Preparation of 2-Acyl- and 2-Alkoxycarbonyl-octahydroindolo[2,3-*a*]-quinolizines

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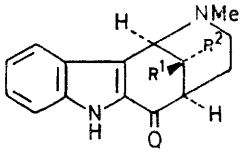
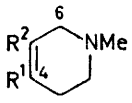
A method for the synthesis of 2-acyl- and 2-alkoxycarbonyl-octahydroindolo[2,3-*a*]quinolizines is described which involves as a key step the isomerisation of a 4-acyl- or 4-alkoxycarbonyl-1-[2-(indol-3-yl)ethyl]-1,2,3,6-tetrahydropyridine to a 4-acyl- or 4-alkoxycarbonyl-1-[2-(indol-3-yl)ethyl]-1,2,3,4-tetrahydropyridine (not isolated). This, in turn, in reacting as a cyclic enamine, provides by protonation an electrophilic centre for closure on to the indole α-position. The 4-acyl-1-[2-(indol-3-yl)ethyl]-1,2,3,6-tetrahydropyridines can be cyclised in an alternative manner to give compounds comprising four of the five skeletal rings of the *Iboga* alkaloids.

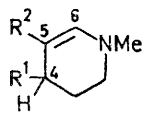
We recently described the syntheses,[1] in racemic form, of the 2-acylindole alkaloids dasycarpidone (1a) and 3-*epi*-dasycarpidone (1b) and their 3-de-ethyl analogue (1c). The key process in the syntheses of these compounds involved the isomerisation of a 1,2,3,6-tetrahydropyridine (2) to a 1,2,3,4-tetrahydropyridine †



(1)



(2)



(3)

	R^1	R^2
a;	Et	H
b;	H	Et
c;	H	H

(3) (not isolated). This species was then able, in subsequent reaction as a cyclic enamine and addition of a proton at C-5, to provide the means for generating the electrophilic character at C-6 required for ring closure on to an indole nucleus.

The isomerisation was achieved by activating the C-6 protons for abstraction by a 4-acyl group in conjugation with the double bond. Thus, treatment of a 4-acyl-1,2,3,6-tetrahydropyridine (2; R^1 = indol-2-ylcarbonyl, R^2 = Et or H) with strong base followed by water gave a species (3; R^1 = indol-2-ylcarbonyl, R^2 = Et or H) as a non-isolable [1] intermediate. In the de-ethyl-series (2; R^2 = H) the isomerisation *and* further protonation at C-5 *and* cyclisation could be brought about smoothly, simply by treatment with acetic acid, a sequence which probably proceeds by way of proton-catalysed enolisation and reketonisation to (3; R^2 = H) as a first step.

We have now extended the synthetic concept just outlined to provide another [4] means for the preparation of the octahydroindolo[2,3-*a*]quinolizine system which is present in many indole alkaloids. This approach to the nucleus produces compounds carrying a substituent at C-2, of potential value in the syntheses of alkaloids containing such skeleta.

Cyclisations to 2-Benzoyloctahydroindolo[2,3-a]*quinolizines.*—The bromide (4a) obtained from 1-bromo-2-(indol-3-yl)ethane [5] and 4-benzoylpyridine was reduced [6] with sodium borohydride to give the alcohol (5a). Manganese dioxide converted the allylic alcohol into the conjugated ketone (5b). Treatment of this ketone with either methanolic sodium methoxide or

† There is evidence [2] that 1,2,3,4-tetrahydropyridines are thermodynamically less stable than their 1,2,3,6-tetrahydropyridine isomers.[3]

[1] A. Jackson, N. D. V. Wilson, A. J. Gaskell, and J. A. Joule, *J. Chem. Soc.* (*C*), 1969, 2738.

[2] E. Wenkert, K. G. Dave, F. Haglid, R. G. Lewis, T. Oishi, R. V. Stevens, and M. Terashima, *J. Org. Chem.*, 1968, **33**, 747.

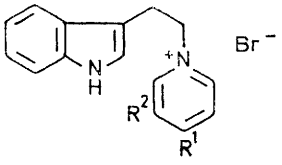
[3] However, see also S. Danishefsky and R. Cavanaugh, *J. Org. Chem.*, 1968, **33**, 2959.

[4] A. Lettis, M.-M. Janot, and D. Van Stolk, *Bull. Soc. chim. France*, 1958, 551; J. Thesing and W. Festag, *Experientia*, 1959, **15**, 127; E. E. van Tamelen and J. B. Hester, *J. Amer. Chem. Soc.*, 1959, **81**, 3805; Y. Ban and M. Seo, *Tetrahedron*, 1961, **16**, 5; E. Wenkert, R. A. Massey-Westropp, and R. G. Lewis, *J. Amer. Chem. Soc.*, 1962, **84**, 3732; J. H. Supple, O. A. Nelson, and R. E. Lyle, *Tetrahedron Letters*, 1963, 1645; K. T. Potts and I. D. Nasri, *J. Org. Chem.*, 1964, **29**, 3407; E. Winterfeldt, *Chem. Ber.*, 1964, **97**, 2463; Cs. Szántay, L. Töke and M. Honti,, *Tetrahedron Letters*, 1965, 1665; H. J. Teuber, *Angew. Chem. Internat. Edn.*, 1965, **4**, 260; E. Wenkert, K. G. Dave, and F. Haglid, *J. Amer. Chem., Soc.*, 1965, **87**, 5461; E. E. Markaryan, *Chem. Abs.*, 1966, **64**, 17,562f; E. Winterfeldt and H. Radunz, *Chem. Ber.*, 1967, **100**, 1680; J. A. Beisler, *Tetrahedron*, 1970, **26**, 1961.

[5] R. C. Elderfield and B. Fisher, *J. Org. Chem.*, 1958, **23**, 949.

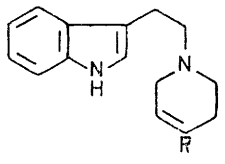
[6] R. E. Lyle and P. S. Anderson, *Adv. Heterocyclic Chem.*, 1966, **6**, 55.

sodium hydride–dimethyl formamide yielded an unstable material (see later) from which, by treatment with methanol–glacial acetic acid, a mixture of the stereoisomeric, ring-closed derivatives (6a) and (7a) was obtained.



(4)

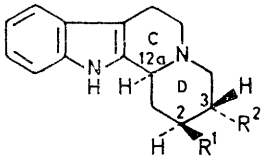
	R^1	R^2
a;	Bz	H
b;	Ac	H
c;	$-C(Me)\cdot O\cdot CH_2\cdot CH_2\cdot O-$	H
d;	MeO_2C	H
e;	H	OMe



(5)

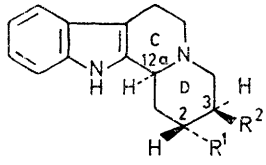
	R
a;	PhCH·OH
b;	Bz
c;	H
d;	MeCH·OH
e;	Ac
f;	$-C(Me)\cdot O\cdot CH_2\cdot CH_2O-$
g;	MeO_2C

The instability of the intermediate precluded a full characterisation; nevertheless, mass spectral measurements on freshly prepared material and its chemical reactivity are in full accord with an enamine formulation (8). The mass spectrum, while still having an important (17%) ion corresponding to cleavage *a* [in (8)] showing the tetrahydropyridine ring to be attached to the indole still only *via* the two-carbon chain at the β-position, had as a base peak an ion at *m/e* 105 ($PhCO^+$) from the now favoured allylic fission at *b* [in (8)]. The corresponding ion in the spectrum of the starting material was relatively unimportant (16%).



(6)

	R^1	R^2
a;	Bz	H
b;	H	Et
c;	PhCH·OH	H
d;	Ac	H
e;	MeO_2C	H
f;	$HO\cdot CH_2$	H
g;	$AcO\cdot CH_2$	H



(7)

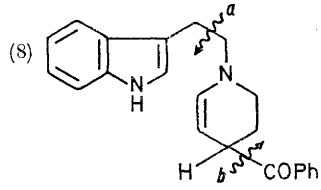
	R^1	R^2
a;	Bz	H
b;	H	Et
c;	PhCH·OH	H
d;	Ac	H
e;	MeO_2C	H
f;	$HO\cdot CH_2$	H
g;	$AcO\cdot CH_2$	H

Chemical confirmation for the formulation as a cyclic enamine for the unstable intermediate came from its reduction with sodium borohydride and its reaction with acid. The reduction gave the piperidine alcohol (9a) identified by a comparison of its acetate with that of authentic material prepared by the catalytic reduction of the salt (4a). Since the conjugated ketone (5b) gave *only* the unsaturated alcohol (5a) on treatment with sodium borohydride the formation of (9a) from the methoxide product is evidence that the double bond is in the enamine position where it would be expected to be reduced by borohydride in a hydroxylic solvent.[6]

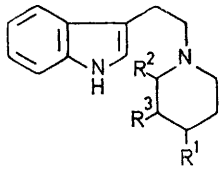
Compound (8) required only treatment with glacial acetic acid at room temperature for a short time to effect cyclisation. The conjugated ketone was recovered unchanged from solution in acetic acid after a comparable time at room temperature. This further substantiates the view that the unstable material is an enamine which easily protonates to lead to ring closure.

It seems then that in this system the 1,2,3,4-tetrahydropyridine can be formed (MeOH–MeO^-) by a thermodynamically controlled equilibration [2a] of the 1,2,3,6-tetrahydropyridine conjugated ketone.

Two other less likely possibilities for the structure of the unstable intermediate should be mentioned. The

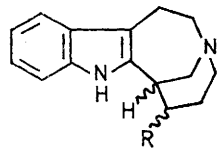


(8)



(9)

	R^1	R^2	R^3
a;	PhCH·OH	H	H
b;	Bz	OH	H
c;	Bz	H	MeO
d;	H	H	MeO



(10)

	R
a;	Bz
b;	Ac

first of these is the carbinolamine (9b) (or its methyl ether). Though this structure is consistent with the chemical evidence and the spectroscopic data, it would be necessary to postulate loss of water, either thermally or after ionisation, to meet the observation that the molecular ion observed in the mass spectrum corresponds to the enamine formulation, *i.e.* *M* for (9b) — H_2O.

The second possibility is the formulation (9c), which could be formed by a Michael-type addition to the starting conjugated ketone. In order to test the feasibility of the capability of such a structure to show the chemical properties of the intermediate, we prepared (see Experimental section) the model compound (9d). The methoxy-model was unchanged by treatment with sodium borohydride or glacial acetic acid. Neglecting any special factors, which would have to be associated with the presence of the benzoyl residue, it thus seems that a 3-methoxypiperidine would not react in the way in which the unstable intermediate behaves.

With the transformation of (2; R^1 = indol-2-ylcarbonyl, R^2 = H) directly to the cyclised system (1c) with acid in mind,[1] the conjugated ketone (5b) was treated with methanol–glacial acetic acid and indeed a clean conversion into a mixture of the octahydroindolo[2,3-*a*]quinolizines (6a) and (7a) took place in high yield. This process must involve a series of prototropic equilibria starting with enolisation of the unsaturated ketone system, leading to an immonium species necessary for a final, irreversible ring-closure

step. It is significant that neither the alcohol (5a) nor a compound (5c) having no substituent at C-4 were changed by comparable treatment with acetic acid.

The cyclised structures of the products were clearly evident from their spectra. Both compounds showed u.v. absorption corresponding to a sum of indole and benzoyl chromophores, and the normal phenyl ketone i.r. absorption. In their mass spectra, in addition to ions for the loss of the C-2 substituent, fragment ions appeared at $M - 1$, and *m/e* 184, 170, 169, and 156 all of which are typical [7] of tetrahydro-β-carboline derivatives. Further, the n.m.r. spectra did not show either indole α-proton or ethylenic hydrogen signals.

The relative stereochemistry of the two isomers (relative stereochemistry of 2- and 12a-H) follows from their n.m.r. and i.r. spectra and from their relative thermodynamic stabilities. The isomer assigned structure (7a) displayed a downfield signal at τ 6·04 for 12a-H whereas the other isomer (6a) gave no aliphatic hydrogen signal below τ 6·5. In general the relevant angular proton in *cis*-octahydroindolo[2,3-*a*]quinolizine systems resonates at much lower field (below τ 6·2) than one in an analogous *trans*-fused system.[8] In the present case the isomer (6a) can adopt a favoured *trans*-C–D ring junction stereochemistry while all groups attached to the D-ring are equatorial. The other isomer (7a) cannot do this without at least one axial D-ring substituent. Of a comparable pair of stereoisomers,[9] the 3-ethyloctahydroindolo[2,3-*a*]quinolizines (6b) and (7b), isomer (6b), in which the ethyl substituent is equatorial when the molecule adopts a *trans*-C–D ring junction, showed strong Bohlmann absorption and no especially low n.m.r. signal for 12a-H. In the other isomer (7b), weaker Bohlmann absorption and an n.m.r. signal at τ 6·22 for 12a-H led to the suggestion [9] that this isomer takes up a conformation intermediate between simple *cis*- and *trans*-C–D ring junctions. In so doing it partially loses the stereochemical requirements for strong Bohlmann absorption [10] and partially acquires those necessary for a low-field 12a-H signal.

It seems that in the present situation isomer (7a) similarly adjusts its overall conformation to minimise interactions and hence displays a low-field signal for 12a-H and much weaker bands in the 2600—2850 cm^{-1} region than its isomer.

Chemical substantiation for the stereochemical assignments was obtained from equilibration studies on the isomers. In both acid [glacial acetic acid at 140°; ratio of (6a) to (7a) 8 : 1] and base [MeO^-–MeOH at 30°; ratio of (6a) to (7a) 1·6 : 1] the isomer assigned as (6a), *i.e.* the isomer which can have both a *trans*-C–D ring junction *and* an equatorial C-2 substituent, was the more stable. That the acetic acid equilibration was effected by epimerisation at C-2 and not at C-12a [11] was shown by the failure of the alcohols (6c) and (7c) to equilibrate in refluxing methanol–glacial acetic acid.

When the acid treatment of (5b) was stopped after 10 min (80% conversion) the ratio of (6a) to (7a) was the same as that after complete reaction (45 min). Since this ratio favours (6a) by more than the equilibrium value it is clear that the more stable isomer is also formed faster. In closely similar cyclisations no stereospecificity [9] and highly stereospecific formation of the less stable isomer [12] have been reported. Clearly not all the factors governing such cyclisations are yet understood,

Cyclisation to 2-Acetyloctahydroindolo[2,3-a]*quinolizines.*—The acetyl analogues (6d) and (7d) were prepared along similar lines. Reaction of 1-bromo-2-(indol-3-yl)ethane with 4-acetylpyridine gave a salt (4b) which was reduced with sodium borohydride to (5d) and then oxidised to (5e). This conjugated ketone was obtained in better overall yield by reaction of the bromo-compound with the ethylene acetal of 4-acetylpyridine to give (4c), reduction then giving (5f) which by a final transacetalisation with acetone gave (5e). Complex mixtures were obtained by sequential treatment with base and acid; however, cyclisation proceeded smoothly in methanol–glacial acetic acid to give a mixture of the stereoisomers (6d) and (7d).

The structure and relative stereochemistry of the two products follows from a series of arguments parallel to those employed for the benzoyl analogues (see Experimental section for relevant spectral measurements). Thus, both had mass spectra typical of tetrahydro-β-carbolines, saturated ketonic carbonyl i.r. bands, indolic u.v. spectra, and no n.m.r. signals for olefinic or indole-α-hydrogen. The isomer to which structure (7d) is assigned had a low-field resonance for 12a-H at τ 6·25 and weaker Bohlmann absorption than had isomer (6d). As in the benzoyl series, the more stable [MeOH–MeO^-, room temp.; ratio of (6d) to (7d) 7·8 : 1] isomer was formed faster, the product ratio at the end of cyclisation being 5 : 1 in favour of (6d).

Cyclisation to 2-Methoxycarbonyloctahydroindolo[2,3-a]*quinolizines.*—The preparation of the esters * (6e) and (7e) by our method proved to be more difficult than the preparation of the ketones just described; nevertheless the compounds were finally obtained in good yield. The starting material (5g) was directly obtained from the salt (4d) by borohydride reduction without the need for an oxidative step. Methanol–glacial acetic acid was without effect on the conjugated

* The hydrochloride of one of these esters has been prepared [13] by an alternative method.

[7] H. Budzikiewicz, C. Djerassi, and D. H. Williams, 'Structure Elucidation of Natural Products by Mass Spectrometry,' vol. 1, Alkaloids, Holden-Day, San Francisco, 1964.

[8] M. Uskovic, H. Bruderer, C. von Planta, T. Williams, and A. Brossi, *J. Amer. Chem. Soc.*, 1964, **86**, 3364; W. E. Rosen and J. N. Schoolery, *ibid.*, 1961, **83**, 4816.

[9] E. Wenkert and B. Wickberg, *J. Amer. Chem. Soc.*, 1962, **84**, 4914.

[10] J. Skolik, P. J. Kreuger, and M. Wiewiorowski, *Tetrahedron*, 1968, **24**, 5439 and references cited therein.

[11] A. J. Gaskell and J. A. Joule, *Tetrahedron*, 1967, **23**, 4063.

[12] G. C. Morrison, W. Cetenko, and J. Shavel, *J. Org. Chem.*, 1967, **32**, 4089.

[13] Y. Ban and T. Kimuna, *Chem. and Pharm. Bull.* (*Japan*), 1968, **16**, 549.

ester over periods of time comparable to those employed successfully to cyclise the conjugated ketones. However, after reflux for two days followed by re-esterification with methanolic hydrogen chloride (see also later) the two isomeric esters (6e) and (7e) were formed cleanly. Treatment of the conjugated ester with sodium hydride in dry dimethylformamide also resulted, after subsequent treatment with methanolic hydrogen chloride, in a good yield of a mixture of the esters (6e) and (7e). It is not yet clear at what stage hydrolysis of the ester group occurs in these two alternative cyclisation sequences. The product esters were only partially hydrolysed by treatment with methanol–glacial acetic acid under the conditions of their preparation. It was shown that the starting conjugated ester was unchanged by methanolic hydrogen chloride and thus it can at least be concluded that treatment with both acetic acid and strong base transformed starting material into a new compound which *either* then cyclised *or* could be subsequently cyclised by methanolic hydrogen chloride.

It is of interest that the ratio of (6e) to (7e) from the base–acid cyclisation sequence varied with the rigour of drying of the dimethylformamide. No equilibration of the product esters occurred in methanolic hydrogen chloride and the differing ratio must then reflect some effect in the cyclisation step. When fewer precautions were taken, the isomer (7e), the less stable isomer (see later), was the major product. This contrasts with the foregoing ketone product ratios. The greater the rigour of drying, the greater the percentage of isomer (6e) in the product mixture and thus the more parallel with the ketone cyclisations the process became.

Again, the relative stereochemistry of the two product esters follows from spectral measurements on the esters, their lithium aluminium hydride reduction products (6f) and (7f), and the *O*-acetates (6g) and (7 g) of these. The arguments follow exactly parallel lines to those for their benzoyl and acetyl analogues (see Experimental section for details).

Additional chemical evidence for the relative stereochemistry of the two esters and indeed for the presence of a tetrahydro-β-carboline nucleus came from their oxidation with mercury(II) acetate. This reagent oxidises [14] such compounds to dihydro-β-carbolinium salts with characteristic u.v. absorption. Systems with *trans*-C–D ring junctions react faster than those with *cis*-junctions. In the present instance isomer (6e) reacted faster than isomer (7e).

The synthetic work just described has focused our attention on the more general question of the relative stabilities [2a] of 1,2,3,6- and 1,2,3,4-tetrahydropyridines and the influence of substituents, *e.g.* 4-acyl groups. We hope to report further on this matter elsewhere.

Cyclisation to Compounds with Partial Iboga *Skeleta.*—In the course of our investigations of conditions to effect acid-catalysed cyclisation of the 4-acyl-1,2,3,6-tetrahydropyridines (5b) and (5e), we found that they could be made to undergo an alternative type of closure with mineral acid. A large variety of acidic conditions have failed to bring about a comparable closure of the corresponding ester (5 g). When the conjugated phenyl ketone (5b) was treated with 2N-hydrochloric acid and the conjugated methyl ketone (5e) with 10N-hydrochloric acid two pairs of isomers were formed to which we assign the structures (10a) and (10b) respectively.

The structural assignments for these compounds, which contain four of the five skeletal rings of the *Iboga* alkaloids, are supported by their spectra. Their u.v. spectra were typically indolic, their n.m.r. spectra showed no signals for ethylenic or indole-α-hydrogen, and their i.r. carbonyl bands were 25—50 cm^{-1} higher than in the precursory conjugated ketones. Combined with the absence of Bohlmann absorption in any of the four compounds, their mass spectral fragmentation, which was not tetrahydro-β-carboline in type, and their method of preparation, these data are most consistent with the formulations (10a) and (10b). As models clearly show, in these structures the ring system does not permit the correct orientation of nitrogen lone pair and C(α)-H for Bohlmann absorption. Equilibration studies [MeO^-–MeOH; room temperature; ratio of major product (10a) to minor product (10a) 2·5 : 1; ratio of major product (10b) to minor product (10b); 4·9 : 1] showed that in each case the more abundant isomer produced was also the more stable; however, neither spectral data nor an inspection of models permit an assignment of the relative stereochemistry of the two pairs of stereoisomers. Compounds with this ring system, but without the acyl substituent, have been synthesised [15] by a completely different route. Their mass spectra are entirely comparable with those of (10a) and (10b).

It was shown that the 2-benzoyloctahydroindolo-[2,3-*a*]quinolizines were not converted into the compounds (10a) by treatment with 2N-acid and, in a reverse sense, compounds (10a) were not transformed into the tetrahydro-β-carboline derivatives by refluxing acetic acid. The alternative type of ring closure must involve interaction of the indole α-position with the *O*-protonated-αβ-unsaturated ketone system. Precedents for such cyclisations exist.[16] The acetic acid-catalysed closures described in the first part of this paper must also involve *O*-protonation as the first of a series of steps. The factor(s) which dictate the different pathways in the two cases may be associated with ion pairing in acetic acid.

EXPERIMENTAL

For general comments see ref. 1.

4-Benzoyl-1-[2-(indol-3-yl)ethyl]pyridinium Bromide (4a).—A solution of 4-benzoylpyridine (4·8 g) and 1-bromo-2-(indol-3-yl)ethane [5] (5·3 g) in ethanol (20 ml) was refluxed for

[14] See for example, W. F. Trager, J. D. Phillipson, and A. H. Beckett, *Tetrahedron*, 1968, **24**, 2681.

[15] Do Khac Manh Duc and M. Fétizon, *Bull. Soc. chim. France*, 1966, 771; 1969, 4154.

[16] G. C. Morrison, R. O. Waite, and J. Shavel, *J. Org. Chem.*, 1967, **32**, 2555; H. Zinnes, F. R. Zuleski, and J. Shavel, *ibid.* 1969, **34**, 3165.

6 h. After a further 24 h at room temperature the solution was poured into dry ether (200 ml) and the product was filtered off and recrystallised, to give the *salt* (4a) (4·35 g), m.p. 196—198° (decomp.) (from EtOH), $\lambda_{max.}$ 218 and 272 nm (log ε 4·66 and 4·22), $\nu_{max.}$ (Nujol) 3220br, and 1660s cm^{-1} (Found: C, 64·8; H, 4·9; N, 6·6. $C_{22}H_{19}BrN_2O$ requires C, 64·9; H, 4·7; N, 6·9%).

1,2,3,6-*Tetrahydro*-4-(α-*hydroxybenzyl*)-1-[2-(*indol*-3-*yl*)-*ethyl*]*pyridine* (5a).—(a) The bromide (4a) (3·8 g) was reduced in ethanol solution with excess of sodium borohydride for 2 h at room temperature. Solvent was evaporated off and the residue was partitioned between ether and water. The ethereal layer was extracted with 2N-hydrochloric acid, and the acid extract was made basic and extracted with ether. The dried ether extract was evaporated to give the *alcohol* (5a), (2·03 g), m.p. 141—144° (from Me_2CO), $\lambda_{max.}$ 221, 275, 282, and 290 nm (log ε 4·61, 3·74, 3·78, and 3·72), $\nu_{max.}$ ($CHCl_3$) 3600s, 3480s, 2810s, and 2765m cm^{-1}, τ[(CD_3)CO] 0·06br (1H, HN), 4·23 (1H, s, HC:C), 5·64br (1H, HO), and 6·93 (2H, d, *J* 2 Hz, C:CH·C*H*$_2$N), *m/e* 332 (M^+, 2%), 314(6), 203(15), 202(100), 173(23), 144(9), 130(10), 105(19), 77(12), and 42(16), metastable ions at 297·1 (332 → 314) and 148·2 (202 → 173) (Found: C, 79·2; H, 7·8; N, 8·5. $C_{22}H_{24}N_2O$ requires C, 79·6; H, 7·3; N, 8·45%).

(b) The ketone (5b) (17 mg) was reduced with sodium borohydride (50 mg) in methanol for 1·5 h at −78° and then with more reagent (80 mg) at room temperature for 24 h. The solution was evaporated and the residue was partitioned between aqueous potassium carbonate and ether. The ethereal layer gave the alcohol (5a) (15 mg) identical in all respects with that prepared in (a).

4-*Benzoyl*-1,2,3,6-*tetrahydro*-1-[2-(*indol*-3-*yl*)*ethyl*]*pyridine* (5b).—The alcohol (5a) (270 mg) in methylene dichloride (50 ml) was oxidised with manganese dioxide[17] (2·7 g) for 30 min at room temperature. The oxidant was filtered off and the filtrate was evaporated to give the *ketone* (5b) (190 mg) (amorphous), $\lambda_{max.}$ 221 and 289 nm (log ε 4·58 and 3·75), $\lambda_{infl.}$ 242, 282, and 290 nm, $\nu_{max.}$ (CCl_4) 3490s, 3380br,d, 2805s, 2770m, 2730m, and 1655s cm^{-1}, τ 1·77br (1H, HN), 2·98br (1H, s, sharpened on addition of D_2O, indolyl-2-H), 3·48br (1H, HC:C), 6·66 (2H, d, *J* 3 Hz, C:CH·C*H*$_2$N), *m/e* 330 (M^+, 20%), 225(18), 201(16), 200(100), 144(13), 143(8), 105(16), and 77(13) [Found: *M* (mass spectrometry) 330·1728; $C_{22}H_{22}N_2O$ requires *M*, 330·1732].

2-*Benzoyloctahydroindolo*[2,3-a]*quinolizines* (6a) *and* (7a).—A solution of the ketone (5b) (410 mg) in degassed methanol (15 ml) and degassed glacial acetic acid (50 ml) was heated under reflux for 45 min. The solution was evaporated and the residue was partitioned between aqueous potassium carbonate and chloroform. The dried organic phase was evaporated to give a gum (400 mg) purified by dry column chromatography on silica gel MFC. Elution with ethyl acetate gave firstly the *isomer* (6a) (217 mg), m.p. 178—180° (from aqueous MeOH), $\lambda_{max.}$ 227, 275, 282, and 290 nm (log ε 4·56, 3·90, 3·92, and 3·85), $\nu_{max.}$ ($CHCl_3$) 3470s, 2800s, 2750s, 2700w, 2670w, and 1680s cm^{-1}, τ 1·97br (1H, HN), 2·0—3·05 (9H, m, *H*Ar), and 6·5—8·3 (12H, m), *m/e* 330 (M^+, 83%), 329(47), 225(100), 210(32), 197(59), 184(66), 170(14), 169(24), 156(27), 105(19) 96(20), and 77(22) (Found: C, 79·5; H, 6·8; N, 7·9. $C_{22}H_{22}N_2O$ requires C, 80·0; H, 6·7; N, 8·5%), and secondly the *isomer* (7a) (88 mg), m.p. 171—173° (from aqueous MeOH), $\lambda_{max.}$ 227, 275, 282, and 290 nm (log ε 4·60, 3·91, 3·92, and 3·85), $\nu_{max.}$ ($CHCl_3$) 3470s, 2815m, 2765w, and 1680s cm^{-1}, τ 1·98br (1H, HN), 2·0—3·1 (9H, m, *H*Ar), 6·04 [1H, d (finely split further), *J* 8 Hz, 12a-H], and 6·45—8·2 (11H, m), *m/e* 330 (M^+, 91%), 329(42), 225(100), 223(29), 210(27), 197(96), 184(98), 170(13), 169(29), 156(31), 105(24), 96(22), and 77(24) (Found: C, 75·6; H, 7·1; N, 7·9. $C_{22}H_{22}N_2O$,MeOH requires C, 76·3; H, 7·25; N, 7·75%).

2-(α-*Hydroxybenzyl*)*octahydroindolo*[2,3-a]*quinolizines* (6c) *and* (7c).—These were prepared by reduction of the ketones (6a) and (7a) (5 mg) with sodium borohydride in 95% ethanol at room temperature for 1 h to give respectively the *alcohol* (6c) (5 mg) (amorphous) separated into diastereoisomers by t.l.c., with benzene–ethyl acetate–methanol (8 : 8 : 1) as eluant to give one *diastereoisomer* (R_F 0·5) (amorphous) $\lambda_{max.}$ 225, 283, and 290 nm, $\lambda_{infl.}$ 275 nm, *m/e* 332 (M^+, 91%), 331(65), 226(19), 225(100), 223(13), 197(10), 196(10), 184(18), 170(7), 169(12), and 156(12) [Found: *M* (mass spectrometry) 332·1884. $C_{22}H_{24}N_2O$ requires *M*, 332·1889] and the other *diastereoisomer* (R_F 0·4), $\lambda_{max.}$ 225, 283, and 290 nm, $\lambda_{infl.}$ 275 nm, *m/e* 332 (M^+, 84%), 331(66), 226(20), 225(100), 223(14), 197(10), 196(10), 184(18), 170(7), 169(14), and 156(12), and the *alcohol* (7c) (5 mg) (amorphous) single isomer on several t.l.c. systems, $\lambda_{max.}$ 226, 274, 282, and 290 nm, $\nu_{max.}$ ($CHCl_3$) 3610m, 3475s, 2810w, and 2755w cm^{-1}, *m/e* 332 (M^+, 78%), 331(64), 226(19), 225(100), 223(14), 197(11), 196(11), 184(19), 170(8), 169(14), and 156(13) [Found: *M*, (mass spectrometry) 332·1886. $C_{22}H_{24}N_2O$ requires *M*, 332·1889] (Found: *m/e* 225·1398. $C_{15}H_{17}N_2$ requires *m/e* 225·1392).

4-*Benzoyl*-1,2,3,4-*tetrahydro*-1-[2-(*indol*-3-*yl*)*ethyl*]*pyridine* (8); *the* '*Unstable Intermediate*.'—To a solution of degassed 1% sodium methoxide in methanol (15 ml) refluxing under nitrogen, was added the ketone (5b) (50 mg) in degassed methanol (15 ml). After being refluxed for 20 min the solution was neutralised with 2% acetic acid in methanol. Solvent was evaporated off and the residue was partitioned between aqueous potassium carbonate and chloroform. The dried chloroform extract was analysed by t.l.c.; no starting material was present. Streaking was observed in all t.l.c. systems employed. In a trial purification by t.l.c. no improvement in purity was observed. The mass spectrum was measured immediately after isolation; *m/e* 330 (M^+, 19%), 329(7), 225(30), 202(9), 200(17), 197(11), 184(17), 183(37), 145(31), 144(52), 130(26), 105(100), and 77(43).

4-(α-*Hydroxybenzyl*)-1-[2-(*indol*-3-*yl*)*ethyl*]*piperidine* (9a) *and its Acetate*.—(a) The salt (4a) (200 mg) in ethanol (20 ml) was hydrogenated over platinum at 60 lb in^{-2} for 40 h. The solution was filtered and evaporated. The residue was partitioned between aqueous potassium carbonate and chloroform to give the *alcohol* (9a) as a brown gum (180 mg), characterised as its acetate (see later).

The alcohol (9a) (180 mg) was treated with acetic anhydride–pyridine (4 : 1; 3 ml) at room temperature overnight. Solvent was evaporated off and the residue was partitioned between aqueous potassium carbonate and chloroform to give a brown gum purified by t.l.c. Development with ethyl acetate gave the *acetate of* (9a), R_F 0·2—0·5 (109 mg) (amorphous), $\lambda_{max.}$ 221, 274sh, 282, and 290 nm, $\nu_{max.}$ ($CHCl_3$) 3480s, 2940s, 2855m, 2810m, 2770m, and 1733vscm^{-1}, τ($CDCl_3$) 1·37br (1H, s, HN), 3·16br (1H, s,

[17] M. Harfenist, A. Bavley, and W. A. Lazier, *J. Org. Chem.*, 1954, **19**, 1608.

sharpened after addition of D_2O, indolyl-2-H), 4·49 (1H, d, J 7 Hz, AcO·C*H*), and 7·97 (3H, s, $MeCO_2$), *m/e* 376 (M^+, 1%), 247(16), 246(100), 186(15), 144(13), 143(9), 130(21), 117(8), 115(9), 91(11), 77(9), 43(48), 42(19), and 41(8), metastable ions at 169·1 (246 → 204) and 140·9 (246 → 186) [Found: M, (mass spectrometry) 376·2138. $C_{24}H_{28}N_2O_2$ requires M, 376·2151], (Found: *m/e* 246·1489. $C_{15}H_{20}NO_2$ requires *m/e* 246·1494).

(b) The ketone (5b) (154 mg) in degassed methanol (4·5 ml) was added to a refluxing 1% solution (40 ml) of sodium methoxide in degassed methanol and the refluxing was continued under nitrogen for 20 min. The solution was cooled to −78° and exactly neutralised with 10% acetic acid in methanol; sodium borohydride (0·5 g) in methanol (15 ml) was then added. After 1·5 h at −78°, the solution was warmed to room temperature and neutralised with acetic acid, and a second portion of sodium borohydride (0·5 g) was added. After 1 day at room temperature the solution was evaporated and the residue was partitioned between aqueous potassium carbonate and ether. The ether phase was dried and evaporated to give the *alcohol* (9a) (143 mg).

The acetate (123 mg) was prepared as just described and was identical in all respects with the acetate described in (a).

1-[2-(*indol*-3-*yl*)*ethyl*]-3-*methoxypyridinium Bromide* (4e).—3-Methoxypyridine (2·7 g) and 1-bromo-2-(indol-3-yl) ethane (5·5 g) were allowed to react in ethanol (10 ml) at room temperature for 24 h. Solvent was evaporated off and the crystalline residue gave the *salt* (4e) (from MeOH) (4·83 g), m.p. 178—182°, $\lambda_{max.}$ 290, 282, and 219 nm (log ε 3·92, 3·94, and 4·55), $\nu_{max.}$ (Nujol) 3310m and 3210m cm^{-1} (Found: C, 54·7; H, 5·6; N, 7·6; Br, 22·7. $C_{16}H_{17}BrN_2O,H_2O$ requires C, 54·7; H, 5·41; N, 7·98; Br, 22·8%).

1-[2-(*indol*-3-*yl*)*ethyl*]-3-*methoxypiperidine* (9d).—The salt (4e) (200 mg) was hydrogenated in ethanol over platinum at 60 lb in^{-2} for 65 h. The solution was filtered and evaporated and the residue was partitioned between aqueous potassium carbonate and ether. The dried organic phase was evaporated to give a gum which was purified by t.l.c. with methanol–ethyl acetate (2 : 1)–triethylamine (1%) as eluant. The *piperidine* (9d) (78 mg) (amorphous) had R_F 0·3—0·6, $\lambda_{max.}$ (EtOH) 223, 276sh, 283, and 291 nm, $\nu_{max.}$ ($CHCl_3$) 3480s, 2940s, 2820m, and 1095s cm^{-1}, τ($CDCl_3$) 1·40br (1H, s, NH), 1·30—2·05 (4H, m, *H*Ar), 3·12br (1H, s, sharpened after addition of D_2O, indolyl-2-H), and 6·63 (3H, s, MeO), *m/e* 258 (M^+, 4%), 130(21), 129(8), 128(100), 96(9), 85(11), 83(17), 77(7), 55(7), 47(9), 42(8), and 41(10) [Found: M, (mass spectrometry), 258·1730. $C_{16}H_{22}N_2O$ requires 258·1732] (Found: *m/e* 128·1078. $C_7H_{14}NO$ requires *m/e* 128·1075).

4-*Acetyl*-1-[2-(*indol*-3-*yl*)*ethyl*]*pyridinium Bromide* (4b).—4-Acetylpyridine (0·62 g) and 1-bromo-2-(indol-3-yl)ethane (0·79 g) were heated together at 100° for 2 h. The resulting solid was recrystallised to give the salt (4b) (1·1 g), m.p. 225—228° (from MeOH) $\nu_{max.}$ (Nujol) 3180br,d and 1692s (Found: C, 58·9; H, 4·8. $C_{17}H_{17}BrN_2O$ requires C, 59·1; H, 4·9%).

1,2,3,6-*Tetrahydro*-4-(1-*hydroxyethyl*)-1-[2-(*indol*-3-*yl*)-*ethyl*]*pyridine* (5d).—The bromide (4b) (1·1 g) in ethanol (20 ml) was reduced with excess of sodium borohydride at room temperature for 2 h. The solution was evaporated and the residue was partitioned between ether and water The organic phase was extracted with 2N-hydrochloric acid, and the aqueous extract was made basic and extracted with ether to give the *alcohol* (5d) (0·86 g), m.p. 133—135° (from Me_2CO), $\lambda_{max.}$ 225, 282, and 290 nm (log ε 4·23, 3·63, and 3·48), $\nu_{max.}$ ($CHCl_3$) 3200br cm^{-1}, τ 2·50br (1H, HN), 2·34 (1H, m, indolyl-4-H), 3·01 (1H, d, J 2 Hz, s after addition of D_2O, indolyl-2-H), 4·30 (1H, m, HC:C), 5·72 [1H, q, J 7 Hz, *H*C(Me)·OH], and 8·68 (3H, d, J 7 Hz, *Me*CH·OH], *m/e* 270 (M^+, 4%), 140(75), 130(80), and 43(100) (Found: C, 74·95; H, 8·05; N, 10·2. $C_{17}H_{22}N_2O$ requires C, 75·5; H, 8·2; N, 10·35%).

4-*Acetyl*-1,2,3,6-*tetrahydro*-1-[2-(*indol*-3-*yl*)*ethyl*]*pyridine* (5e).—(a) The alcohol (5d) (150 mg), dicyclohexylcarbodiimide (682 mg), and orthophosphoric acid (crystalline; 219 mg) were dissolved in dimethyl sulphoxide and left at room temperature for 2 days. The solution was poured into 2N-hydrochloric acid extracted with ether, made basic, and then extracted with ether again. Evaporation of the ethereal extract gave the *ketone* (5e) (110 mg), m.p. 116—118° (from C_6H_6–light petroleum), $\lambda_{max.}$ 225, 283, and 290 nm (log ε 4·47, 3·74, and 3·67), $\nu_{max.}$ (Nujol) 3140m, 1660s, and 1645m cm^{-1}, τ 1·78br (1H, HN), 2·42 (1H, indolyl-4-H), 2·6—2·95 (3H, *H*Ar), 3·02br (1H, s, sharpened after addition of D_2O, indolyl-2-H), 3·24 (1H, m, HC:C), 6·7 (2H, m, C:CH·CH_2N), and 7·72 (3H, s, MeCO), *m/e* 268 (M^+, 12%), 138(100), 130(9), and 43(20) [Found: M, (mass spectrometry), 268·1568; $C_{17}H_{20}N_2O$ requires M, 268·1576].

(b) The ethylene acetal of 4-acetylpyridine was prepared by refluxing the reactants in benzene solution in the presence of a trace of toluene-*p*-sulphonic acid. 4-Acetylpyridine ethylene acetal (2·2 g) and 1-bromo-2-(indol-3-yl)ethane (3·0 g) were heated together at 100° for 8 h. The resulting amorphous *salt* (4c) was used directly for the next step.

The salt (4c) (195 mg) in methanol (25 ml) was reduced with excess of sodium borohydride at room temperature until the colour had been discharged. The solution was diluted with water and extracted with chloroform. The organic extract was evaporated and the residue subjected to t.l.c. with ethyl acetate–benzene–methanol (2 : 2 : 1) as eluant to give 4-*acetyl*-1,2,3,6-*tetrahydro*-1-[2-(*indol*-3-*yl*)-*ethyl*]*pyridine ethylene acetal* (5f) (89 mg) (amorphous), $\lambda_{max.}$ 228, 282, and 290 nm, $\nu_{max.}$ ($CHCl_3$) 3480s, 2805m, and 2765w cm^{-1}, τ 1·22br (1H, HN), 2·43 (1H, indolyl-4-H), 2·6—3·0 (3H, m, *H*Ar), 3·08 (1H, d, J 1 Hz, indolyl-2-H), 3·16 (1H, m, HC:C), and 8·53 (3H, s, MeCO), *m/e* 312 (M^+, 5%), 182(100), 130(65), and 42(60) [Found: M, (mass spectrometry), 312·1835. $C_{19}H_{24}N_2O_2$ requires M, 312·1838].

The acetal (5f) was treated with toluene-*p*-sulphonic acid in acetone at 0° for 2 days whereby the ketone (5e) was obtained (95%).

2-*Acetyloctahydroindolo*[2,3-a]*quinolizines* (6d) *and* (7d).—A solution of the ketone (5e) (255 mg) in degassed methanol (5 ml) and degassed acetic acid (25 ml) was refluxed for 1 h. Solvent was removed and the residue was partitioned between chloroform and aqueous potassium carbonate. The dried organic layer was evaporated and the residue was purified by dry column chromatography and then t.l.c. with ethyl acetate–benzene–methanol (2 : 2 : 1) as eluant to give the *ketone* (6d) (160 mg) (amorphous), $\lambda_{max.}$ 226, 283, and 290 nm, $\lambda_{infl.}$ 276 nm, $\nu_{max.}$ ($CHCl_3$) 3470s, 2810s, 2760s, 2700s, 2670w, and 1712s cm^{-1}, τ 1·54br (1H, HN), 2·5—3·05 (4H, m, *H*Ar), and 7·86 (3H, s, MeCO), *m/e* 268 (M^+, 88%), 267(65), 241(14), 226(20), 225(100), 223(16), 210(16), 197(27), 196(14), 184(55), 170(12), 169(22), 168(14),

156(20), and 43(31), metastable ions at 170·9 (198 → 184), 126·4 (268 → 184), and 106·7 (268 → 169) [Found: *M* (mass spectrometry), 268·1565. $C_{17}H_{20}N_2O$ requires *M*, 268·1576] (Found: *m/e* 225·1389. $C_{15}H_{17}N_2$ requires 225·1392.) (Found: *m/e* 184·0997. $C_{12}H_{12}N_2$ requires *m/e* 184·1000), and the *ketone* (7d) (26 mg) (amorphous), $\lambda_{max.}$ 225, 283, and 290 nm, $\lambda_{infl.}$ 276 nm, $\nu_{max.}$ ($CHCl_3$) 3470s, 2815m, 2760w, and 1710s cm^{-1}, τ 1·76 (1H, s, HN), 2·5—3·1 (4H, m, *H*Ar), 6·25 (1H, m, 12a-H), and 7·79 (3H, s, MeCO), *m/e* 268 (M^+, 82%), 267(58), 226(18), 225(100), 223(22), 197(40), 196(14), 185(14), 184(68), 183(16), 170(14), 169(22), 168(16), 156(22), 130(34), and 43(86), metastable ion at 170·9 (198 → 184) [Found: *M* (mass spectrometry), 268·1568. $C_{17}H_{20}N_2O$ requires *M*, 268·1576).

1-[2-(*Indol*-3-*yl*)*ethyl*]-4-*methoxycarbonylpyridinium Bromide* (4d).—Methyl isonicotinate (2·1 g) and 1-bromo-2-(indol-3-yl)ethane (3·4 g) were set aside in ethanol (30 ml) at room temperature for 5 days. The crystals (two crops, 1·6 and 1·9 g) were recrystallised to give the orange salt (4d), m.p. 290—300° (decomp.) (from aqueous MeOH), $\lambda_{max.}$ 220, 273, and 289 nm (log ε 4·66, 4·00, and 3·86), $\nu_{max.}$ (Nujol) 3200br and 1738s cm^{-1} (Found: C, 53·45; H, 5·0; N, 7·5. $C_{17}H_{17}N_2O_2Br$ requires C, 53·8; H, 5·05; N, 7·4%).

1,2,3,6-*Tetrahydro*-1-[2-(*indol*-3-*yl*)*ethyl*]-4-*methoxycarbonylpyridine* (5g).—The bromide (4d) (2·2 g) was reduced, in suspension in methanol (40 ml), with excess of sodium borohydride at room temperature for 2 h. The solution was concentrated and extracted with chloroform. The organic extract was evaporated and the residue was partitioned between 2N-hydrochloric acid and ether. The aqueous layer was made basic and extracted with chloroform and the organic extract was dried and evaporated to give the *ester* (5 g) (1·25 g), m.p. 111—112° (from aqueous MeOH), $\lambda_{max.}$ 223, 282, and 290 nm (log ε 4·32, 3·77, and 3·71), $\nu_{max.}$ ($CHCl_3$) 3480s, 2810w, 1710s, and 1660w cm^{-1}, τ 1·64br (1H, HN), 2·38 (1H, q, HC:C), and 6·22 (3H, s, MeO), *m/e* 284 (M^+, 3%) 161(20), 154(49), 144(4), 143(3), and 130(100) (Found: C, 70·8; H, 7·1; N, 10·0. $C_{17}H_{20}N_2O_2$ requires C, 71·8; H, 7·1; N, 9·85%).

2-*Methoxycarbonyloctahydroindolo*[2,3-a]*quinolizines* (6e) *and* (7e).—(a) To a stirred suspension of sodium hydride (0·9 g) in dry dimethylformamide (50 ml) at 110° was added a solution of the ester (5g) (3·5 g) in dimethylformamide (35 ml). After a further 10 min at 110° the mixture was cooled to 0° and methanol (10 ml) in dimethylformamide (20 ml) was added. Solvent was then evaporated off and the residue was treated with saturated methanolic hydrogen chloride (100 ml) at reflux overnight. Solvent was removed and the residue was partitioned between chloroform and aqueous potassium carbonate. The dried organic extract was evaporated and the residue was purified by chromatography on silica gel. Elution with benzene–ethyl acetate (1 : 4) afforded the *ester* (6e) (1·24 g), m.p. 79—82° (from aqueous MeOH), $\lambda_{max.}$ 225, 282, and 290 nm (log ε 4·34, 3·80, and 3·73), $\nu_{max.}$ ($CHCl_3$) 3480s, 2815m, 2760m, and 1730s cm^{-1}, τ 1·96br (1H, HN), 2·4—3·0 (4H, *H*Ar), 6·23 (3H, s, MeO), and 6·58 (1·5H, s, *Me*OH of solvation), *m/e* 284 (M^+, 90%), 283(100), 225(32), 223(30), 197(28), 170(30), 169(32), and 157(26) (Found: C, 69·1; H, 7·5; N, 9·4. $C_{17}H_{20}N_2O_2,\frac{1}{2}MeOH$ requires C, 69·8; H, 7·4; N, 9·3%); elution with ethyl acetate afforded a mixture of (6e) and starting material, and, finally, elution with ethyl acetate–methanol (9 : 1) gave the *ester* (7e) (0·42 g), m.p. 110—114° (from aqueous MeOH), $\lambda_{max.}$ 225, 282, and 290 nm (log ε 4·35, 3·85, and 3·78), $\nu_{max.}$ ($CHCl_3$) 3475s, 2810m, 2760m, and 1725s cm^{-1}, τ 1·89br (1H, HN), 2·4—3·0 (4H, m, *H*-Ar), 6·18 (3H, s, MeO), 6·25 (1H, d, *J* 9 Hz, 12a-H), *m/e* 284 (M^+, 90%), 283(100), 225(33), 197(42), 170(17), 169(12), and 156(15) (Found: C, 71·4; H, 7·09; N, 9·7. $C_{17}H_{20}N_2O_2$ requires C, 71·8; H, 7·1; N, 9·85%).

(b) A solution of the ester (5 g) (2·5 mg) in degassed glacial acetic acid (2 ml) and degassed methanol (0·6 ml) was refluxed under nitrogen for 2 days. The solution was evaporated and the residue was partitioned between water and chloroform. The aqueous layer was freeze-dried, methanol (5 ml) was added and the solution was saturated with hydrogen chloride and then refluxed overnight. Solvent was evaporated off and the residue was partitioned between aqueous potassium carbonate and chloroform. The dried organic phase was evaporated to give a mixture of the two esters (6e) and (7e) (t.l.c. comparison).

2-*Hydroxymethyloctahydroindolo*[2,3-a]*quinolizines* (6f) *and* (7f) *and their* O-*Acetates* (6g) *and* (7g).—The esters, (6e) (71 mg) and (7e) (200 mg), were reduced with excess of lithium aluminium hydride in refluxing tetrahydrofuran (15 ml) for 30 min. The solutions were cooled, water was added, and the organic material was extracted with chloroform. Evaporation of the dried organic extracts gave, respectively, the *alcohol* (6f) (56 mg), m.p. 248—250° (from C_6H_6), $\lambda_{max.}$ 225, 282, and 290 nm (log ε 4·45, 3·83, and 3·76) (Found: C, 75·6; H, 7·8; N, 10·2. $C_{16}H_{20}N_2O$ requires C, 75·0; H, 7·9; N, 10·9%) and the *alcohol* (7f) (63 mg), m.p. 259—262° (from $CHCl_3$), $\lambda_{max.}$ 225, 282, and 290 nm (log ε 4·47, 3·79, and 3·72) (Found: C, 73·9; H, 7·9; N, 10·7. $C_{16}H_{20}N_2O$ requires C, 75·0; H, 7·9; N, 10·9%).

The acetates were prepared in 90% yields by treatment with acetic anhydride–pyridine (1 : 1) at room temperature overnight followed by evaporation, partition between chloroform and aqueous potassium carbonate and evaporation of the dried organic extracts to give respectively the *acetate* of (6f) (amorphous), $\nu_{max.}$ ($CHCl_3$) 3460m, 2800m, 2740m, and 1720s cm^{-1}, τ 1·90br (1H, HN), 2·5—3·0 (4H, m, *H*Ar), 6·06 (2H, d, *J* 5 Hz, CH_2·OAc), and 7·95 (3H, s, MeCO), *m/e* 298 (M^+, 76%), 297(100), 225(33), 197(35), 170(37), 169(65), 168(45), 156(37), 57(33), 55(39), 43(100), and 41(43) [Found: *M* (mass spectrometry), 298·1682. $C_{18}H_{22}N_2O_2$ requires *M*, 298·1681] and *acetate* of (7f) (amorphous), $\nu_{max.}$ ($CHCl_3$) 3460m (Bohlmann absorptions not sufficiently strong to be resolved) and 1720s cm^{-1}, τ 2·05br (1H, HN), 2·5—3·0 (4H, *H*Ar), 5·50 (1H, m, 12a-H), 6·03br (2H, CH_2·OAc), and 7·97 (3H, s, MeCO), *m/e* 298 (M^+, 31%), 297(39), 237(41), 197(32), 170(49), 169(89), 168(45), 167(36), 156(49), 154(37), 115(37), 43(100), and 41(32) [Found: *M* (mass spectrometry), 298·1682. $C_{18}H_{22}N_2O_2$ requires *M*, 298·1681].

Benzoyl-substituted Partial Iboga *Compounds* (10a).—The phenyl ketone (5b) (40 mg) was heated in solution in 2N-hydrochloric acid–dioxan (4 : 1) (3 ml) in a sealed tube for 2 h at 95°. The resulting solution was diluted, basified, and extracted with chloroform to give a gum (43 mg) which was purified by t.l.c. with benzene–ethyl acetate–methanol (2 : 2 : 1) as eluant (twice) to give the *major isomer* (10a) (22 mg), R_F 0·3, further purified by t.l.c. elution with methanol, m.p. 199—202° (from MeOH), $\lambda_{max.}$ 228 and 284 nm (log ε 4·50 and 3·83), $\lambda_{infl.}$ 290 nm, $\nu_{max.}$ ($CHCl_3$) 3460s and 1689s cm^{-1}, *m/e* 330 (M^+, 94%), 225(100),

197(32), 182(40), 169(24), 168(32), 167(27), 157(29), 156(57), 144(29), 105(33), and 77(27), metastable ion at 153·2 (182 → 167) [Found: *M* (mass spectrometry), 330·1734. $C_{22}H_{22}N_2O$ requires 330·1732) and the *minor isomer* (10a) (8 mg), R_F 0·6, further purified by t.l.c. elution with ethyl acetate–triethylamine (9 : 1) (amorphous), $\lambda_{max.}$ 284 and 291 nm, $\nu_{max.}$ (CCl_4) 3470s, 3400br, and 1689s cm^{-1}, *m/e* 330 (M^+, 90%), 225(100), 197(33), 182(37), 169(20), 168(32), 167(25), 157(24), 156(50), 144(27), 105(35), and 77(28), metastable ion at 153·2 (182 → 167) [Found: *M* (mass spectrometry), 330·1734. $C_{22}H_{22}N_2O$ requires *M*, 330·1732) (Found: *m/e* 225·1393. $C_{15}H_{17}N_2$ requires *m/e* 225·1392).

Acetyl-substituted Partial Iboga *Compounds* (10b).—The ketone (5e) (32 mg) was treated with 10N-hydrochloric acid (1 ml.) for 1·5 h at room temperature. The solution was made basic and extracted with chloroform. T.l.c. of the dried, evaporated extract with ethyl acetate–triethylamine (9 : 1) as eluant (three elutions) gave the minor *isomer* (10b) (5 mg) (R_F 0·5), further purified by t.l.c. with methanol as eluant), (amorphous), $\lambda_{max.}$ 224, 284, and 291 nm, $\nu_{max.}$ (CCl_4) 3395br, 3470s, and 1712s cm^{-1}, *m/e* 268 (M^+, 100%), 225(87), 198(20), 182(42), 168(24), 167(19), 157(29), 156(47), 144(27), and 43(22), metastable ions at 189·0 (268 → 225), 153·2 (182 → 167), 147·1 (225 → 182), and 92·1 (225 → 144) [Found: *M* (mass spectrometry), 268·1576. $C_{17}H_{20}N_2O$ requires *M*, 268·1576] (Found: *m/e* 225·1395. $C_{17}H_{20}N_2$ requires *m/e* 225·1392) and the *major isomer* (10b) (18 mg), R_F 0·25, further purified by t.l.c. with two elutions with methanol) (amorphous), $\lambda_{max.}$ 226, 284, and 291 nm, $\nu_{max.}$ (CCl_4) 3460s and 1705s cm^{-1}, τ 1·78br (1H, HN), 2·4—3·0 (4H, *H*Ar), 8·07 (3H, s, MeCO), *m/e* 268 (M^+, 100%), 225(70), 198(17), 182(32), 168(16), 157(24), 156(24), 144(20), and 43(54), metastable ions as for minor isomer [Found: *M* (mass spectrometry), 268·1578. $C_{17}H_{20}N_2O$ requires *M* 268·1576].

2-*Acetyl*-1,2-*epoxyoctahydroindolo*[2,3a]*quinolizine*.— The methyl ketone (5e) (25 mg) was treated with potassium hydroxide (320 mg) in methanol (15 ml) at room temperature for 1 h. The solution was diluted with water and extracted with ether. The ethereal extract was evaporated and the residue was purified by t.l.c. whereby the *epoxyketone* (4·5 mg) was obtained (amorphous), $\lambda_{max.}$ 227, 281, and 294 nm, $\nu_{max.}$ ($CHCl_3$) 3460m, (weak, non resolved, Bohlmann absorption) and 1710s cm^{-1}, *m/e* 282 (M^+, 25%) 281(20), 253(15), 239(25), 210(10), 197(11), 184(100), 170(25), 169(25), and 156(40), metastable ions at 280 (282 → 281), 227·5 (281 → 253), 202·6 (282 → 239), 162·4 (239 → 197), 133·8 (253 → 184), and 120·1 (282 → 184) [Found: *M* (mass spectrometry), 282·137005. $C_{17}H_{18}N_2O_2$ requires *M*, 282·136820] (Found: *m/e* 253·1340. $C_{16}H_{17}N_2O$ requires *m/e* 253·1341) (Found: *m/e* 184·0098. $C_{12}H_{12}N_2$ requires *m/e* 184·1000).

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