Photocyclisation of Enamides. Part VII.[1] A New Synthesis of the Protoberberine Alkaloids [2]

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N-Acylation of the 3,4-dihydro-1-methylisoquinolines (Ia and b) occurred smoothly to afford the enamides (IIa—k), which underwent ready photocyclisation to give the berbin-8-ones (IVa—d) and (Va—m). Reduction of the berbinones (IVc) and (Vd), (Vh), and (Vj) gave (±)-xylopinine (VIb), (±)-tetrahydropalmatine (VIc), and (±)-sinactine (VId), respectively.

In the light of research on the photocyclisation of enamides,[1] which has been recognised as a useful route to nitrogen-containing heterocycles, we became interested in 1-alkyl-3,4-dihydroisoquinolines, which have a cyclic imine structure and are known [3] to undergo ready *N*-acylation to afford *N*-acyl-1-alkylidene-1,2,3,4-tetrahydroisoquinolines. These can be regarded as enamides capable of undergoing photocyclisation since they possess a 6π-electron hexatriene system. The photocyclisation reaction has already been applied to enamides of the carbamate type in syntheses of aporphine alkaloids, such as nuciferine and glaucine,[4] and very recently to enamides † from 3,4-dihydroisoquinolines in studies independent of ours. We report here further examples of ready photocyclisation of *N*-aroyl-1-methylene-1,2,3,4-tetrahydroisoquinolines to berbin-8-ones. The potential of this route to protoberberine alkaloids [5] was established

† While this manuscript was in preparation, Lenz [5] described the photochemistry of 2-aroyl-1-methylene-1,2,3,4-tetrahydroisoquinolines.

[1] Part VI, I. Ninomiya, T. Naito, H. Ishii, T. Ishida, M. Ueda, and K. Harada, *J.C.S. Perkin I*, 1975, 762.

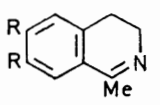
[2] Preliminary communications (*a*) I. Ninomiya and T. Naito, *J.C.S. Chem. Comm.*, 1973, 137; (*b*) I. Ninomiya, H. Takasugi, and T. Naito, *Heterocycles*, 1973, **1**, 17.

[3] I. Baxter and G. A. Swan, *J. Chem. Soc.*, 1965, 4014.

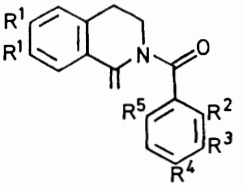
[4] (*a*) M. P. Cava, S. C. Havlicek, A. Lindert, and R. J. Spangler, *Tetrahedron Letters*, 1966, 2937; (*b*) M. P. Cava, M. J. Mitchell, S. C. Havlicek, A. Lindert, and R. J. Spangler, *J. Org. Chem.*, 1970, **35**, 175; (*c*) M. P. Cava, P. Stern, and K. Wakisaka, *Tetrahedron*, 1973, **29**, 2245; (*d*) N. C. Yang, A. Shani, and G. R. Lenz, *J. Amer. Chem. Soc.*, 1966, **88**, 5369.

[5] G. Lenz, *J. Org. Chem.*, 1974, **39**, 2839, 2846.

by total syntheses of (±)-xylopinine (VIb), (±)-tetrahydropalmatine (VIc), and (±)-sinactine (VId).

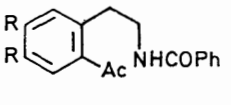


(I)
a; R = H
b; R = OMe



(II)

a; $R^1 = R^2 = R^3 = R^4 = R^5 = H$
b; $R^1 = OMe$, $R^2 = R^3 = R^4 = R^5 = H$
c; $R^1 = R^3 = R^4 = OMe$, $R^2 = R^5 = H$
d; $R^2 = OMe$, $R^1 = R^3 = R^4 = R^5 = H$
e; $R^1 = R^2 = OMe$, $R^3 = R^4 = R^5 = H$
f; $R^1 = R^2 = R^5 = OMe$, $R^3 = R^4 = H$
g; $R^2 = R^3 = R^5 = OMe$, $R^1 = R^4 = H$
h; $R^1 = R^2 = R^3 = R^5 = OMe$, $R^4 = H$
i; $R^1 = R^5 = OMe$, $R^2R^3 = OCH_2O$, $R^4 = H$
j; $R^1 = OMe$, $R^4 = NO_2$, $R^2 = R^3 = R^5 = H$
k; $R^1 = OMe$, $R^2 = CO_2Me$, $R^3 = R^4 = R^5 = H$



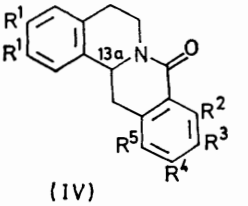
(III)
a; R = H
b; R = OMe

Treatment of the 3,4-dihydro-1-methylisoquinolines (Ia and b) with benzoyl chloride afforded products (IIa and b) in good yields, which showed i.r. absorption at 1 630—1 635 cm^{-1} (enamide) and n.m.r. doublets at δ 5.28—5.40 and 4.45—4.51 (each J 1.5—2 Hz, olefinic protons). These data confirmed that the products (IIa and b) were 2-benzoyl-1,2,3,4-tetrahydro-1-methyleneisoquinolines; they were found to be rather unstable to acid, readily giving the oxo-amides (IIIa and b) when stirred with dilute acid at room temperature.[3]

Irradiation of a methanolic solution of the enamides (IIa and b) with a low-pressure mercury lamp at room temperature for several hours yielded two types of products (IVa and b) and (Va and b), which were separated by chromatography on alumina. The products (IVa and b) exhibited i.r. absorption at 1 642—1 645 cm^{-1} (six-membered lactam carbonyl group) and n.m.r. signals at δ 4.70—5.15 (6- and 13a-H) and 8.18—8.20 (9-H). Further, one of these products (IVa) was reduced with lithium aluminium hydride to give the known berbine (VIa), identical with an authentic sample,[6] thus establishing the structure of (IVa). The products (Va and b) exhibited n.m.r. signals at δ 8.43—8.47 (m, 9-H) and at 6.75—7.28 (s, 13-H), but lacked an olefinic proton signal. These data suggest the didehydrolactam structures shown. Since reduction of the didehydrolactam (Va) with lithium aluminium hydride followed by sodium borohydride also afforded the berbine (VIa), this type of photocyclisation provides a novel synthetic route to the berbine system.

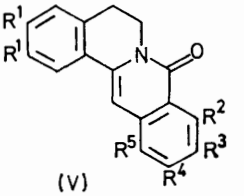
[6] A. L. Margni, D. Giacopello, and V. Deulofeu, *J. Chem. Soc.* (*C*), 1970, 2578.
[7] N. Nakanishi, *Japan J. Pharmacol.*, 1962, **12**, 208.

By applying the above method, we synthesised (±)-xylopinine,[2a] which is known to exhibit interesting biological activity,[7] in two steps from the enamide (IIc). Irradiation of the enamide (IIc), prepared from (Ib) and veratroyl chloride, afforded three products, one major (Vd) in 40% yield and two minor [(IVc) and (Vc)] each in 5% yield, which were separated by repeated chromatography on silica gel. Either successive



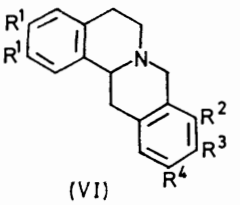
(IV)

a; $R^1 = R^2 = R^3 = R^4 = R^5 = H$
b; $R^1 = OMe$, $R^2 = R^3 = R^4 = R^5 = H$
c; $R^1 = R^3 = R^4 = OMe$, $R^2 = R^5 = H$
d; $R^1 = OMe$, $R^2 = R^3 = R^4 = R^5 = H$, 13a - CO_2Me



(V)

a; $R^1 = R^2 = R^3 = R^4 = R^5 = H$
b; $R^1 = OMe$, $R^2 = R^3 = R^4 = R^5 = H$
c; $R^1 = R^4 = R^5 = OMe$, $R^2 = R^3 H$
d; $R^1 = R^3 = R^4 = OMe$, $R^2 = R^5 = H$
e; $R^1 = R^2 = OMe$, $R^3 = R^4 = R^5 = H$
f; $R^2 = R^3 = OMe$, $R^1 = R^4 = R^5 = H$
g; $R^2 = R^5 = OMe$, $R^1 = R^3 = R^4 = H$
h; $R^1 = R^2 = R^3 = OMe$, $R^4 = R^5 = H$
i; $R^1 = R^2 = R^5 = OMe$, $R^3 = R^4 = H$
j; $R^1 = OMe$, $R^2R^3 = OCH_2O$, $R^4 = R^5 = H$
k; $R^1 = R^2 = OMe$, $R^5 = OH$, $R^3 = R^4 = H$
l; $R^1 = OMe$, $R^4 = NO_2$, $R^2 = R^3 = R^5 = H$
m; $R^1 = OMe$, $R^2 = CO_2Me$, $R^3 = R^4 = R^5 = H$



(VI)

a; $R^1 = R^2 = R^3 = R^4 = H$
b; $R^1 = R^3 = R^4 = OMe$, $R^2 = H$
c; $R^1 = R^2 = R^3 = OMe$, $R^4 = H$
d; $R^1 = OMe$, $R^2R^3 = OCH_2O$, $R^4 = H$

reductions of the major photoproduct (Vd) with lithium aluminium hydride and sodium borohydride, or reduction

of the lactam (IVc) with lithium aluminium hydride, afforded the corresponding amine (VIb), identical with natural xylopinine.[8]

We then required a regiospecific method of photocyclisation for further application of this method. Some cases of regiospecific photocyclisation have been described,[5,9] particularly with the compounds having an *ortho*-methoxy-group; we therefore examined the photocyclisation of the 2'-methoxy-enamides (IId and e), prepared from (Ia and b) and 2-methoxybenzoyl chloride. We thus obtained the didehydrolactams (Va and b) as sole products in 46—50% yields. Further, the 2',6'-dimethoxy-enamide (IIf) photocyclised as expected to afford only the didehydrolactam (Ve), in 56% yield, one *ortho*-methoxy-group having been lost. Analogously, photocyclisation of the 2',3',6'-trimethoxy-enamides (IIg and h) afforded two types of photocyclised product (Vf and h, and Vg and i) in the ratio *ca.* 2.5 : 1. The structures of these photoproducts were deduced mainly from their n.m.r. spectra. Further, the product (Vh) was reduced successively with lithium aluminium hydride and sodium borohydride to give the tertiary amine (VIc), which was identified as (±)-tetrahydropalmatine by direct comparison with the natural alkaloid.[10]

Many protoberberine alkaloids possess a 9,10-methylenedioxy-group, *e.g.* sinactine (VId). In order to synthesise this type of alkaloid by our method, it was necessary to prevent cyclisation to the 'root' of a methylenedioxy-group. The enamide (IIi) was therefore prepared, from (Ib) and 6-methoxy-2,3-methylenedioxybenzoyl chloride,[11] and irradiated. Two photocyclisation products (Vj and k) were obtained, in 44 and 21% yield, respectively, which were separated readily by chromatography. The major product (Vj), shown to contain two methoxy- and a methylenedioxy-group and an olefinic proton from its n.m.r. spectrum, was reduced as above to give the tertiary amine (VId), which was identical with natural (—)-sinactine.[12] The minor product (Vk) was shown to have a phenolic hydroxy-group from its i.r. absorption at 3 250—3 000 cm^{-1} and n.m.r. peak at δ 9.58, and two adjacent protons at positions 10 and 11 from n.m.r. signals at δ 7.08 and 6.79 (each d, *J* 8.5 Hz), thus establishing its structure. Methylation of the phenolic lactam (Vk) with methyl iodide gave the tetramethoxy-lactam (Vi), identical with the product of photocyclisation of the enamide (IIh). These results indicate that cyclisation of the enamide (IIi), substituted both *ortho*-positions by a methoxy- and

[8] A. R. Battersby, D. J. LeCourt, S. Garratt, and R. I. Thrift, *Tetrahedron*, 1961, **14**, 46.

[9] (*a*) I. Ninomiya, T. Kiguchi, and T. Naito, *J.C.S. Chem. Comm.*, 1974, 81; (*b*) Y. Kanaoka and K. Ito, *ibid.*, 1973, 647; (*c*) I. Ninomiya, H. Takasugi, and T. Naito, *Heterocycles*, 1973, **1**, 17; (*d*) R. G. F. Giles and M. V. Sargent, *J.C.S. Chem. Comm.*, 1974, 215; (*e*) Y. Tamura, S. Fukumori, S. Kato, and Y. Kita, *ibid.*, p. 285.

[10] Ch. Tani, I. Imanishi, and J. Nishijo, *Yakugaku Zasshi*, 1970, **90**, 407.

[11] F. P. Doyle, K. Hardy, J. H. C. Naylor, M. J. Soulal, E. R. Stove, and H. R. J. Waddington, *J. Chem. Soc.*, 1962, 1453.

[12] R. D. Haworth and W. H. Perkin, *J. Chem. Soc.*, 1926, 1769.

TABLE 1

Enamides (IIa—k)

Compd.	Yield (%)	M.p. [B.p.] (°C) (solvent)	Formula	Analyses (%) [a] C	H	N
(IIa)	87	[180; 8 × 10^{-3} mmHg]	$C_{17}H_{15}NO$	81.45 (81.9	5.95 6.05	5.7 5.6)
(IIb)	81	125—126 (PhH–n-C_6H_{14})	$C_{19}H_{19}NO_3$	73.7 (73.75	6.15 6.2	4.35 4.55)
(IIc)	80	Viscous oil	$C_{21}H_{23}NO_5$	*b*		
(IId)	90	[203; 4 mmHg]	$C_{18}H_{17}NO_3$	*b*		
(IIe)	62	153.5—154 (PhH–Et_2O)	$C_{20}H_{21}NO_4$	70.7 (70.8	6.15 6.25	4.1 4.15)
(IIf)	62	167—169 (PhH–Et_2O)	$C_{21}H_{23}NO_5$	68.4 (68.3	6.4 6.3	3.9 3.8)
(IIg)	50	103—104.5 (Et_2O)	$C_{20}H_{21}NO_4$	70.5 (70.8	6.3 6.25	4.3 4.15)
(IIh)	92	163—164.5 (PhH–Et_2O)	$C_{22}H_{25}NO_6$	66.15 (66.15	6.3 6.3	3.55 3.5)
(IIi)	80	207—208 (PhH–Et_2O)	$C_{21}H_{21}NO_6$	66.0 (65.8	5.55 5.5	3.7 3.7)
(IIj)	85	215—217 ($CHCl_3$–Et_2O)	$C_{19}H_{18}N_2O_5$	64.35 (64.4	4.95 5.1	7.9 7.9)
(IIk)	63	136—138 (MeOH–Et_2O)	$C_{21}H_{21}NO_5$	68.6 (68.65	5.65 5.75	3.95 3.8)

[a] Required values in parentheses. [b] Because of its instability, the compound was not obtained in pure state.

TABLE 2

Spectral data

Compd.	$\nu_{max.}$($CHCl_3$)/ cm^{-1} (C:C·N·CO)	N.m.r. [δ($CDCl_3$)]
(IIa)	1 630	5.40 and 4.51 (2 H, each d, *J* 1.5 Hz, H_2C=C), 4.10 (2 H, t, *J* 6 Hz, 3-H_2), and 3.02 (2 H, t, *J* 6 Hz, 4-H_2)
(IIb)	1 635	7.01 (1 H, s, 8-H), 6.68 (1 H, s, 5-H), 5.28 (1 H, d, *J* 2 Hz, *trans*-N·C:CH; intensity increased *ca.* 24% by irradiation of 8-H), 4.45 (1 H, d, *J* 2 Hz, *cis*-N·C:CH), and 3.90 and 3.89 (each 3 H, s, OMe × 2)
(IIc)	1 620	7.20 (1 H, s, 8-H), 6.80 (1 H, s, 5-H), 5.50 and 4.43 (2 H, each br, s, H_2C=C), and 3.80 (12 H, s, OMe × 4)
(IId)	1 625	
(IIe)	1 630	6.98 (1 H, s, 8-H), 6.67 (1 H, s, 5-H), 5.20 (1 H, s-like, *trans*-N·C:CH; intensity increased 23% by irradiation of 8-H), 4.60 (1 H, s-like, *cis*-N·C:CH), and 3.88, 3.83, and 3.44 (each 3 H, s, OMe × 3)
(IIf)	1 633	6.91 (1 H, s, 8-H), 5.10 (1 H, s-like, *trans*-N·C:CH; intensity increased 21% by irradiation of 8-H), 4.64 (1 H, s-like, *cis*-N·C:CH), and 3.88 (3 H), 3.83 (3 H), and 3.51 (6 H) (each s, OMe × 4)
(IIg)	1 630	5.32 and 4.85 (2 H, each s-like, H_2C=C), and 3.77 (6 H) and 3.35 (3 H) (each s, OMe × 3)
(IIh)	1 635	6.93 (1 H, s, 8-H), 6.81 and 6.44 (2 H, ABq, *J* 9 Hz, 4'- and 5'-H), 6.64 (1 H, s, 5-H), 5.13 and 4.79 (2 H, each d, *J* 1 Hz, H_2C=C), and 3.87, 3.81, 3.77, 3.75, and 3.43 (each 3 H, s, OMe × 5)
(IIi)	1 630	6.95 (1 H, s, 8-H), 6.61 (1 H, s, 5-H), 6.65 and 6.18 (2 H, ABq, *J* 8 Hz, 3'- and 4'-H), 5.85 (2 H, m, O·CH_2·O), 5.17 and 4.67 (2 H, each br, s, H_2C=C), and 3.85, 3.83, and 3.40 (each 3 H, s, OMe × 3)
(IIj)	1 640 1 530 (NO_2) 1 350 (NO_2)	
(IIk)	1 730 (CO_2Et) 1 635	

a methylenedioxy-group, occurred not only at the 'root' of the methoxy-group but also at the 'root' of the methylenedioxy-group. The latter was followed by spontaneous cleavage and elimination of a C_1 unit, thus affording a phenolic product.[9a]

Photocyclisation of the enamides (IIj and k), which have an electron-attracting substituent on the benzene ring, proceeded very slowly to give the corresponding berbin-8-ones (Vl) and (IVd and Vm) in poor yields. Isolation of the 13a-methoxycarbonyl-lactam (IVd) from photocyclisation of the enamide (IIk), which carries an *ortho*-ester group, provided proof of the occurrence of a thermal [1,5] sigmatropic shift [13] of an ester group, and indicated an electrocyclic mechanism for the photocyclisation of this type of enamide.

In a future paper we will report total syntheses of 13-methylprotoberberine alkaloids.

EXPERIMENTAL

^{1}H N.m.r. spectra were measured for solutions in deuteriochloroform with a Varian A-60D instrument (tetramethylsilane as internal reference). M.p.s were determined with

TABLE 3

Cyclisation products (IV) and (V)

Compd.	Yields (%) (starting enamide)	M.p. (°C) (solvent)	Formula	Analysis (%) [a] C	H	N
(IVa)	40 (IIa)	169—170 (Et_2O–CH_2Cl_2) (lit.,[15] 169—170)				
(IVb)	18 (IIb)	141—142 (PhH–Et_2O) (lit.,[16] 142)				
(IVc)	5 (IIc)	190—192 (MeOH–Et_2O) (lit.,[5] 188—189)	$C_{21}H_{23}NO_5$	M^+ 369.154 (369.158)		
(IVd)	8 (IIk)	205—206 (MeOH)	$C_{21}H_{21}NO_5$	68.6 (68.65	5.7 5.75	3.85 3.8)
(Va)	20 (IIa)	102—102.5 (Et_2O—n-C_6H_{14})				
	50 (IId)	(lit.,[6] 101—102)				
(Vb)	24 (IIb)	191—192 (EtOH)				
	46 (IIe)	(lit.,[16] 189—190)				
Vc)	5 (IIc)	184—185 (MeOH) (lit.,[17] 189—190)	$C_{21}H_{21}NO_5$	68.9 (68.65	5.95 5.75	3.5 3.8)
(Vd)	40 (IIc)	196.5—198 (MeOH) (lit.,[17] 198—199)	$C_{21}H_{21}NO_5$	M^+ 367.142 (367.141)		
(Ve)	56 (IIf)	179.5—181.5 (EtOAc–Et_2O)	$C_{21}H_{23}NO_5$	71.3 (71.2	5.55 5.7	4.35 4.15)
(Vf)	25 (IIg)	146—148 (Et_2O)	$C_{19}H_{17}NO_3$	M^+ 307.120 33 (307.120 84)		
(Vg)	10 (IIg)	164—166 (Et_2O)	$C_{19}H_{17}NO_3$	M^+ 307.120 33 (307.120 84)		
(Vh)	*ca.* 20 (IIh)	[Mixture with (Vi)]				
(Vi)	8 (IIh)	211—212 (MeOH)	$C_{21}H_{21}NO_5$	68.5 (68.65	5.65 5.75	3.85 3.8)
(Vj)	44 (IIi)	247.5—249 ($CHCl_3$–MeOH) (lit.,[12] 240—241)				
(Vk)	21 (IIi)	280—281 (Me_2CO)	$C_{20}H_{19}NO_5$	67.85 (68.0	5.3 5.4	4.2 3.95)
(Vl)	8 (IIj)	> 300 ($CHCl_3$–MeOH)	$C_{19}H_{16}N_2O_5$	64.2 (64.75	4.35 4.6	7.95 7.95)
(Vm)	5 (IIk)	247—249 (MeOH)	$C_{21}H_{19}NO_5$	68.95 (69.05	5.2 5.25	3.9 3.85)

[a] Required values in parentheses.

[13] P. Schmidt, R. W. Hoffmann, and J. Backes, *Angew. Chem. Internat. Edn.*, 1972, **11**, 514.

TABLE 4

Spectral data

Compd.	$\nu_{max.}$(CHCl$_3$)/cm^{-1} (N·CO)	N.m.r. [δ(CDCl$_3$)]
(IVa)	1 645	8.20 (1 H, m, 9-H), and 5.12—4.72 (2 H, m, 13a- and 6-H)
(IVb)	1 642	8.18 (1 H, m, 9-H), 6.75 (1 H, s, 1- or 4-H), 6.71 (1 H, s, 4- or 1-H), 5.15—4.70 (2 H, m, 13a- and 6-H), and 3.90 (6 H, s, OMe × 2)
(IVc)	1 640	7.67 (1 H, s, 9-H), 6.73 (3 H, s, 1-, 4-, and 12-H), 5.20—4.65 (2 H, m, 6- and 13a-H), and 3.93 (9 H) and 3.91 (3 H) (each s, OMe × 4)
(IVd)	1 733 (CO_2Et), 1 655	8.15 (1 H, m, 9-H), 7.21 (1 H, s, 1-H), 6.71 (1 H, s, 4-H), 5.30—4.90 (1 H, m, 6-H), 3.92, 3.88, and 3.52 (each 3 H, s, OMe × 3), and 3.90 and 3.15 (2 H, ABq, *J* 15.5 Hz, 13-H$_2$)
(Va)	1 640	8.47 (1 H, m, 9-H), 8.00—7.30 (7 H, m, aromatic), 7.03 (1 H, s, 13-H), 4.41 (2 H, t-like, 6-H$_2$), and 3.02 (2 H, t-like, 5-H$_2$)
(Vb)	1 645	8.43 (1 H, m, 9-H), 7.28, 6.87, and 6.75 (3 H, each s, 1-, 4-, and 13-H), and 3.97 and 3.91 (each 3 H, s, OMe × 2)
(Vc)	1 640	8.20 (1 H, d, *J* 9 Hz, 9-H), 7.35, 7.13, and 6.75 (3 H, each s, 1-, 4-, and 13-H), 7.12 (1 H, d, *J* 9 Hz, 10-H), 4.35 (2 H, t-like, 6-H$_2$), 4.00 (3 H), 3.97 (6 H), and 3.93 (3 H) (each s, OMe × 4), and 2.93 (2 H, t-like, 5-H$_2$)
(Vd)	1 640	7.80 (1 H, s, 9-H), 7.25, 6.91, 6.80, and 6.73 (4 H, each s, 13- and other aromatic H), and 4.02 (9 H) and 3.95 (3 H) (each s, OMe × 4)
(Ve)	1 650	7.49 (1 H, t, *J* 8 Hz, 11-H), 7.25 (1 H, s, 1-H), 7.20 (1 H, dd, *J* 8.5 and 1.5 Hz, 12-H), 6.93 (1 H, dd, *J* 8.5 and 1.5 Hz, 10-H), 6.73 (2 H, s-like, 4- and 13-H), and 3.98, 3.95, and 3.90 (each 3 H, s, OMe × 3)
(Vf)	1 655	7.78 (1 H, m, 1-H), 7.50—7.20 (5 H, m, aromatic), 6.89 (1 H, s, 13-H), and 4.03 and 3.93 (each 3 H, s, OMe × 2)
(Vg)	1 655	7.90 (1 H, m, 1-H), 7.55—7.20 (4 H, m, 13- and other aromatic H), 7.03 and 6.83 (2 H, ABq, *J* 9 Hz, 10- and 11-H), and 3.95 and 3.91 (each 3 H, s, OMe × 2)
(Vh)	1 655	7.28 (2 H), 6.73 (2 H), 7.23 (1 H) (each s, 13- and aromatic H), 4.33 (2 H, t-like, 6-H$_2$), 4.03 (3 H), 3.95 (3 H), and 3.93 (6 H) (each s, OMe × 4), and 2.91 (2 H, t-like, 5-H$_2$)
(Vi)	1 655	7.31, 7.18, and 6.71 (3 H, each s, 13- and aromatic H), 6.98 and 6.75 (2 H, ABq, *J* 9 Hz, 10- and 11-H), 4.33 (2 H, t, *J* 6.5 Hz, 6-H$_2$), 3.98 (3 H), 3.97 (3 H), and 3.93 (6 H) (each s, OMe × 4), and 2.90 (2 H, t, *J* 6.5 Hz, 5-H$_2$)
(Vj)	1 650	7.21, 7.10, 7.07, 6.75, and 6.72 (5 H, each s, 13- and aromatic H), 6.28 (2 H, s, O·CH$_2$·O), 4.30 (2 H, t-like, 6-H$_2$), 3.98 and 3.93 (each 3 H, s, OMe × 2), and 2.90 (2 H, t-like, 5-H$_2$)
(Vk)	(Nujol) 3 250—3 000br (OH), 1 640	[(CD$_3$)$_2$SO] 9.58br (1 H, OH), 7.37, 7.18, and 6.94 (3 H, each s, 1-, 4-, and 13-H), 7.08 and 6.79 (2 H, ABq, *J* 8.5 Hz, 10- and 11-H), 4.15 (2 H, t-like, 6-H$_2$), 3.88, 3.83, and 3.78 (each 3 H, s, OMe × 3), and 2.90 (2 H, t-like, 5-H$_2$)
(Vl)	(Nujol) 1 660, 1 530sh (NO_2), 1 350(NO_2)	
(Vm)	1 730 (CO_2Et), 1 650	7.70—7.25 (4 H, m), 6.88 (1 H, s), and 6.73 (1 H, s) (13- and aromatic H), and 4.03, 3.97, and 3.92 (each 3 H, s, OMe × 3)

a Kofler hot-stage apparatus. The photochemical reactions were carried out as described in Part I.[14]

General Procedure for the Preparation of Enamides (IIa—k).—To a solution of the 3,4-dihydro-1-methylisoquinoline (Ia or b) (0.01 mol) and triethylamine (0.015 mol) in anhydrous benzene (100 ml), a solution of the appropriate aroyl chloride (0.01 mol) in anhydrous benzene (50 ml) was added dropwise with stirring. After refluxing for 2 h, the mixture was cooled and filtered to remove triethylamine hydrochloride. Evaporation left a residue, which was either distilled or recrystallised to give the *enamide* (IIa—k) (Tables 1 and 2).

General Procedure for Irradiation of the Enamides (IIa—k).—A 0.02M-solution of the enamide (IIa—k) in methanol was irradiated for several hours in a quartz vessel until disappearance of the starting enamide was indicated by t.l.c. The solvent was removed and the residue was chromatographed on alumina or silica gel to give the photocyclised products [(IVa—d) and (Va—m); Tables 3 and 4].

Reduction of the Photocyclised Lactams (IVa *and* c) *and* (Va, d, h, *and* j).—*Berbine* (VIa). (a) *From the lactam* (IVa). To a solution of the lactam (IVa) (249 mg) in anhydrous ether (30 ml), lithium aluminium hydride (150 mg) was added in small portions with cooling. The mixture was refluxed for 1.5 h, then cooled in ice and the excess of hydride was decomposed with water. The aqueous layer was extracted with ether. The combined extracts were washed with brine, dried, and evaporated to give a viscous residue, which was triturated with and recrystallised from ethanol to afford the amine (VIa) (188 mg, 80%), m.p. 84—85° (lit.,[6] 85—86°), identical with an authentic sample.

(b) *From the didehydrolactam* (Va). By the procedure given in (a), reduction of the didehydrolactam (Va) (247 mg) with lithium aluminium hydride (150 mg) afforded an oil, which was reduced with sodium borohydride (150 mg) in methanol (40 ml) to give the amine (VIa) (120 mg, 50%), identical with that obtained in (a).

(±)-*Xylopinine* (VIb). (a) *From the lactam* (Vd). By the procedure given for (Va), successive reductions of the lactam (Vd) with lithium aluminium hydride and sodium borohydride afforded a solid which crystallised from ether to afford the amine (VIb) (20%), m.p. 157—158° (lit.,[8] 157—158°) (Found: M^+, 355.178. $C_{21}H_{25}NO_4$ requires M, 355.178), identical with authentic (±)-xylopinine.

(b) *From the lactam* (IVc). Reduction of the lactam (IVc) with lithium aluminium hydride afforded the amine (VIb) in 30% yield, identical with the sample obtained in (a).

(±)-*Tetrahydropalmatine* (VIc). By the procedure given for (Va), successive reductions of a mixture of the lactams (Vh and i) with lithium aluminium hydride and sodium borohydride afforded an oil, which was purified by preparative t.l.c. on silica gel. The fraction of higher R_F value was recrystallised from methanol to give the amine (VIc) (15%) as needles, m.p. 149.5—150.5° (lit.,[10] 148°), identical with natural (±)-tetrahydropalmatine.

(±)-*Sinactine* (VId). By the procedure given for (Va), successive reductions of the lactam (Vj) with lithium aluminium hydride and sodium borohydride afforded a yellow solid, which crystallised from ethanol to give the amine (VId) (54%) as needles, m.p. 169—170° (lit.,[12] 169—170°), identical with natural (−)-sinactine (Found: C, 70.75; H, 6.2; N, 4.15. Calc. for $C_{20}H_{21}NO_4$: C, 70.8; H, 6.25; N, 4.15%). (±)-Sinactine hydrochloride melts at 241—242° (decomp.).

Methylation of the Phenolic Lactam (Vk).—A mixture of the lactam (Vk) (177 mg), potassium carbonate (690 mg), and methyl iodide (710 mg) in acetone (80 ml) was refluxed for 10 h. After cooling, the mixture was filtered and the filtrate evaporated. The yellow residue was recrystallised from methanol to give the tetramethoxylactam (Vi) (173 mg, 94%) as yellow needles, m.p. 211—212°, identical with the product (Vi) obtained from photocyclisation of the enamide (IIh).

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