Dye-sensitized Photo-oxygenation of the *Aspidosperma* Alkaloids Vincadifformine and Tabersonine. A New, Convenient Approach to Vincamine †

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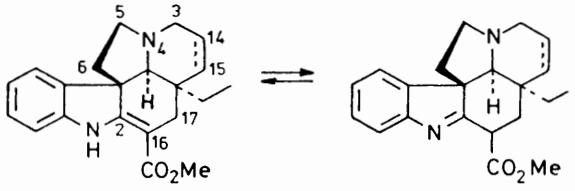
The dye-sensitized photo-oxygenation of (−)-vincadifformine (1) and (−)-tabersonine (3) is described. Reaction takes place through the intermediate formation of 16-hydroperoxyindolenines, which decompose to give 2,16-*seco*-products or which can be efficently trapped by reductants to give a new stereoselective synthesis of the 16-hydroxy-[3*H*]indoles (10) and (14). These compounds are the key precursors to the eburnane alkaloids vincamine (4) and Δ^{14}-vincamine (6). Suitable experimental conditions give compounds (4) and (6) in good yields directly from their *Aspidosperma* precursor.

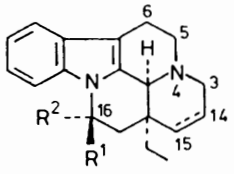
ACCORDING to Wenkert and Wickberg's biosynthetic hypothesis,[2] the useful cerebral vasodilator alkaloid vincamine (4) is formed by oxidation of the appropriate precursor (−)-vincadifformine (1) into the hydroxy-[3*H*]-indole (10), followed by the acid-catalyzed *Aspidosperma* →eburnane skeletal rearrangement. This transformation



(1) N(4) = —:
(2) N(4) = ---O
(3) N(4) = —:; Δ^{14}

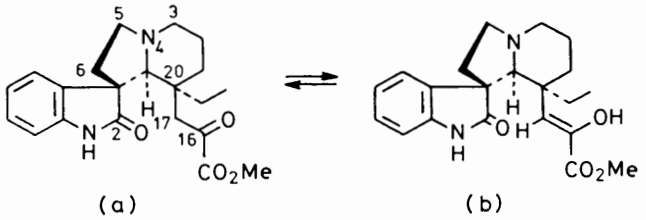
has been realized *in vitro* by Le Men *et al.*[3] through a multi-step procedure which involves oxidation of compound (1) with peroxy-acids to give the hydroxy-[3*H*]-indole *N*(4)-oxide (11), triphenylphosphine-induced deoxygenation of which gives compound (10), and subsequent treatment with acetic acid to give the rearrangement. The same reaction has been performed in a single step by protecting the *N*(4) centre from the oxidation with mineral acids in polar solvents [4] or, more efficiently in terms of yield and ease of implementation, by ozonation.[5]

Recently, Lévy *et al.*[6] reported that irradiation of methanol solution of (1)·HCl in the presence of oxygen



(4) R^1 = OH, R^2 = CO_2Me
(5) R^1 = CO_2Me, R^2 = OH
(6) R^1 = OH. R^2 = CO_2Me; Δ^{14}
(7) R^1 = CO_2Me, R^2 = OH; Δ^{14}

and the dyestuff Methylene Blue (MB) with an HP Hanovia lamp resulted in a mixture of vincamine (4) and its 16-epimer (5) in 5.7% yield, the major product being the oxoindole (8a) (40%). Furthermore, irradiation of

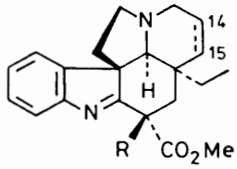


(a) (b)

(8) N(4) = —:
(9) N(4) = ----O

vincadifformine itself, under the same conditions, gave extensive decomposition which led to a complex mixture of products, one of which could be isolated successfully in small amounts and identified as compound (8a).

The paper of Lévy *et al.*[6] prompted us to report our



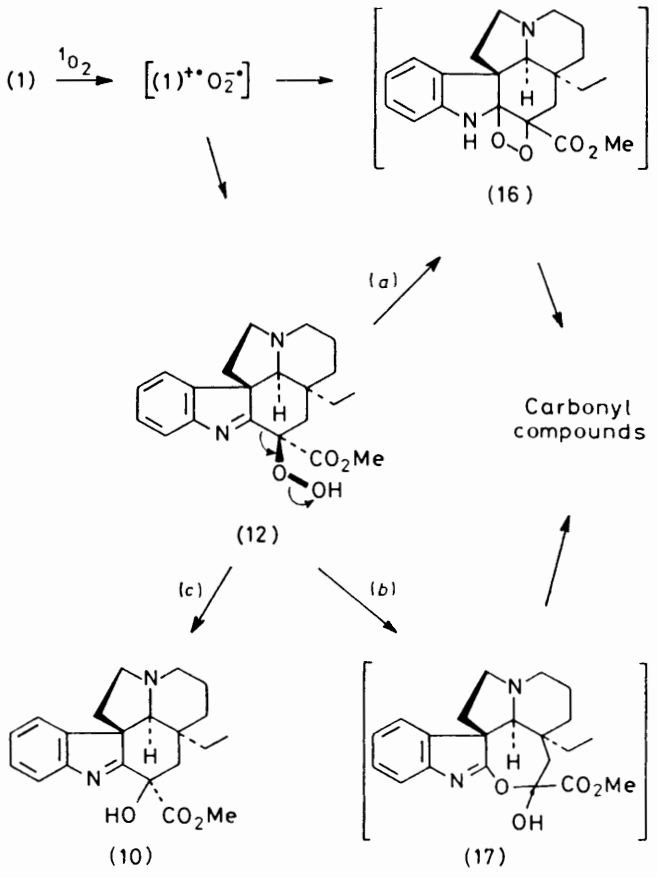
(10) R = OH; N(4) = —:
(11) R = OH; N(4) = ·····O
(12) R = OOH; N(4) = —:
(13) R = OOH; N(4) = ·····O
(14) R = OH; N(4) = —:; Δ^{14}
(15) R = OH; N(4) = ·····O; Δ^{14}

findings in the field of the sensitized photo-oxidation of vincadifformine (1) and tabersonine (3) which culminated in an experimentally feasible synthesis of the pivotal intermediates (10) and (14) and, as a result, of vincamine (4) and its Δ^{14}-analogue (6).

† The numbering system used in this paper is one proposed by J. Le Men and N. I. Taylor, *Experientia*, 1965, **21**, 508.

RESULTS AND DISCUSSION

Apart from a few exceptions, sensitized oxidations proceed *via* the sensitizer triplet state, according two major classes of reactions classified by Gollnick and Schenck [7] as ' Type 1 ' and ' Type 2 '. In the first class the triplet sensitizer interacts with the substrate and directly abstracts hydrogen atoms to form radicals which subsequently react with the triplet ground-state oxygen ($^3O_2$,$^3\Sigma_g^-$) (Backstrom-type photosensitized autoxidation). In the second class, the excited sensitizer transfers energy to give singlet oxygen ($^1O_2$,$^1\Delta_g$) so that a direct reaction can occur with the substrate (photosensitized oxygen transfer).



SCHEME 1

In principle, the presence of an allylic methine hydrogen atom in the protomeric form of vincadifformine (1) should be particularly favourable for hydrogen abstraction initiated by irradiation or by the decomposition of peroxides (Type 1 autoxidation). However, irradiation of a solution of compound (1) in cyclohexane in the presence of oxygen and a typical $^3(n, \pi^*)$-sensitizer, such as benzophenone (E_T 68.5 kcal mol^{-1}), which is known to be a strong hydrogen abstractor,[8] gave no products which resulted from the oxygenation at C-16 (*vide infra*).

There are indications that all additions of $^1O_2$ (Type 2) to electron-rich systems might proceed by electron transfer from the donor (*e.g.*, vincadifformine) to $^1O_2$ to give a radical cation–superoxide anion pair $[(1)^{+\bullet}\ O_2^{-\bullet}]$ or a charge-transfer (CT) complex.[9] Recombination of the ion pair would give a dioxetan [*e.g.* compound (16)], followed by retrocycloaddition to carbonyl compounds or hydroperoxide [*e.g.* compound (12)], depending on the nature of the substituents attached to the reaction centres and on the bulkiness of more distant parts of the molecule (Scheme 1). The collapse of the allylic hydroperoxide (12) in non-aqueous solvents resulting in C–C bond cleavage might occur either through the intramolecular nucleophilic addition across the C–N double bond [10] or through skeletal rearrangement initiated by migration to oxygen (Hock–Criegee cleavage [11]) *via* compound (17). Alternatively, the hydroperoxide (12) can be reduced photochemically or by intermolecular interactions to the corresponding hydroxy-compound (10).

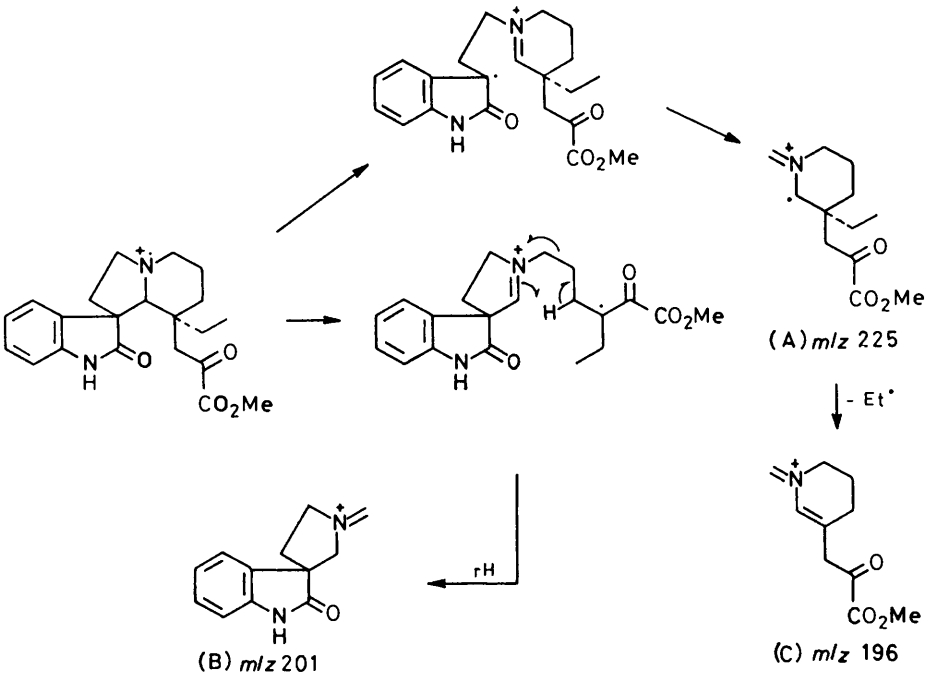
When a solution of compound (1) (4×10^{-2}M) in MeOH which contained Rose Bengal (6.5×10^{-5}M) as sensitizer (E_T 39.5 kcal mol^{-1}) was irradiated for 1 h from −70 to 20 °C employing a 350 W tungsten lamp through Pyrex in the presence of oxygen, the oxoindole (8) was formed in 70—85% yields. The physical data for this compound were in close agreement with those reported by Lévy *et al.*[6] In particular, the mass peaks at *m/z* 225, 201, and 196 due to the ions (A), (B), and (C), supported the 2,16-*seco*-structure (Scheme 2).

The oxoindole (8) proved to be stereochemically labile. In fact, in chloroform (12 h at room temperature), a mixture of at least three closely running diastereoisomers [high-performance thin layer chromatography (h.p.t.l.c.)] was detected. By virtue of ready interconvertibility (*e.g.* on silica gel) their separation was not attempted. However, the stereochemical integrity at C-7 and C-21 [*i.e.*, (7*R*), (21*S*)] in compound (8) *vs.* vincadifformine (1) was established by means of circular dichroism (c.d.) measurements (recorded immediately after isolation of the oxoindole). The curve obtained was closely related to that reported for the oxoindole alkaloids mitraphylline and rhyncophylline.[12]

Other sensitizers (*e.g.*, Methylene Blue, fluorescein, Eosin Y, and riboflavin) were less efficient in this transformation and gave the oxoindole (8) in 10—60% yields. Besides compound (8), the only other product identified was (−)-3-oxovincadifformine (18)[13] ($M^{+\bullet}$ at *m/z* 352). The remainder of the product was a complex mixture with no evidence (t.l.c.) for the formation of compound (10) or its acid-induced rearranged products (4) and (5).

The proposed route for the formation of compound (18) involves the interaction of N(4) either with $^1O_2$ or with excited sensitizer molecules, followed by reaction of the resulting α-amino-radical (or radical cation) with ground-state oxygen.[14]

If the formation of the oxoindole (8) requires the intermediacy of the 16-hydroperoxy-[3*H*]indole (12), it should be possible for a suitable reducing agent to trap intermediate (12) and so give the desired hydroxy-derivative (10). Triethyl phosphite and sodium thiosulphate were used as reductants, in addition to thiourea which is the only reported [15] compound used for the *in*



SCHEME 2

situ reduction of allylic hydroperoxides during their photochemical generation.* The results obtained on the photosensitized oxygenation of compounds (1) and (3) are summarised in Table 1.

As with the photo-oxygenation without reductants, the best conversion of compound (1) and the highest selectivity in the functionalisation at C-16 were obtained with Rose Bengal and hematoporphyrin (E_T 37 kcal mol^{-1}), whereas MB and fluorescein seem to be less suitable for this conversion. For preparative purposes sodium thiosulphate is the reductant of choice since it is transformed into sodium tetrathionate, sparingly soluble in the reaction medium.

TABLE 1

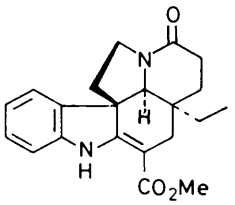
Dye-sensitized photo-oxygenation of 4 × 10^{-2}M solutions of compounds (1), (2), and (3)

Expt.	Substrate	Sensitizer [a] [molarity (× 10^{-5})]	Reductant [molarity (× 10^{-2})]	Reaction time (min)	Substrate recovered (%)	Products [yield (%)]
1 [b]	(1)	RB [6.5]		60		(8) [85]; (18) [6]
2 [b]	(1)	EY [6.5]		60		(8) [60]; (18) [10]
3 [b]	(1)	RF [6.5]		80		(8) [58]; (18) [10]
4 [b]	(1)	MB [6.5]		120	59	(8) [10]; (18) [14]
5 [b]	(1)	FL [6.5]		120	63	(8) [10]; (18) [8]
6 [b]	(1)	RB [6.5]	Thiourea [4]	40	28	(8) [33]; (10) [29]
7 [b,c]	(1)	RB [6.5]	$(EtO)_3P$ [12]	45		(10) [67]
8 [c,d]	(1)	RB [15]	$Na_2S_2O_3$ [6]	60		(10 [82]; (4) [46]; [e] (5) [30] [e]
9 [b,c]	(1)	HP [6.5]	$(EtO)_3P$ [8]	6		(8) [22]; (10) [46]
10 [c,d]	(1)	HP [0.65]	$Na_2S_2O_3$ [6]	60		(8) [8]; (10) [62]; (4) [38]; (5) [25] [e]
11 [b]	(1)	EY [6.5]	$(EtO)_3P$ [6]	40		(10) [60]
12 [b]	(1)	MB [6.5]	$(EtO)_3P$ [4]	120	79	(8) [6]; (10) [4]
13 [b]	(1)	FL [6.5]	$(EtO)_3P$ [6]	40	75	(8) [7]; (10) [1]
14 [b]	(3)	RB [6.5]	$(EtO)_3P$ [12]	20		(14) [88]; (6) [41]; [e] (7) [44] [e]
15 [b]	(2)	RB [6.5]		30		(11) [64]; (9) [33]; (11) [95] [f]
16 [g]	(2)	RB [6.5]		35		(9) [49]; (11) [23]; (9) [72] [h]

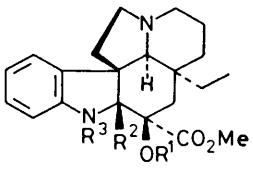
[a] RB, Rose Bengal; EY, Eosin Y; RF, riboflavin; HP, hematoporphyrin; MB, Methylene Blue; FL, fluorescein. [b] MeOH. [c] NaOH (2 N, 1 ml) was added. [d] MeOH–H_2O (6 : 1). [e] After direct acidic work-up of the irradiated mixture. [f] After reduction of the irradiated mixture with KI–AcOH. [g] $CHCl_3$. [h] After refluxing the irradiated mixture prior to work-up.

The 16-hydroxy-[3*H*]indole (10) was an authentic singlet-oxygen product as evidenced by ineffectiveness of a free-radical scavenger (2,6-di-t-butylphenol), by inhibition of formation with the singlet oxygen quencher 1,4-diazabicyclo[2.2.2]octane (DABCO), and by competitive inhibition by 1,4-dimethylfuran (DMF), a reactive $^1O_2$ acceptor.

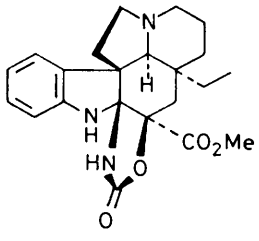
* The efficient oxidation of iodine ions in the presence of water with singlet oxygen to iodine precluded their use as reductant (A. G. Kepka and L. I. Grossweiner, *Photochem. Photobiol.*, 1973, **18**, 49).



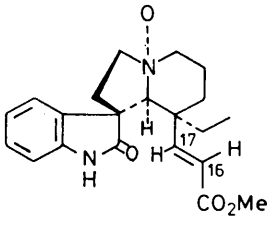
(18)



(19) $R^1 = R^2 = R^3 = H$
(20) $R^1 = R^3 = Ac, R^2 = H$
(21) $R^1 = R^2 = H, R^3 = Me$
(22) $R^1 = R^3 = H, R^2 = CN$
(23) $R^1 = OH, R^2 = OMe, R^3 = H$



(24)



(25)

The compound (10) was left stereochemically uncharacterized until Lévy *et al.*[16] disclosed the (16*R*)-configuration. We have reached the same conclusions in an independent way by examination of the spectroscopic data (in particular c.d. and ^{13}C n.m.r. spectra) of some derivatives of compound (10). Reduction of compound (10) with $NaBH_3CN$ in acetic acid at room temperature gave, in quantitative yield, the known 16-hydroxy-indoline (19) [16] and then treatment with acetic anhydride in the presence of *NN*-dimethylaminopyridine (DMAP) in dichloromethane at room temperature afforded the *NO*-diacetate (20) [δ_H ($CDCl_3$) 7.98 (dd, *J* 8 and 1 Hz, 12-H), 4.58br (s, 2-H), 2.38 (s, MeCON), and 2.16 (s, CO_2Me)]. Concurrent reduction and *N*-methylation to compound (21) was achieved by reducing compound (10) with $NaBH_3CN$ and 40% aqueous formaldehyde. Treatment of compound (10) with an excess of potassium cyanate in dichloromethane in the presence of the phase-transfer catalyst 18-crown-6 (1,4,7,10,13,16-hexaoxocyclo-octadecane) gave, in fair yields, the oxazolidin-2-one (24), m.p. 170—174 °C. Compound (24) exhibited the characteristic absorption of an oxazolidin-2-one group ($\nu_{max.}$ 1 750 cm^{-1}) in its i.r. spectrum as well as the molecular ion (*m/z* 397) and fragmentation peak due to the extrusion of HNCO (*m/z* 354). The oxazolidinone structure was confirmed by its ^{13}C n.m.r. spectrum, particularly in the downfield α- and β-substituent shifts [17] observed at C-2 (δ 13.6), C-7 (4.3), and C-16 (5.5 p.p.m.) [compare with 16-hydroxy-indoline (19) (Table 2)]. Likewise, under the conditions used for potassium cyanide, compound (10) gave the expected 2-cyano-derivative (22) [*m/z* 381 ($M^{+\cdot}$), $\nu_{max.}$ 2 225 cm^{-1}] which reverted quantitatively to compound (10) by exposure to silver tetrafluoborate in acetonitrile in the dark.[19]

Unequivocal evidence that all the derivatives possess a *cis*-B/C ring junction is given by their chiroptical data (see Experimental section). In particular, the c.d. spectrum of the *NO*-diacetate (20) shows a pair of Cotton effects ($\Delta\varepsilon_{259}$ +6.6 and $\Delta\varepsilon_{222}$ −5.9) centred at λ 243 nm. Since the longest wavelength Cotton effect (259 nm) is positive, the absolute configuration of compound (20) is 2*R* in comparison with splendoline and isosplendoline [20] the c.d. spectra of which are of similar sign and shape.

TABLE 2

^{13}C N.m.r. chemical shifts [a, b]

	(2)	(6)	(7)	(9)	(25)	(10)	(11)	(14)	(15)	(19)	(21)	(22)	(24)	(1) [c]	(10) [d]
C-2	165.3	131.5	132.6	178.3	176.9	187.0	182.0	186.0	180.6	74.4	82.0	73.7	88.0	167.8	187.2
C-3	66.4	43.7	43.6	66.8	69.4	53.6	65.0	52.0	63.2	53.0	53.0	52.8	54.2	51.7	53.6
C-5	65.4	49.5	49.6	58.7	60.2	52.0	64.9	54.0	67.3	51.7	51.6	51.5	52.9	50.7	52.0
C-6	43.0	16.6	17.0	34.7	34.7	33.8	32.4	34.0	33.1	42.9	44.0	38.0	37.0	45.3	33.8
C-7	56.6	106.2	106.1	53.3	54.0	62.1	59.2	60.9	60.4	52.9	53.5	57.1	57.2	55.5	62.6
C-8	136.3	129.1	128.8	134.0	132.8	144.9	145.6	145.0	145.1	135.0	135.3	132.6	135.4	138.0	145.1
C-9	125.6	118.3	117.9	122.7 [e]	124.0	121.9	124.0	121.3	126.2	123.1	122.7	123.2	123.2	121.0	128.0
C-10	121.8	121.7	121.4	122.5 [e]	122.5	127.7	127.8	127.8	128.2	118.6	119.0	120.3	120.1	120.5	126.4
C-11	128.2	120.2	120.1	128.3	128.9	126.2	126.7	126.2	127.3	128.3	128.3	129.0	127.8	127.4	121.9
C-12	108.6	110.4	112.8	109.7	108.6	120.9	120.3	120.7	120.8	108.9	108.8	109.7	108.9	109.3	121.0
C-13	142.5	134.2	136.8	141.8 [f]	141.8	153.5	152.4	153.2	153.1	149.9	153.2	147.3	144.7	143.4	153.7
C-14	19.1	125.3	125.7	15.7	16.5	21.3	18.1	122.6	118.3	21.3	21.3	20.9	21.2	22.2	21.3
C-15	32.2 [e]	128.0	126.5	24.7 [g]	22.7 [e]	33.1	31.2	134.5	132.6	34.5 [e]	35.1 [e]	34.2 [e]	29.8 [e]	32.9	33.1
C-16	88.7	82.0	84.0	140.2 [f]	120.4	77.7	73.3	76.9	73.4	77.3	76.7	79.4	82.8	92.8	77.7
C-17	27.5	43.7	45.6	109.7	148.3	45.0	40.7	49.4	46.3	37.3	36.6	38.5	32.4	25.6	45.0
C-18	6.8	8.4	8.4	8.5	8.1	7.1	6.8	8.2	8.6	7.7	7.7	7.7	7.1	7.3	7.1
C-19	33.2 [e]	34.8	35.1	28.0 [g]	30.3 [e]	31.8	34.8	30.7	33.1	35.9 [e]	35.8 [e]	36.0 [e]	33.2 [e]	29.3	31.8
C-20	38.3	36.8	38.2	40.0	42.3	36.3	37.4	38.9	41.1	35.2	34.4	35.1	34.4	38.2	36.3
C-21	88.7	57.4	56.9	83.3	84.4	78.0	89.9	72.6	85.2	72.5	74.8	74.6	76.9	72.7	78.0
CO_2Me	168.3	172.9	171.7	163.6	165.8	171.0	173.4	171.5	173.6	174.5	174.2	173.7	170.7	169.2	171.3
$CO_2\mathit{Me}$	51.0	53.9	52.4	52.0	51.3	52.9	52.1	52.8	50.3	52.3	52.1	52.8	52.9	50.9	52.8
NMe					26.2						37.5				
CN												120.6			
CO_2N													156.6		

[a] At 25.2 MHz. [b] In $CDCl_3$ [except for compound (9) in CD_3OD–$(CD_3)_2SO$ (1 : 1) and for compound (11) in $(CD_3)_2SO$]. [c] Ref. 16. [d] Ref. 18. [e-g] The assignments of these signals may be reversed.

Consequently, the stereochemical requirement of oxazolidinone ring-closure in compound (24) dictates that the 16-hydroxy-group is β-oriented.

The stereochemistry produced by photo-oxygenation of compound (1) is undoubtedly due to steric inhibition of the ethyl group (axially oriented) at C-20 towards the singlet oxygen approach on the α-face of the molecule. This stereochemical assignment is also consistent with the ^{13}C n.m.r. spectral data of compounds (19), (21), (22), and (24) and are collated in Table 2.

Important is the dependence of the C-6 shift on the structural features. In compounds (19) and (21) this value is close to that of vindoline (δ_C 43.4 p.p.m.) while, on substitution at C-2, we observe an upfield shift (δ_C 5—7 p.p.m.) for C-6, which has hydrogen atoms that are 1,3-diaxially disposed towards the C-2 substituent. The fact that Δδ (C-6) values of voafolidine *vs.* voafoline [21] are nearly identical with those of compound (24) *vs.* vindoline shows the stereochemistry of the B/C ring-junction in all the derivatives (19), (21), and (22) to be *cis*, with the C-2 substituent β-oriented.

The 16-hydroxy-[3*H*]indole (10), isolated from the irradiated solution, was quantitatively converted (by heating in acetic acid) into the (kinetic) 3 : 2 mixture of vincamine (4) and 16-*epi*-vincamine (5). Interestingly, the preparation of compounds (4) and (5) might be improved if the isolation of compound (10) could be avoided. In fact, direct acidic work-up of the irradiated mixture furnished the expected eburnanes in better yields (Table 1).

Since the formation of undesired by-products implied the participation of the N(4) lone-pair, it was felt that formation of the intermediate *N*(4)-oxide (of hitherto unknown stereochemistry) should prevent either the quenching of $^1O_2$ by a CT mechanism or the undesired oxidation of alkyl groups at the position α to N(4). The (4*S*)-configuration of compound (2) was assigned on the basis of its ^1H n.m.r. spectrum which showed a downfield shift of an aromatic proton at δ 8.32 (1 H, dd, *J* 7 and 1 Hz, 9-H) *vs.* δ 7.20 in compound (1). Molecular models showed that 9-H is diamagnetically deshielded by a through-space interaction with the α-oriented *N*-oxide function.[22]

When the Rose Bengal-sensitized photo-oxygenation of compound (2) in methanol (Expt. 15) was monitored with t.l.c., it was found that the starting material was replaced within 30 min by a mixture of *ca.* equal amounts of compound (11) and a less mobile component, which appeared as a purple spot when the plate was sprayed with *NN*-dimethyl-*p*-phenylenediammonium hydrochloride solution (hydroperoxide test).[23] Attempted isolation of the more polar compound brought about its total decomposition with the fortuitous result that only the hydroxy-[3*H*]indole *N*-oxide (11) was obtained. Taking into account that the above transformation was more efficiently achieved by brief exposure to potassium iodide in acetic acid at room temperature, this sensitive product was tentatively assigned the structure 16-hydroperoxy-[3*H*]indole *N*(4)-oxide (13).

The solvent affected the reaction strongly. In fact, chloroform (Expt. 16), gave a *ca.* 1 : 1 mixture (t.l.c.) of the presumed hydroperoxide *N*(4)-oxide (13) and the ketone *N*(4)-oxide (9), m.p. 174—176 °C. The oxoindole structure for compound (9) was inferred from its u.v. spectrum [$\lambda_{max.}$ (MeOH) 218 (log ε 4.40), 251 (4.18), and 285sh nm (3.21)] and mass spectrum [molecular ion at *m/z* 386 ($C_{21}H_{26}N_2O_8$) along with a cluster of peaks at *m/z* 370 ($M^{+\cdot}$ −16), 369 ($M^{+\cdot}$ −17), and 368 ($M^{+\cdot}$ −18), usually associated with *N*-oxides [24]].

Surprisingly, the ^{13}C n.m.r. spectrum did not seem to confirm this assignment. Along with the absence of the ketone carbonyl C-16 signal (*cf.* δ_C 191.9 p.p.m. in ethyl pyruvate) and the methylene C-17 signal, the spectrum contained two other signals at δ_C 140.2 and 109.7 p.p.m., as a singlet and a doublet, respectively, in the single-frequency off-resonance decoupled (SFORD) spectrum. The chemical shifts of C-16 and C-17, as well as their multiplicities, are those expected for the substitution of a hydrogen atom by a hydroxy-group on C-16 in the related acrylic ester *N*(4)-oxide (25) * which led consistently to a downfield shift of *ca.* 21 p.p.m. in the C-16 signal and an upfield shift of *ca.* 38 p.p.m. in the C-17 signal [*e.g.* compound (25) compared with compound (9b)] (Table 2), as shown by Wenkert *et al.*[25] Strong support for this structural assignment is given by the ^1H n.m.r. spectrum of compound (9) which shows a one-proton singlet at δ 4.72, assignable to the 17-H hydrogen in the enolized form (9b). This value compares with that for the same proton in the model compound (25) (δ 5.96, *J* 15 Hz) and agrees well with the calculated value, using the additivity rule.[26]

That enolization occurred in compound (8) is shown by ^1H n.m.r. spectrum which contains, apart from the expected signals, a *ca.* one-proton singlet at δ 5.30 that can be ascribed to 17-H. The conditions required for epimerization of compound (8) are surprisingly mild (*vide supra*) and, by comparison, oxoindole alkaloids (*e.g.*, carapanaubine and rauvoxine) failed to undergo significant equilibration [path (*a*) in Scheme 3] under the same conditions.[27]

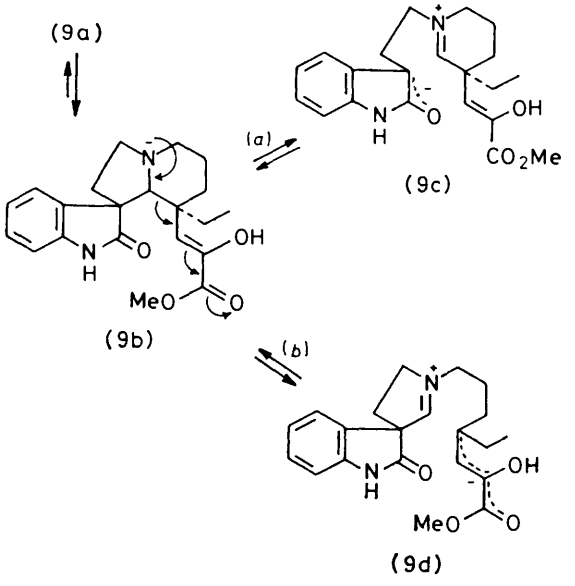
Therefore, it appears that the dominant factor in the observed scrambling of stereochemistry is the highly favourable interconversion through the intermediate (9d) [path (*b*) in Scheme 3].

Compound (9) was the only isolable product when the irradiation mixture was refluxed prior to the usual work-up; otherwise compound (9) was accompanied by the known 16-hydroxy-[3*H*]indole *N*(4)-oxide (11).

Brief comment is needed on the observed dichotomy between the behaviour of compounds (1) and (2) on changing from chloroform to methanol solvents. This is probably due to the internal dipolar interaction (see the Figure) between the N(4) centre and the distal oxygen atom of the hydroperoxide (13); it must be sufficiently long-lived to experience intermolecular reversible addition of the participant solvent (methanol) across the C=N bond to give compound (23). The presence of methanol

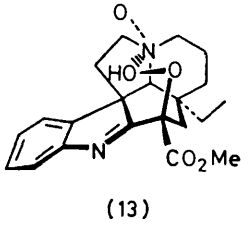
* The synthesis of compound (25) will be reported elsewhere.

is sufficient to direct the collapse of the hydroperoxide (13) towards the reduction product (11) [path (*c*) in Scheme 1] at the expense of cleavage products [paths (*a*) and (*b*), Scheme 1]. Attempts to isolate the adduct (23) or the hydroperoxide (13) were fruitless, although products derived from such a methanol addition have precedent.[28]



SCHEME 3

The above photo-oxygenation was extended to Δ^{14}-vincadifformine [compound (3), tabersonine] which cleanly afforded the indolenine (14) in 88% yield (Expt. 14), without the interference of other sensitive functional groups. Acidic work-up of the irradiated mixture, without the isolation of compound (14), gave a *ca.* 1 : 1 mixture (85%) of compounds (6) and (7), which occur in the root bark of *Crioceras dipladeniiflorus*.[29]



(13)

FIGURE

The observed locospecificity[30] in the photo-oxygenation of compound (3) which involves charge transfer to oxygen, is determined by the 'π-electron richness'[31] (*e.g.*, $\pi_{C=C}$ ionization potential) of the β-anilino-acrylic double bond *vs.* the disubstituted Δ^{14}-bond.

In conclusion, dye-sensitized photo-oxygenation of the *Aspidosperma* alkaloids vincadifformine (1) and tabersonine (3) under suitable conditions in the presence of reducing agents constitutes a useful method for their conversion into eburnane alkaloids.

EXPERIMENTAL

M.p.s are uncorrected and were determined in open ended capillaries. I.r. spectra were obtained on a Beckman 1021 spectrophotometer. U.v. spectra are for solutions in methanol on a Perkin-Elmer model 141 polarimeter. Circular dichroism spectra were determined in methanol on a Roussel–Jouan Dichrograph III. ^{1}H N.m.r. spectra were recorded on Varian EM-360, XL-100, or Bruker 90 instruments. ^{13}C N.m.r. spectra were obtained from a Varian XL-100 pulsed Fourier-transform spectrometer; chemical shifts are in p.p.m. downfield from internal $SiMe_4$. Partial proton-decoupling was used to distinguish between individual carbon atoms. Mass spectra (DIS; 70 eV) were measured on Varian 112 and CH-7 spectrometers (temperature of registration is given). T.l.c. were performed on 0.25 mm thick layers of silica gel GF_{254} (Merck) on glass plates. Solvent systems were (A) benzene–ethanol–ammonia (*d*, 0.88) (89 : 10 : 1) and (B) chloroform–methanol–ammonia (*d*, 0.88) (40 : 10 : 1). Compounds were detected on developed chromatograms by fluorescence quenching with λ 254 or 365 nm and later visualized with cerium(IV) ammonium sulphate (CAS, 1% in 85% phosphoric acid);[32] R_F (solvent systems A or B) and colour (CAS spray on t.l.c.) of products are given. Preparative layer chromatography (p.l.c.) was performed with silica gel G-60 (Merck) on glass plates (20 × 20 cm) and activated at 120 °C for 30 min prior to use. Flash chromatography (FC) was carried out as described by Still *et al.*[33] and performed with silica gel S (Merck) 230—400 mesh. All solvents were purified by standard procedures before use. 98% *m*-CPBA was obtained from commercially available material washed with phosphate buffer (pH 7.5), filtered, and dried under reduced pressure at room temperature. (−)-Vincadifformine *N*(4)-oxide (2)[3] and (−)-3-oxovincadifformine (18)[13] were prepared by the reported procedures. Photo-irradiation was performed by means of an OSRAM Concentra 350 W wire lamp (35°) at 20 °C (water cooling) with oxygen gas bubbled through the solution. The reaction mixtures were prepared by dissolving the substrate (0.1—1.0 g) and reductant, if required, into the diluted sensitizer solution (see Table 1) and the resulting mixtures were irradiated. After the products had been obtained, t.l.c. was performed. The standard work-up procedure involved filtration of sodium tetrathionate (Table 1, Expts. 8 and 10) and evaporation (<35 °C). The crude irradiated material was filtered through a pad of alumina Camag using chloroform–methanol (19 : 1) to remove the sensitiser and the products were isolated by p.l.c. or FC.

Photo-oxidation of (−)-*Vincadifformine* (1) *to give the Oxoindole* (8) *and* 3-*Oxovincadifformine* (18) (*Table* 1, *Expt.* 1).—According to the above procedure, (−)-vincadifformine (1) (100 mg, 0.29 mmol) was irradiated in a methanolic solution of Rose Bengal (6.5×10^{-5}M) (7.5 ml) for 1 h. P.l.c. (A) gave the ketone (8) (93 mg, 85%); R_F 0.32 (no colour); $\nu_{max.}$ (chloroform) 3 300, 1 720, and 1 705 cm^{-1}; $\lambda_{max.}$ (log ε) 215 (4.48), 248 (4.18), and 283 nm (3.21) [lit.,[6] $\nu_{max.}$ 3 300, 1 720, and 1 705 cm^{-1}; $\lambda_{max.}$ (log ε) 216 (4.15), 253 (3.94), and 277 nm (3.32)]; δ ($CDCl_3$) 0.77 (3 H, t, *J* 7 Hz, 19-Me), 3.84 (3 H, s, CO_2Me), 5.30 (s, 17-H), 6.75—7.60 (4 H, m, Ar-H), and 8.98br (1 H, s, exch. D_2O, 1-H); *m/z* (250 °C) 370 ($M^{+\bullet}$, 3%), 310 (31), 283 (22), 201 (17), 160 (31), 159 (19), 144 (17), 130 (19), and 124 (100); Δε ($\lambda_{max.}$) 13.0 (225 nm), −2.3 (255), and 2.4 (283); and the known 3-oxovincadifformine (18)[13] (6.2 mg; 6%), identical

with, in all respects, an authentic sample (t.l.c. and i.r. and ^{1}H n.m.r. spectroscopy).

Photo-oxidation of (−)-*Vincadifformine* (1) *in the Presence of Sodium Thiosulphate to give the* 16-*Hydroxy*-[3H]*indole* (10), *Vincamine* (4), *and* 16-epi-*Vincamine* (5) (*Expt.* 8).—Irradiation of (−)-vincadifformine (1) (1 g, 2.96 mmol) in a solution of Rose Bengal (1.5×10^{-4}M) in methanol–water (6 : 1, 75 ml) in the presence of sodium thiosulphate (701 mg, 4.44 mmol) and 2N NaOH *(1 ml) gave, after FC [benzene–triethylamine (97 : 3)], the 16-hydroxy-[3*H*]indole (10) (857 mg, 82%), R_F (A) 0.52 (orange), m.p. 112 °C (di-isopropyl ether); $\lambda_{max.}$ (log ε) 224 (4.28) and 267 nm (3.60); $[\alpha]_D$ −151° (*c* 1, chloroform); [lit.,[16] m.p. 73—75 °C; $\lambda_{max.}$ (log ε) 223 (4.28) and 272 (3.65); $[\alpha]_D$ −174°]; δ ($CDCl_3$) 0.49 (3 H, m, 19-Me), 2.28 and 2.76 (2 H, AB q, *J* 15 Hz, 17-H), 2.64 (1 H, s, 21-H), 3.96 (3 H, s, CO_2Me), 7.16—7.46 (3 H, m, Ar-H), 7.66 (1 H, dd, *J* 7 and 1 Hz, 9-H), and 8.10 (1 H, m, exch. D_2O, OH); *m/z* (280 °C) 354 ($M^{+\cdot}$, 34%), 336 (5), 325 (6), 295 (32), 266 (31), and 124 (100) (Found: C, 70.95; H, 7.35; N, 7.9. $C_{21}H_{26}N_2O_3$ requires C, 71.18; H, 7.34; N, 7.91%). To the irradiated mixture was added water–acetic acid (8 : 1, 75 ml), which contained sodium acetate trihydrate (2 g), and the mixture was heated to 70 °C for 20 min. The usual work-up (ammonia, chloroform extraction) afforded, after FC [dichloromethane–methanol (19 : 1)] (+)-vincamine (4) (480 mg, 46%), R_F (A) 0.45 (yellow), m.p. 233 °C (methanol); and (+)-16-*epi*-vincamine (5) (312 mg, 30%), R_F (A) 0.28 (yellow), m.p. 183—184 °C (methanol).

Photo-oxidation of (−)-*Tabersonine* (3) *in the Presence of Triethyl Phosphite to give the* 14,15-*Didehydro*-16-*hydroxy*-[3*H*]*indole* (14), 14,15-*Didehydrovincamine* (6), *and* 14,15-*Didehydro*-16-epi-*vincamine* (7) (*Expt.* 14).—Photo-oxygenation of (−)-tabersonine (3) (1 g, 2.97 mmol) in the presence of triethyl phosphite (1.5 ml), as previously described for compound (1), yielded the 16-hydroxy-[3*H*]indole (14) (919 mg, 88%) as an amorphous solid; R_F (A) 0.46 (orange); $\nu_{max.}$ (chloroform) 3 500, 2 810, 2 790, 1 740, and 1 610 cm^{-1}; $\lambda_{max.}$ (log ε) 222 (4.24) and 270 nm (3.65); $[\alpha]_D$ −134° (*c* 1.4, chloroform); δ ($CDCl_3$) 0.48 (3 H, m, 19-Me), 2.68br (1 H, s, 21-H), 3.99 (3 H, s, CO_2Me), 5.60br (1 H, d, *J* 10 Hz, 15-H), 5.70 (1 H, ddd, *J* 10, 4, and 1 Hz, 14-H), 7.24—7.48 (3 H, m, Ar-H), and 7.66 (1 H, dd, *J* 7 and 1 Hz, 9-H); *m/z* (200 °C) 352 ($M^{+\cdot}$, 3%), 334 (15), 305 (100), 181 (15), and 170 (30); identical in all respects to that obtained from 14,15-didehydro-16-hydroxy-[3*H*]-indole *N*(4)oxide (15). Acidic work-up of the irradiated mixture, as previously described for compound (10), yielded (+)-14,15-didehydrovincamine (6) (428 mg, 41%); R_F (A) 0.49 (yellow), m.p. 216—218 °C (methanol) [lit.,[13] 221—223 °C] and (+)-14,15-didehydro-16-*epi*-vincamine (7) (460 mg, 44%); R_F (A) 0.41 (yellow), m.p. 183—185 °C (methanol) [lit.,[13] 181—182 °C].

Photo-oxidation of (−)-*Vincadifformine* N(4)-*Oxide* (2) to *give* 16-*Hydroxy*-[3*H*]*indole* N(4)-*Oxide* (11) *and the Ketone* N(4)-*Oxide* (9) (*Expts.* 15 *and* 16).—Irradiation of (−)-vincadifformine *N*(4)-oxide (2) (1 g, 2.80 mmol) in Rose Bengal (6.5×10^{-5}M) in methanol (75 ml) afforded a nearly 1 : 1 mixture (t.l.c.) of two products. Usual work-up and FC [chloroform–methanol (8 : 2)], gave 16-*hydroxy*-[3H]-*indole* N(4)-*oxide* (11) (667 mg, 64%); R_F (B) 0.44 (no colour), m.p. 195—198 °C (acetone), $[\alpha]_D$ −137° (*c* 1.4, chloroform); $\lambda_{max.}$ (log ε) 222 (4.15) and 268 nm (3.66) [lit.,[3] m.p. 178—180 °C, $[\alpha]_D$ −107° (*c* 0.9, methanol); $\lambda_{max.}$ (log ε) 223 (4.29) and 270 nm (3.73)]; δ ($CDCl_3$) 0.63 (3 H, m, 19-H), 2.34 and 2.42 (2 H, AB q, *J* 15 Hz, 17-H), 3.70br (1 H, s, 21-H), 3.86 (3 H, s, CO_2Me), 7.12 (1 H, ddd, *J* 7, 7, and 1 Hz, 10-H), 7.48 (1 H, dd, *J* 7 and 1 Hz, 12-H), and 8.03 (1 H, dd, *J* 7 and 1 Hz, 9-H); *m/z* (250 °C) 370 ($M^{+\cdot}$, 16%), 354 (13), 352 (77), 341 (16), 295 (10), and 124 (100) (Found: C, 68.25; H, 7.05; N, 7.55. $C_{21}H_{26}N_2O_4$ requires C, 68.11; H, 7.03; N, 7.57%), identical (by t.l.c.) with an authentic sample; and the *N*-oxide (9) (357 mg, 33%), R_F (B) 0.42 (no colour), m.p. 174—176 °C (acetone–methanol); $\nu_{max.}$ (Nujol) 1 725 and 1 710 cm^{-1}; $\lambda_{max.}$ (log ε) 218 (4.40), 251 (4.18), and 285sh nm (3.21); $[\alpha]_D$ −53° (*c* 1.4; methanol); δ ($CDCl_3$) 0.63 (3 H, t, *J* 7 Hz, 19-Me), 3.60 (3 H, s, CO_2Me), 4.72 (1 H, s, 17-H), 6.80 (1 H, dd, *J* 7 and 1 Hz, 12-H), 7.18 (2-H, dt + dt, *J* 7 and 1 Hz, 10-H and 11-H), and 7.51 (1 H, dd, *J* 7 and 1 Hz, 9-H); *m/z* (250 °C) 386 ($M^{+\cdot}$, 1%), 384 (2), 370 (22), 368 (18), 311 (6), 309 (9), 281 (50), and 124 (100); $\Delta\varepsilon$ ($\lambda_{max.}$) +7.8 (225), −15.5 (255), and +0.66 (290) (Found: C, 65.1; H, 6.75; N, 7.25. $C_{21}H_{26}N_2O_5$ requires C, 65.28; H, 6.73; N, 7.25%).

Addition of excess potassium iodide in acetic acid to the irradiated mixture afforded, after usual work-up, the *N*(4)-oxide (11) in nearly quantitative yield.

When the photo-oxygenation was carried out in chloroform according to the above procedure, a nearly 1 : 1 mixture of the ketone *N*(4)-oxide (9) and the hydroperoxide [R_F (B) 0.38; monitored by t.l.c.] was obtained after 35 min. Usual work-up yielded the *N*(4)-oxide (11) (238 mg, 23%) and the ketone *N*(4)-oxide (9) (531 mg, 49%). Refluxing the irradiated mixture for 1 h prior to work-up gave the ketone (9) as the only isolable product (783 mg).

Oxidation of (−)-*Tabersonine* (3) *with* m-*Chloroperbenzoic Acid* (m-*CPBA*) *to give the* 14,15-*Didehydro*-16-*hydroxy*-[3H]-*indole* N(4)-*Oxide* (15).—*m*-CPBA (1.1 g, 6.55 mmol) was added over a 20 min period to a stirred solution of (−)-tabersonine (1 g, 2.9 mmol) in benzene (150 ml) under a nitrogen atmosphere. The mixture was stirred continuously for 24 h at room temperature, after which the solvent was removed under reduced pressure (<40 °C). The residue was charged onto a column of activated Dowex 1-X8 (3 g, 100—200 mesh) (washed with methanol) to obtain, after removal of the solvent, 800 mg of the residue. FC (chloroform–methanol (8 : 2)] afforded the pure N(4)-*oxide* (15) (418 mg, 38%); R_F (B) 0.54 (orange), m.p. 160 °C (decomp.) (acetone); $\nu_{max.}$ (chloroform) 3 500, 1 735, and 1 605 cm^{-1}; $\lambda_{max.}$ (log ε) 222 (4.15) and 270 nm (3.63); δ ($CDCl_3$) 0.70 (3 H, *J* 7 Hz, 19-Me), 1.30 (1 H, q, *J* 7 Hz, 19-H_S), 1.38 (1 H, q, *J* 7 Hz, 19-H_R), 2.30 and 2.58 (2 H, AB q, *J* 15 Hz, 17-H), 3.86br (1 H, s, 21-H), 3.98 (3 H, s, CO_2Me), 5.64br (1 H, d, *J* 10 Hz, 15-H), 5.82br (1 H, d, *J* 10 Hz, 14-H), 7.30br (1 H, t, *J* 7 Hz, 11-H), 7.36 (1 H, t, *J* 7 Hz, 10-H), 7.58br (1 H, d, *J* 7 Hz, 12-H), and 8.38br (1 H, d, *J* 7 Hz, 9-H); *m/z* (180 °C) 368 ($M^{+\cdot}$, 1%), 352 (7), 335 (26), 305 (100), 181 (22), and 170 (28) (Found: C, 68.65; H, 6.55; N, 7.6. $C_{21}H_{24}N_2O_4$ requires C, 68.48; H, 6.53; N, 7.61%).

Reduction of the N(4)-*Oxide* (15) *with Raney Nickel to give the* 16-*Hydroxy*-[3H]*indole* (14).—The *N*(4)-oxide (15) (1 g, 2.7 mmol) was dissolved in acetone (150 ml) to which was added a suspension of Raney nickel in acetone * with vigorous stirring. The resulting mixture was filtered on a short column of Celite and thoroughly washed with acetone. After removal of the solvent, the crude products were chromatographed by FC [benzene–triethylamine (97 : 3)] to give

* Added to avoid photobleaching of the sensitiser.

* To avoid over-reduction of compound (15) the Raney nickel was previously deactivated by heating in acetone to boiling point.

the 16-hydroxy-[3*H*]indole (14) (700 mg, 73%) as an amorphous solid, identical in all respects with that obtained from the photo-oxygenation of (−)-tabersonine (3) in the presence of triethyl phosphite (Expt. 14).

Reduction of 16-*Hydroxy*-[3H]*indole* (10) *by* $NaBH_3CN$ *to give the* 16-*Hydroxy-indoline* (19).—A mixture of methanol (50 ml), acetic acid (3 ml), sodium acetate trihydrate (2.1 g), and compound (10) (1 g, 2.8 mmol) was stirred during the addition, over 30 min at room temperature, of $NaBH_3CN$ (100 mg, 3.1 mmol). After 45 min overall, water (50 ml) was added and the mixture was concentrated to half-volume under reduced pressure. The pH was adjusted to 8.0 by addition of dilute ammonia and extraction with dichloromethane gave the pure *indoline* (19) (985 mg, 98%); R_F (A) 0.46 (dark orange), m.p. 102 °C (di-isopropyl ether); $\lambda_{max.}$ (log ε) 211 (4.23), 244 (3.95), and 300 nm (3.60) (lit.,[16] m.p. 75—77 °C; $\lambda_{max.}$ 215, 255, and 305 nm); $\nu_{max.}$ (chloroform) 3 420, 2 810, 1 725, and 1 605 cm^{-1}; $[\alpha]_D$ +27° (*c* 1; chloroform); δ ($CDCl_3$) 0.51 (3 H, t, *J* 7 Hz, 19-Me), 1.77 and 2.17 (2 H, AB q, *J* 15 Hz, 17-H), 2.31br (1 H, s, 21-H), 3.78 (3 H, s, CO_2Me), 4.03br (1 H, s, 2-H), 4.50 (1 H, m, exch. D_2O, OH), 6.50br (1 H, d, *J* 7 Hz, 12-H), 6.68br (1 H, t, *J* 7 Hz, 10-H), 7.06br (1 H, t, *J* 7 Hz, 11-H), 7.10 (1 H, d, *J* 7 Hz, 9-H), and 9.0—9.6 (1 H, m, exch. D_2O, 1-H); *m/z* (80 °C) 356 ($M^{+\bullet}$, 1.2%), 348 (0.5), 297 (1.1), 254 (26), 226 (4), and 124 (100); Δε ($\lambda_{max.}$) +3.25 (221), +6.3 (244), +0.55 (270), and +2.05 (304) (Found: C, 70.65; H, 7.9; N, 7.85. $C_{21}H_{28}N_2O_3$ requires C, 70.78; H, 7.86; N, 7.86%).

Acetylation of the Indoline (19) *to give* 16-*Hydroxy-indoline* N(1),O(16)-*Diacetate* (20).—Compound (19) (100 mg, 0.28 mmol) was dissolved in a mixture of acetic anhydride (1 ml) and pyridine (2 ml) in the presence of 4-dimethylaminopyridine (34 mg). After 12 h, water (30 ml) was added, the mixture was basified to pH 9.0 using dilute ammonia, and extracted with dichloromethane. Evaporation of the extract and p.l.c. (A) yielded the diacetate (20) as an amorphous *solid*; R_F (A) 0.54 (no colour); $\lambda_{max.}$ (log ε) 209 (4.15), 252 (3.83), 280 (3.60), 289 (3.56), and 304sh nm; δ ($CDCl_3$) 0.84 (3 H, m, 19-Me), 2.16 (3 H, s, AcO), 2.38 (3 H, s, AcN), 3.44 (3 H, s, CO_2Me), 4.58br (1 H, s, 2-H), 7.0—7.4 (3 H, m, Ar-H), and 7.98 (1 H, dd, *J* 7 and 1 Hz, 12-H); *m/z* (100 °C) 398 ($M^{+\bullet}$ −42, 1%), 338 (8.9), 335 (0.4), 297 (0.7), 254 (6.2), 144 (6.7), and 124 (100); Δε ($\lambda_{max.}$) +3.4 (210), −5.9 (222), −4.4 (231), +6.6 (259), and −0.7 (290).

16-*Hydroxy*-[3H]*indole* (10) *and* $NaBH_3CN$ *in the Presence of Formaldehyde:* 16-*Hydroxy*-N(1)-*methyl-indoline* (21).—16-Hydroxy-[3*H*]indole (10) (1 g, 2.8 mmol) was reduced with $NaBH_3CN$, as described above, and then aqueous formaldehyde was added to the mixture (40% w/v) (2.1 ml). The resulting solution was stirred while further $NaBH_3CN$ (300 mg) was added at room temperature over 60 min. Usual work-up and FC [benzene–triethylamine (97 : 3)] yielded the pure *indoline* (21) (858 mg, 83%); R_F (A) 0.48 (red), m.p. 137—139 °C (diethyl ether); $\nu_{max.}$ (chloroform) 3 400, 2 810, 1 735, and 1 601 cm^{-1}; $\lambda_{max.}$ (log ε) 214 (4.15), 251 (4.00), and 304 nm (3.50); $[\alpha]_D$ +14.5° (*c* 1.4, chloroform); δ ($CDCl_3$) 0.54 (3 H, m, 19-Me), 2.42br (1 H, s, 21-H), 2.69 (3 H, s, 1-Me), 3.64br (1 H, s, 2-H), 3.88 (3 H, s, CO_2Me), 6.48br (1 H, d, *J* 7 Hz, 12-H), 6.76br (1 H, t, *J* 7 Hz, 10-H), and 7.0—7.2 (2 H, m, Ar-H); *m/z* (180 °C) 370 ($M^{+\bullet}$, 17%), 352 (16), 311 (6), 293 (6), 268 (32), 226 (45), 158 (24), and 124 (100); Δε ($\lambda_{max.}$) +9.5 (248), +0.2 (274), and +0.6 (309) (Found: C, 71.4; H, 8.15; N, 7.55. $C_{22}H_{30}N_2O_3$ requires C, 71.35; H, 8.11; N, 7.56%).

16-*Hydroxy*-[3H]*indole* (10) *and Potassium Cyanide gave* 2-*Cyano*-16-*hydroxyindoline* (22).—To a stirred mixture of compound (10) (200 mg, 0.56 mmol) and 18-crown-6 ether (210 mg) in dichloromethane (25 ml) under nitrogen, was added potassium cyanide (370 mg, 15.6 mmol) in one portion. The mixture was stirred continuously for 24 h at room temperature. The mixture was then exhaustively washed with water, dried (Na_2SO_4), and the solvent removed under reduced pressure. FC of the residue [dichloromethane–acetonitrile (4 : 1)] gave the pure *cyano-derivative* (22) (150 mg, 69%); R_F (A) 0.54 (crimson), m.p. 215 °C (acetone–di-isopropyl ether); $\nu_{max.}$ (chloroform) 3 300, 2 930, 2 850, 2 225, 1 730, and 1 600 cm^{-1}; $\lambda_{max.}$ (log ε) 207 (3.76), 244 (3.85), and 296 nm (3.48); $[\alpha]_D$ +204° (*c* 1, chloroform); δ ($CDCl_3$) 0.41 (3 H, t, *J* 7 Hz, 19-Me), 1.10br (1 H, q, *J* 7 Hz, 19-H_S), 1.26br (1 H, q, *J* 7 Hz, 19-H_R), 1.82 and 2.10 (2 H, AB q, *J* 15 Hz, 17-H), 3.80 (3 H, s, CO_2Me), 5.38br (1 H, s, exch. D_2O, OH), 7.18br (1 H, d, *J* 7 Hz, 9-H), 6.90br (1 H, t, *J* 7 Hz, 10-H), 7.22br (1 H, t, *J* 7 Hz, 11-H), and 9.20 (1 H, m, exch. D_2O, 1-H); *m/z* (180 °C) 381 ($M^{+\bullet}$, 2%), 354 (4), 295 (4), 252 (4), and 124 (100); Δε ($\lambda_{max.}$) +12.6 (213), +16.2 (243), +1.1 (267), and +4.45 (297) (Found: C, 69.15; H, 7.05; N, 11.05. $C_{22}H_{27}N_3O_3$ requires C, 69.30; H, 7.08; N, 11.02%). The *title compound* (22) (50 mg) was stirred in the dark overnight in acetonitrile (5 ml) in the presence of silver tetrafluoroborate (80 mg). The mixture was then concentrated to small volume, poured into water, and the pH adjusted to 9 with dilute ammonia. Usual work-up and p.l.c. (A) gave pure compound (10) in quantitative yield.

16-*Hydroxy*-[3H]*indole* (10) *with Potassium Cyanate to give the Oxazolidinone* (24).—To a stirred mixture of 16-hydroxy-[3*H*]indoline (10) (200 mg, 0.56 mmol) and 18-crown-6 ether (210 mg) under nitrogen, was added potassium cyanate (100 mg, 1.23 mmol) in one portion and the mixture was stirred for 24 h at room temperature. Usual work-up and FC [chloroform–methanol (19 : 1)] gave the *oxazolidinone* (24) (152 mg, 68%); R_F (A) 0.32 (crimson), m.p. 173 °C (decomp.) (ethyl acetate); $\nu_{max.}$ (chloroform) 3 438, 2 910, 2 855, 1 750, 1 740, and 1 600 cm^{-1}; $\lambda_{max.}$ (log ε) 216 (3.78), 242 (3.86), and 297 nm (3.53); $[\alpha]_D$ +37.8° (*c* 1, chloroform); δ ($CDCl_3$) 0.57 (3 H, t, *J* 7 Hz, 19-Me), 2.40br (1 H, s, 21-H), 3.86 (3 H, s, CO_2Me), 4.54 (1 H, s, exch. D_2O, 1-H), 6.49br (1 H, d, *J* 7 Hz, 12-H), 6.73br (1 H, t, *J* 7 Hz, 10-H), 6.80 (1 H, s, exch. D_2O, CO_2NH), 6.92br (1 H, t, *J* 7 Hz, 11-H), and 7.06br (1 H, d, *J* 7 Hz, 9-H); *m/z* (250 °C) 397 ($M^{+\bullet}$; 8%), 354 (8), 336 (2), 295 (10), and 124 (100); Δε ($\lambda_{max.}$) −9.0 (212), +4.55 (244), +1.15 (272), and +2.75 nm (298) (Found: C, 66.3; H, 6.85; N, 10.55. $C_{22}H_{27}N_3O_4$ requires C, 66.50; H, 6.80; N, 10.58%).

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