolizine (**4**) [31% yield from the 1-methylisoquinoline (**1**)] *via* successive reductions with lithium aluminium hydride and sodium borohydride. Fujii *et al.*[8] have already obtained this hydrobenzo[*a*]quinolizine (**4**) as a mixture of stereoisomers (7:1) with respect to the orientation (equatorial or axial) of the 3-methyl group. The n.m.r. spectrum ($CDCl_3$) of the product (**4**) showed signals at δ 0.91 (d, *J* 6 Hz, 3-Me) and 3.01 (br d, *J* 12 Hz, 11b-H); however, no signal was observed in the region around δ 3.8 in deuteriobenzene, thus suggesting[9,10] that this homogeneous amine (**4**) has the B/C-*trans* structure with the 3-methyl group equatorial, as shown in Scheme 1.

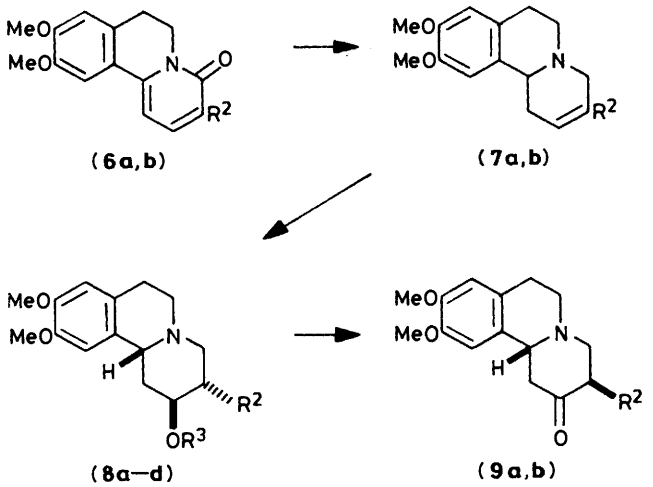
We then investigated the photocyclisation of enamides of the 2,3-disubstituted acryloylenamine type in the hope of preparing 2- or 3-functionalised hydrobenzo[*a*]quinolizines because 3-ethyl-2-oxobenzo[*a*]quinolizines are key intermediates for the synthesis of ipecac alkaloids.[5] Acylation of the 3,4-dihydro-1-methylisoquinoline (**1**) with 3-methoxy-2-methyl-[11] and 2-ethyl-3-methoxy-acryloyl chlorides afforded the unstable enamides (**2c**) and (**2d**) in good yields ($\nu_{max.}$ 1 655 cm^{-1}); these were irradiated without further purification to afford the photocyclised lactams (**3c**) and (**3d**) (62 and 54% respectively). From comparisons of the coupling constants between 2- and 3-H [5.5 Hz in the photocyclised lactam (**3c**) and 6 Hz in the saturated lactam (**5**), readily prepared from (**3c**)] the relative configuration at the 2- and 3-positions was deduced to be *cis* in the lactams (**3c**), (**3d**), and (**5**).

When the photocyclised lactams (**3c**) and (**3d**) were treated with 10% hydrochloric acid, the unsaturated lactams (**6a**) and (**6b**)[12] were obtained [57 and 44% from (**1**)] as the result of elimination of the methanol moiety. Reduction of the



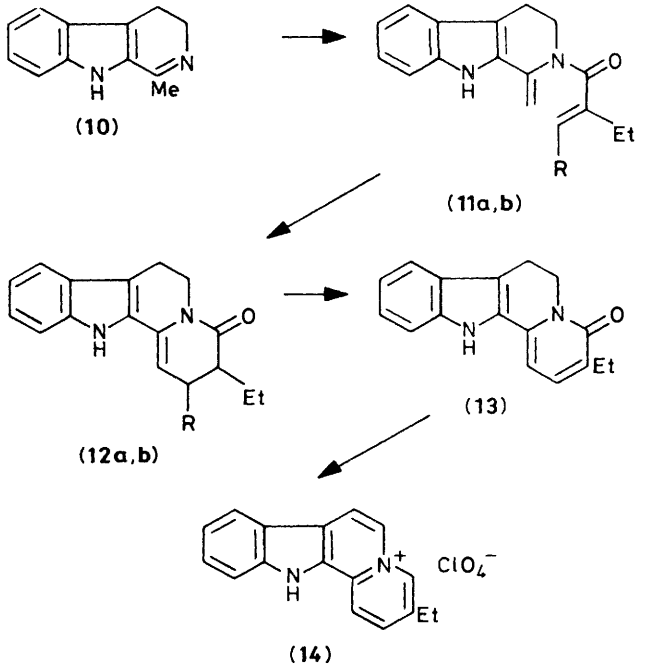
a; R^1 = Me, R^2 = H
b; R^1 = H, R^2 = Me
c; R^1 = OMe, R^2 = Me
d; R^1 = OMe, R^2 = Et

Scheme 1.



a; R^2 = Me, R^3 = H
b; R^2 = Et, R^3 = H
c; R^2 = Me, R^3 = Ac
d; R^2 = Et, R^3 = Ac

Scheme 2.



a; R = H
b; R = OMe

Scheme 3.

unsaturated lactams (**6a**) and (**6b**) with lithium aluminium hydride followed by sodium borohydride afforded the unsaturated amines (**7a**) and (**7b**) [94 and 98% respectively (Scheme 2)]; their structures were deduced from their n.m.r. spectra which showed signals at δ 5.50 [m, 2-H in (**7a**)], 5.57 [m, 2-H in (**7b**)], and 1.68 [br s, 3-Me in (**7a**)]. The amine (**7a**) was then converted into the saturated amine (**4**) by catalytic hydrogenation over platinum dioxide.

Hydroboration of the unsaturated amines (**7a**) and (**7b**) with sodium borohydride in the presence of an excess of boron trifluoride–ether in diglyme solution, followed by treatment with 20% hydrogen peroxide, gave the corresponding alcohols (**8a**) and (**8b**) (53 and 42% respectively), which were characterised as their acetates (**8c**) and (**8d**). The n.m.r. spectra were very similar except for the peaks due to the 3-substituents; the acetate (**8c**) showed peaks at δ 4.80 (q, *J* 3.5 Hz, 2-H) and 3.58 (br d, *J* 9 Hz, 11b-H), which suggest that it has a B/C-*trans* ring structure with the 2-acetoxy and 3-methyl groups in a *trans*-diaxial configuration.[9,10] The above hydroboration of the unsaturated amines (**7a**) and (**7b**), which afforded the homogeneous alcohols (**8a**) and (**8b**), would then be explained as follows: the amines (**7a**) and (**7b**) would initially form the unsaturated amine borane,[13] then the excess of diborane would attack the olefinic double bond at the 2-position from the less hindered β-side to form the corresponding 2-boranes, which would finally be oxidised to give the respective 2-alcohols (**8a**) and (**8b**) homogeneously.

Pfitzner–Moffatt oxidation[14] of the alcohols (**8a**) and (**8b**) afforded the known ketones (**9a**)[15] and (**9b**)[16] which have 3-alkyl groups in a stable equatorial configuration, formed as a result of epimerisation at the 3-position. Since the ketone (**9b**) is an important intermediate for the synthesis of a number of Ipecac alkaloids,[5] the above process provides a new and convenient route to benzo[*a*]quinolizine alkaloids.

Synthesis of Flavopereirine.— Using the synthetic route described above, we carried out a new synthesis of flavopereirine, one of the simplest alkaloids of Strychnos plants.

Harmalane (**10**) was acylated with ethacryloyl chloride to yield the unstable enamide (**11a**) (Scheme 3) which was then irradiated without purification with a high-pressure mercury lamp at room temperature. The photocyclisation proceeded very slowly taking more than 20 h to afford only a poor yield (7.5%) of the photocyclised lactam (**12a**). However, the methoxy-substituted enamide (**11b**), prepared from harmalane (**10**) and 2-ethyl-3-methoxyacryloyl chloride, underwent smooth photocyclisation to afford the unstable lactam (**12b**), which was then treated with 10% hydrochloric acid at room temperature for a few minutes to afford the stable dehydrolactam (**13**) [35% from harmalane (**10**)]. Lithium aluminium hydride reduction of the lactam (**13**) followed by dehydrogenation with palladium on charcoal at 280—300 °C without solvent afforded the fully aromatic compound, isolated as its perchlorate (**14**), which was shown to be identical with natural flavopereirine perchlorate[17] by direct comparison of their i.r. spectra.

Experimental

^{1}H N.m.r. spectra were measured with Varian XL-200 and JEOL PMX-60 instruments for solutions in deuteriochloroform unless otherwise stated (tetramethylsilane as internal reference) and i.r. spectra for solutions in chloroform with a Hitachi 215 spectrophotometer. M.p.s were determined with a Kofler-type hot-stage apparatus. Extracts from the reaction mixtures were dried over anhydrous sodium sulphate. All the photochemical reactions were carried out by irradiation at room temperature either with a low-pressure (120-W) mercury lamp (Eikosha PIL-120) or a high-pressure (300-W) mercury lamp (Eikosha PIH-300). Ether refers to diethyl ether.

(3β,11bβ)-1,3,4,6,7,11b-*Hexahydro*-9,10-*dimethoxy*-3-*methyl*-2H-*benzo*[a]*quinolizine* (**4**).—To a solution of 3,4-dihydro-6,7-dimethoxy-1-methylisoquinoline (**1**) (250 mg) and triethylamine (250 mg) in anhydrous benzene (50 ml), a solution of methacryloyl chloride (125 mg) in anhydrous benzene (10 ml) was added dropwise with stirring. After being refluxed for 1 h, the mixture was cooled and filtered to remove triethylamine hydrochloride. Anhydrous benzene (40 ml) was added to the

filtrate and then the solution was irradiated in a quartz vessel for 5 h. After the solvent had been evaporated, the unstable photocyclised product (**3b**) was reduced with lithium aluminium hydride in ether–tetrahydrofuran in the usual manner to give the unstable enamine, which was then reduced with sodium borohydride (200 mg) in methanol (20 ml) to give the amine (**4**) (100 mg, 31%) as an oil, δ (200 MHz) 6.70 (1 H, s, 11-H), 6.58 (1 H, s, 8-H), 3.84 (6 H, s, OMe × 2), 3.01 (1 H, br d, *J* 12 Hz, 11b-H), 2.27 (1 H, dq, *J* 13 and 3 Hz, 1-H_{eq}), 1.97 (1 H, t, *J* 11 Hz, 4-H_{ax}), 1.47 (1 H, qd, *J* 13 and 4 Hz, 1-H_{ax}), 1.17 (1 H, td, *J*13 and 4 Hz, 2-H_{ax}), and 0.91 (3 H, d, *J* 6 Hz, CMe). Recrystallisation of the perchlorate from ethanol afforded *needles*, m.p. 219—220 °C (Found: C, 53.25; H, 6.65; N, 3.55. $C_{16}H_{24}ClNO_6$ requires C, 53.1; H, 6.7; N, 3.85%).

(2α,3α)-2,3,6,7-*Tetrahydro*-2,9,10-*trimethoxy*-3-*methyl*-4H-*benzo*[a]*quinolizin*-4-*one* (**3c**).—By the procedure given for compound (**4**), the unstable enamide (**2c**) was carefully prepared from the isoquinoline (**1**) (2.45 g) and 3-methoxy-2-methacryloyl chloride (1.83 g), and then irradiated for 20 h to give the lactam (**3c**) (2.24 g, 62%) as *crystals* (from methanol), m.p. 150—153 °C, $\nu_{max.}$ 1 660 cm^{-1} (NCO); δ (200 MHz) 7.12 (1 H, s, 11-H), 6.66 (1 H, s, 8-H), 5.81 (1 H, d, *J* 5.5 Hz, 1-H), 4.25 (1 H, t, *J* 5.5 Hz, 2-H), 3.94 and 3.92 (each 3 H, s, OMe × 2), 3.36 (3 H, s, 2-OMe), and 1.34 (3 H, d, *J* 7 Hz, CMe) (Found: C, 67.3; H, 6.95; N, 4.6. $C_{17}H_{21}NO_4$ requires C, 67.3; H, 7.0; N, 4.6%).

(2α,3α,11bβ)-1,2,3,6,7,11b-*Hexahydro*-2,9,10-*trimethoxy*-3-*methyl*-4H-*benzo*[a]*quinolizin*-4-*one* (**5**).—A solution of the lactam (**3c**) (200 mg) in methanol (50 ml) was hydrogenated over platinum dioxide (30 mg) under hydrogen (1 atm) at room temperature for 5 h. Removal of the catalyst by filtration and evaporation of the solvent left a solid which was recrystallised from methanol–ether to afford the dihydrolactam (**5**) (170 mg, 85%) as *crystals*, m.p. 164—166 °C, $\nu_{max.}$ 1 625 cm^{-1} (NCO); δ (200 MHz) 6.70 and 6.64 (each 1 H, s, 8- and 11-H), 4.63 (1 H, dd, *J* 11 and 5 Hz, 11b-H), 3.88 (6 H, s, OMe × 2), 3.78 (1 H, ddd, *J* 10, 6, and 4 Hz, 2-H), 3.39 (3 H, s, 2-OMe), 2.99 (1 H, br quint., *J* 7 Hz, 3-H), 2.61 (1 H, dt, *J* 11 and 4 Hz, 1-H_{eq}), 1.87 (1 H, td, *J* 11 and 10 Hz, 1-H_{ax}), and 1.20 (3 H, d, *J* 7 Hz, CMe) (Found: C, 66.7; H, 7.35; N, 4.65. $C_{17}H_{23}NO_4$ requires C, 66.85; H, 7.6; N, 4.6%).

6,7-*Dihydro*-9,10-*dimethoxy*-3-*methyl*-4H-*benzo*[a]*quinolizin*-4-*one* (**6a**).—A benzene solution of the enamide (**2c**), prepared from the isoquinoline (**1**) (1.02 g) and 3-methoxy-2-methacryloyl chloride (0.67 g), was irradiated for 20 h and the solution was washed with 10% hydrochloric acid and water, dried, and evaporated to give a solid which was recrystallised from ether–ethanol to afford the *lactam* (**6a**) (770 mg, 57%), m.p. 177—178 °C, $\nu_{max.}$ 1 640 cm^{-1} (NCO); δ 7.23 (1 H, d, *J* 7 Hz, 1-H), 7.15 (1 H, s, 11-H), 6.73 (1 H, s, 8-H), 6.48 (1 H, d, *J* 7 Hz, 2-H), 3.88 (6 H, s, OMe × 2), and 2.18 (3 H, s, CMe) (Found: C, 70.85; H, 6.3; N, 5.2. $C_{16}H_{17}NO_3$ requires C, 70.85; H, 6.3; N, 5.15%).

1,6,7,11b-*Tetrahydro*-9,10-*dimethoxy*-3-*methyl*-4H-*benzo*[a]-*quinolizine* (**7a**).—To a solution of the lactam (**6a**) (710 mg) in anhydrous ether–tetrahydrofuran (1:1; 80 ml), lithium aluminium hydride (500 mg) was added in small portions under cooling. The mixture was refluxed for 1 h. Treatment in the usual way gave the corresponding amine which, without purification, was reduced with sodium borohydride (500 mg) in methanol (100 ml) to afford the amine (**7a**) (640 mg, 94%) as a yellow oil, $\nu_{max.}$ 1 610 cm^{-1} (C=C), δ 6.60 and 6.53 (each 1 H, s, 8- and 11-H), 5.50 (1 H, m, 2-H), 3.80 (6 H, s, OMe × 2), and 1.68 (3 H, br s, CMe). The oil was unstable and the colour changed to reddish brown on standing.

(2β,3α,11bβ)-2-*Acetoxy*-1,3,4,6,7,11b-*hexahydro*-9,10-*dimethoxy*-3-*methyl*-2H-*benzo*[a]*quinolizine* (**8c**).—To a solution of the amine (**7a**) (640 mg) and sodium borohydride (225 mg) in diglyme (4 ml), a solution of 47% boron trifluoride–ether (1.5 g) in diglyme (2.5 ml) was added at 20 °C dropwise under a nitrogen stream. After being stirred at room temperature for 1.5 h, the mixture was treated successively with water (1 ml) and concentrated hydrochloric acid (5 ml) to decompose the excess of the reagent, and 30% sodium hydroxide was then added to make the solution alkaline, followed by 30% hydrogen peroxide (2 ml) dropwise. After the mixture had been heated at 100 °C for 2 h, water (200 ml) was added and the diglyme was removed by azeotropic distillation. The resulting residue was extracted with chloroform, and the extract washed with aqueous sodium hydrogen carbonate, dried, and evaporated. The residue was chromatographed on silica gel with chloroform–methanol (95:5) as eluant to afford the desired hydroxyamine (**8a**) (360 mg, 53%) as an oil; this was then subjected to acetylation to give the acetoxyamine (**8c**) as a yellow oil, $\nu_{max.}$ 1 710 cm^{-1} (Ac); δ ($CDCl_3$; 200 MHz) 6.70 (1 H, s, 11-H), 6.60 (1 H, s, 8-H), 4.80 (1 H, q, *J* 3.5 Hz, 2-H), 3.88 and 3.86 (each 3 H, s, OMe × 2), 3.58 (1 H, br d, *J* 9 Hz, 11b-H), 2.13 (3 H, s, Ac), and 1.10 (3 H, d, *J* 7 Hz, CMe); δ(C_6D_6) 6.72 (1 H, s, 11-H), 6.44 (1 H, s, 8-H), 4.98 (1 H, q, *J* 3.5 Hz, 11b-H), 3.46 and 3.44 (each 3 H, s, OMe × 2), 2.74 (1 H, dd, *J* 11 and 4 Hz, 4-H_{eq}), 2.57 (1 H, dd, *J* 11 and 4 Hz, 4-H_{ax}), 2.28 (1 H, dt, *J* 14 and 3.5 Hz, 1-H_{eq}), 1.98 (1 H, ddd, *J* 14, 11, and 3.5 Hz, 1-H_{ax}), 1.95 (1 H, m, 3-H), 1.76 (3 H, s, Ac), and 1.08 (3 H, d, *J* 7 Hz, CMe). Recrystallisation of the perchlorate from ethanol afforded *needles*, m.p. 186—187 °C (Found: C, 51.5; H, 6.15; N, 3.2. $C_{18}H_{26}ClNO_8$ requires C, 51.5; H, 6.15; N, 3.35%).

(3β,11bβ)-1,3,4,6,7,11b-*Hexahydro*-9,10-*dimethoxy*-3-*methyl*-2H-*benzo*[a]*quinolizin*-2-*one* (**9a**).—The hydroxyamine (**8a**) (360 mg) was dissolved in dimethyl sulphoxide (DMSO) (3 ml) and benzene (3 ml) containing dicyclohexylcarbodi-imide (DCC) (555 mg) and pyridine (0.15 ml). Trifluoroacetic acid (0.1 ml) was added to the above solution and the mixture was then allowed to stand at room temperature overnight. Methanol and water (3:2; 10 ml) was added to stop the reaction and the resulting precipitate was filtered off. The filtrate was made alkaline by adding concentrated ammonium hydroxide, and extracted with chloroform. The extract was dried and evaporated to give a solid which was recrystallised from ether to afford the ketone (**9a**) (226 mg, 63%) as needles, m.p. 138—140 °C (lit.,[15] 129—130 °C), $\nu_{max.}$ 1 710 cm^{-1} (CO); δ 6.63 and 6.53 (each 1 H, s, 8- and 11-H), 3.81 (6 H, s, OMe × 2), and 1.08 (3 H, d, *J* 6 Hz, CMe) (Found: C, 69.65; H, 7.5; N, 5.0. Calc. for $C_{16}H_{21}NO_3$: C, 69.8; H, 7.7; N, 5.1%).

Catalytic Hydrogenation of 1,6,7,11b-*Tetrahydro*-9,10-*dimethoxy*-3-*methyl*-4H-*benzo*[*a*]*quinolizine* (**7a**).—A solution of the amine (**7a**) (110 mg) in methanol (10 ml) was hydrogenated over platinum dioxide (20 mg) under hydrogen (1 atm) at room temperature for 3 h. Removal of the catalyst by filtration and evaporation of the solvent gave an oil which was purified by preparative t.l.c. to afford the amine (**4**), identical (t.l.c., i.r., and n.m.r. spectra) with the amine (**4**) prepared from compound (**3b**).

3-*Ethyl*-6,7-*dihydro*-9,10-*dimethoxy*-4H-*benzo*[a]*quinolizin*-4-*one* (**6b**).—By the procedure described for (**6a**), the enamide (**2d**) was prepared from the isoquinoline (**1**) (512 mg) and 2-ethyl-3-methoxyacryloyl chloride (370 mg) (b.p. 75—80 °C at 15 mmHg) (prepared from methyl 2-ethylacrylate in five steps in 17% yield by the method of G. Shaw[11]) and irradiated without further purification for 5 h. The irradiated solution was washed with 10% hydrochloric acid and water, dried, and

evaporated to give a solid which was recrystallised from ethanol–ether to afford the *lactam* (**6b**) (310 mg, 44%), m.p. 128—129 °C, as pale yellow crystals, $\nu_{max.}$ 1 640 cm^{-1} (NCO); δ 7.15 (1 H, d, *J* 8 Hz, 1-H), 7.10 (1 H, s, 11-H), 6.68 (1 H, s, 8-H), 6.47 (1 H, d, *J* 8 Hz, 2-H), 2.62 (2 H, q, *J* 8 Hz, CH_2CH_3), and 1.22 (3 H, t, *J* 8 Hz, CH_2CH_3) (Found: C, 71.6; H, 6.65; N, 4.85. $C_{17}H_{19}NO_3$ requires C, 71.55; H, 6.7; N, 4.9%).

3-*Ethyl*-1,6,7,11b-*tetrahydro*-9,10-*dimethoxy*-4H-*benzo*[a]-*quinolizine* (**7b**).—By the procedure described for (**7a**), successive reductions of the lactam (**6b**) (310 mg) with lithium aluminium hydride (150 mg) and sodium borohydride (150 mg) afforded the amine (**7b**) (290 mg, 98%), as a yellow oil, $\nu_{max.}$ 1 615 cm^{-1} (C=C); δ 6.67 and 6.60 (each 1 H, s, 8- and 11-H), 5.57 (1 H, m, 2-H), 3.87 (6 H, s, OMe × 2), and 1.07 (3 H, t, *J* 7 Hz, CH_2CH_3). The oil was unstable and the colour changed to reddish brown on standing.

(2β,3α,11bβ)-2-*Acetoxy*-3-*ethyl*-1,3,4,6,7,11b-*hexahydro*-9,10-*dimethoxy*-2H-*benzo*[a]*quinolizine* (**8d**).—By the procedure described for compound (**8a**), hydroboration of the amine (**7b**) (1.3 g) followed by oxidation with 30% hydrogen peroxide gave the hydroxyamine (**8b**) (714 mg, 52%) which was acetylated with acetic anhydride and pyridine to give the acetoxyamine (**8d**) (640 mg, 79%) as *crystals*, m.p. 114—115 °C (from ether), $\nu_{max.}$ 1 720 cm^{-1} (Ac); δ (200 MHz, C_6D_6) 6.69 (1 H, s, 11-H), 6.43 (1 H, s, 8-H), 4.12 (1 H, q, *J* 3 Hz, 2-H), 3.63 (1 H, br d, *J* 11 Hz, 11b-H), 3.44 and 3.43 (each 3 H, s, OMe × 2), 2.72 (1 H, dd, *J* 12 and 3 Hz, 4-H_{eq}), 2.57 (1 H, dd, *J* 12 and 2 Hz, 4-H_{ax}), 2.30 (1 H, dt, *J* 14 and 3 Hz, 1-H_{eq}), 1.86 (1 H, ddd, *J* 14, 11, 3 Hz, 1-H_{ax}), 1.78 (3 H, s, Ac), 1.65 (2 H, m, CH_2CH_3), 1.44 (1 H, m, 3-H), and 0.90 (3 H, t, *J* 7 Hz, CH_2CH_3) (Found: C, 68.7; H, 8.2; N, 4.15. $C_{19}H_{27}NO_4$ requires C, 68.45; H, 8.15; N, 4.2%).

(3β,11bβ)-3-*Ethyl*-1,3.4,6.7,11b-*hexahydro*-9,10-*dimethoxy*-2H-*benzo*[a]*quinolizin*-2-*one* (**9b**).—By the procedure described for compound (**9a**), the hydroxyamine (**8b**) (360 mg) was subjected to Pfitzner–Moffatt oxidation to afford the ketone (**9b**) (247 mg, 69%), m.p. 107—109 °C (lit.,[16] 109—110 °C), as a pale yellow powder, $\nu_{max.}$ 1 710 cm^{-1} (CO); δ 6.63 and 6.58 (each 1 H, s, 8- and 11-H), and 0.93 (3 H, t, *J* 6 Hz, CH_2CH_3).

3-*Ethyl*-2,3,6,7-*tetrahydro*-4H-*indolo*[2,3-a]*quinolizin*-4(12H)-*one* (**12a**).—By the procedure described for compound (**3b**), the enamide (**11a**) was prepared from harmalane (3,4-dihydro-1-methyl-9*H*-pyrido[3,4-*b*]indole) (**10**) (552 mg) and 2-ethylacryloyl chloride (354 mg) and, without purification, was irradiated for 48 h. Evaporation of the solvent and preparative t.l.c. of the resulting residue afforded the lactam (**12a**) (60 mg, 7.5%) as an oil, $\nu_{max.}$ 3 480 (NH), 1 670 and 1 650 cm^{-1} (NCO and C=C–N); δ 8.30 (1 H, br s, NH), 5.47 (1 H, t-like, 1-H), 4.06 (2 H, q-like, 2-H), and 0.96 (3 H, t, *J* 8 Hz, CH_2CH_3). The oil was unstable and the colour changed to reddish brown on standing.

3-*Ethyl*-6,7-*dihydro*-4H-*indolo*[2,3-a]*quinolizin*-4(12H)-*one* (**13**).—By the procedure described for compound (**3b**), the enamide (**11b**) was prepared from harmalane (**10**) (3 g) and 2-ethyl-3-methoxyacryloyl chloride (2.2 g) and, without purification, irradiated for 20 h. The resulting solution was washed with 10% hydrochloric acid and water, and dried. The solvent was evaporated to give a solid which was recrystallised from methanol to afford the *lactam* (**13**) (1.15 g, 27%) as yellow crystals, m.p. 265 °C, $\nu_{max.}$ 1 650 (NCO), 1 595 and 1 570 cm^{-1} (C=C); δ 6.45 (1 H, d, *J* 8 Hz, 2-H), 4.37 (2 H, t, *J* 7 Hz, 6-H), 3.03 (2 H, t, *J* 7 Hz, 7-H), 2.57 (2 H, q, *J* 7 Hz, CH_2CH_3), and 1.17 (3 H, t, *J* 7 Hz, CH_2CH_3) (Found: C, 77.3; H, 6.35; N, 10.5. $C_{17}H_{16}N_2O$ requires C, 77.25; H, 6.1; N, 10.6%).

Flavopereirine Perchlorate (3-*Ethylindolo*[2,3-a]*quinolizin*-5(12H)-*ium Perchlorate*).—To a solution of the lactam (**13**) (200 mg) in anhydrous ether–tetrahydrofuran (5:3, 80 ml) lithium aluminium hydride (200 mg) was added in small portions under ice-cooling. After being refluxed for 8 h, the usual work-up afforded the corresponding amine which was, without purification, dissolved in methanol (5 ml) and saturated with anhydrous hydrogen chloride gas. To the resulting solution, 10% palladium on charcoal (400 mg) was added and then the solvent was evaporated to give a residue which was heated at 280—300 °C for 10 min. After it had been cooled, hot methanol containing a small amount of acetic acid was added and then the catalyst was filtered off. The filtrate was evaporated and the residue was dissolved in 10% sodium hydroxide solution and extracted with chloroform. The extract was washed with water and dried, and acetic acid was added until the yellow colour disappeared. The solution was evaporated and the resulting residue was purified by preparative t.l.c. on silica gel. To a solution of the major fraction in chloroform–methanol, 10% sodium perchlorate was added to afford the pure perchlorate (**14**) (20 mg, 8%), m.p. 301—305 °C (lit.,[17] 319—322 °C); it was identical (i.r. spectrum) with the natural flavopereirine perchlorate.

Acknowledgements

The authors thank the Ministry of Education, Science, and Culture (Japan) for a research grant and also Dr. H. Kaneko of Dainippon Pharm. Co., Research Institute for the gift of flavopereirine perchlorate.

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Received 3rd *January* 1984; *Paper* 4/005