Total Synthesis of Heptacyclic *Aspidosperma* Alkaloids. Part 1. Preliminary Experiments

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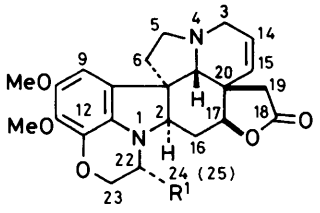
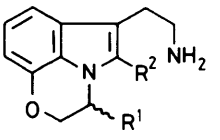
A series of model experiments is described, in which methods for the construction of the alkaloids of the obscurinervine group are developed. The penultimate intermediate (**44**) in a synthesis of the obscurinervidine analogue lacking only the aromatic methoxy groups has been prepared.

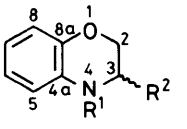
The ultimate objective of the investigations reported here was the total synthesis of members of the heptacyclic group of *Aspidosperma* alkaloids exemplified by obscurinervine (**1**) and obscurinervidine (**2**).[1] Numerous syntheses of the aspidosperma ring system have already been described,[2] but hitherto none of these has resulted in the synthesis of the obscurinervine group, which have an additional, oxazine, ring attached to C-12 and N_a, and an additional asymmetric centre at C-22.



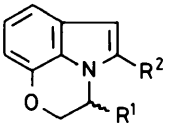
Obscurinervine (**1**) R = Et
Obscurinervidine (**2**) R = Me



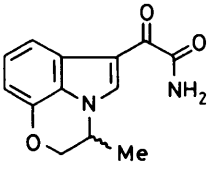
(**3**) R^1 = Me, R^2 = H
(**4**) R^1 = Et, R^2 = H
(**5**) R^1 = Me, R^2 = Me
(**6**) R^1 = Et, R^2 = Me



(**7**) R^1 = H, R^2 = Me
(**8**) R^1 = NH_2, R^2 = Me
(**9**) R^1 = N=CMe_2, R^2 = Me
(**10**) R^1 = H, R^2 = Et
(**11**) R^1 = NH_2, R^2 = Et



(**12**) R^1 = Me, R^2 = CO_2Me
(**13**) R^1 = Me, R^2 = H
(**14**) R^1 = Me, R^2 = Me
(**15**) R^1 = Me, R^2 = CH_2OH
(**16**) R^1 = Et, R^2 = CO_2Me
(**17**) R^1 = Et, R^2 = CO_2H



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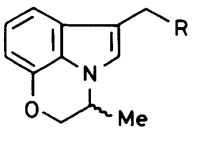
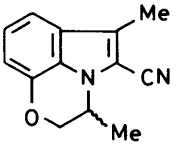
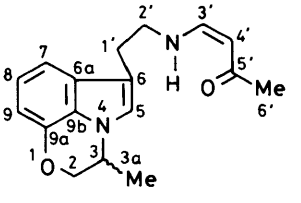


(**19**) R = NMe_2
(**20**) R = CN



(**21**)



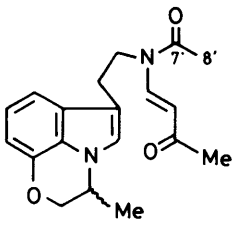
(**22**)

Our initial experiments were directed towards the synthesis of model compounds lacking the two aromatic methoxy groups and in particular the tryptamine analogues (**3**) and (**4**), which belong to the relatively little known pyrrolo[1,2,3-*de*]-2*H*-1,4-benzoxazine ring system.

Reductive cyclization of *o*-nitrophenacetol by hydrogenation (30 atm) over 10% palladised charcoal gave 3-methyl-3,4-dihydro-2*H*-1,4-benzoxazine (**7**),[3] which was nitrosated, and then reduced, by zinc–hydrochloric acid or (preferably) lithium aluminium hydride, to the *N*-amino derivative (**8**). Attempted cyclization of the methyl pyruvate derivative of (**8**) in the presence of formic acid failed, and only the *N*-formyl derivative of the parent benzoxazine (**7**) was isolated. However, the methyl pyruvate hydrazone derivative of (**8**) did cyclise in the presence of methanolic hydrogen chloride to give the tricyclic ester (**12**), but in variable yield. Subsequently, it was found that thermal cyclization in the absence of added hydrogen chloride gave consistent yields of (**12**). Presumably traces of pyruvic acid in the reaction mixture were sufficient to catalyse the Fischer cyclization. Hydrolysis and decarboxylation of (**12**) then gave the parent pyrrolo-benzoxazine derivative (**13**).

As an indole derivative, compound (**13**) should be convertible into the desired tryptamine analogue (**3**) by any of a number of well-tried methods. However, the glyoxylamide (**18**), obtained from (**13**) by reaction with oxalyl chloride followed by ammonia, could not be reduced to (**3**) in satisfactory yield; hence (**13**) was converted into the gramine derivative (**19**), which was quaternized with methyl iodide, treated with potassium cyanide, and the resulting nitrile (**20**) reduced to (**3**) by means of lithium aluminium hydride. A by-product, obtained in small amount in the preparation of (**20**), was the isomeric nitrile (**21**).

Our first attempt to construct the *Aspidosperma* framework from the tryptamine analogue (**3**) involved an adaptation of the elegant route developed by Büchi[4] in the synthesis of vindorosine and vindoline. Accordingly, the amine (**3**) was condensed with 1-chlorobut-1-en-3-one to give the enamino ketone (**22**), which was then acetylated to the substrate (**23**) needed for cyclisation. In consonance with Büchi's experience, the enamino ketone (**22**) existed in the *Z* configuration (δ 4.96, 1 H, d, *J* 8.0 Hz, 20-H; the signal for 21-H is superimposed on the multiplets owing to the aromatic protons), which resisted attempts at cyclization, whereas the *N*-acetyl derivative (**23**) has the *E* configuration (δ 8.01, 1 H, d, *J* 13.7 Hz, and 5.66 1 H, d, *J* 13.7 Hz). Attempts to cyclise (**23**) to the pentacyclic enone (**24**) by means of boron trifluoride–diethyl ether, as used in analogous cyclizations by Büchi, gave very disappointing results. In all the conditions used a complex mixture of products



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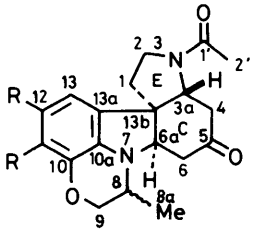
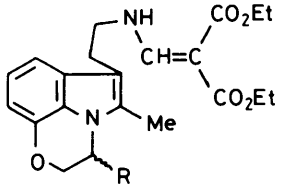
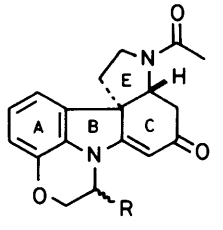


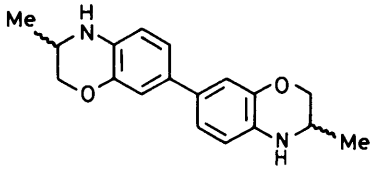
(24a) R = H, α-Me at C-8
(24b) R = H, β-Me at C-8
(25a) R = OMe, α-Me at C-8
(25b) R = OMe, β-Me at C-8



(26) R = Me
(27) R = Et



(28) R = Me
(29) R = $^{8a}CH_2{}^{8b}CH_3$



(30)

was obtained, from which the best yield of (**24**) that was isolated after careful chromatography was only 5%; hence this approach to (**24**) was not further investigated.

Compounds of type (**24**) can also be obtained by Takano cyclization[5] of the derivative (**26**) from the 2-methyltryptamine analogue (**5**) and ethoxymethylenemalonic ester. The initial product of this cyclization is the enamino ketone (**28**), which, it was expected, should be reducible stereospecifically to the desired *cis* B/C pentacyclic ketone (**24**). Accordingly, the synthesis of (**26**) was investigated.

Fischer cyclization of the isopropylidene derivative (**9**) of the *N*-aminobenzoxazine (**8**) was the first method attempted; however, the desired pyrrolobenzoxazine (**14**) could not be isolated, in spite of the fact that a wide variety of well-authenticated acidic catalysts were tried.

One result of interest, however, emerged from these attempts. The use of polyphosphoric acid on (**9**) gave a strongly fluorescent product whose ^{1}H n.m.r. spectrum resembled that of the benzoxazine (**7**) in the high field region, but was deficient in absorptions in the aromatic region. The u.v. spectrum ($\lambda_{max.}$ 292 and 314 nm) exhibited a bathochromic shift relative to that of (**7**) ($\lambda_{max.}$ 256 and 294 nm) and the mass spectrum (M^+, *m/z* 296) clearly indicated a dimeric species. The structure (**30**) was thus assigned to this product. This is reminiscent of the result obtained by Fusco and Sannicolo,[6] who obtained the dimeric compound (**32**) when the non-indolizable tetrahydroquinoline derivative (**31**) was heated with polyphosphoric acid. The free-radical mechanism proposed by these workers to account for the formation of (**32**) is presumably applicable in the conversion of (**9**) into (**30**).

With the aminobenzoxazine (**8**) in hand its conversion into the pyrrolobenzoxazine (**14**) was routinely investigated, but the failure to obtain (**14**) was not particularly surprising; indeed there are several reports in the literature[7] of the failure to cyclise phenylhydrazine derivatives of acetone.

An alternative route to (**14**) suggested itself in the reduction of the ester group in (**12**) to a methyl group. Accordingly, (**12**) was reduced by means of lithium aluminium hydride to the related primary alcohol (**15**); under more vigorous conditions the dimethylpyrrolobenzoxazine (**14**) was obtained, but only in unacceptably poor yield (30%). A much improved yield (82%) of (**14**) was subsequently obtained by the use of RedAl in toluene.

At this stage no further work was done on this approach to (**5**) because a much more direct synthesis was developed *via* application of the Grandberg tryptamine synthesis.[8] This simply involved the cyclization of the derivative of (**8**) with 5-chloropentan-2-one in hot aqueous methanol without the addition of an acid catalyst. By this means the tryptamine analogue (**5**) was obtained directly in acceptable yield (69%), without the need for purification by chromatography.

Reaction of (**5**) with ethoxymethylenemalonic ester gave an essentially quantitative yield of (**26**), which was cyclised by heating in a mixture of acetic anhydride and acetic acid for 70 h; this gave the pentacyclic enamino ketone (**28**) in 49% yield as a mixture of C-8 epimers, both of which existed as a mixture of amide conformers (proton and ^{13}C n.m.r. spectra). In consonance with this, h.p.l.c. analysis revealed the presence of four components in the mixture. Separation by preparative t.l.c. resulted in the isolation of the component of highest R_F value which, although apparently homogeneous at room temperature, gave two peaks on re-analysis by h.p.l.c., owing to equilibration of two amide conformers on the column. The products from this cyclization would be expected to have the more stable *cis* C/E ring junction, as has earlier been observed in analogous cyclizations,[5] and they are therefore formulated as (**28**).

Reduction of (**28**) by means of lithium and t-butyl alcohol in liquid ammonia gave an excellent yield (90—95%) of the desired pentacyclic amino ketone (**24**) which was also obtained as a mixture of C-8 epimers. Its ^{13}C n.m.r. spectrum exhibited a total of 38 signals; in contrast to its precursor (**28**), there was no evidence for the presence of amide conformers at room temperature.

In analogous reductions reported by earlier workers[9] the thermodynamically more stable product was normally obtained; in this case it would clearly have a *cis* B/C ring junction, and it is therefore formulated as (**24**). As expected, its ^{1}H n.m.r. and mass spectra were identical with those of (**24**) prepared earlier by Büchi's route.

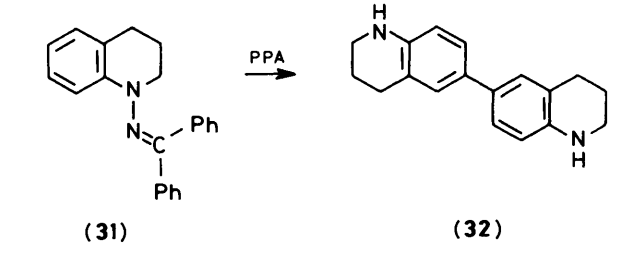
The mass spectrum of (**24**) exhibits an ion at *m/z* 269 (**33**), which is produced by loss of the methyl group (C-8a) to give an ion at *m/z* 311, followed by retro Diels-Alder fission of ring C. Alternatively, retro Diels-Alder fragmentation of ring C followed by loss of N_b leads to ions at *m/z* 199 (**34a**), 186 (**34b**), and 171 (**34c**). A third fragmentation pathway gives an important ion of uncertain structure at *m/z* 240, which is almost certainly produced by loss of ketene, the acetyl group, and a hydrogen atom.

Initially, the pentacyclic ketone (**24**) was obtained as an oily mixture of diastereoisomers, but it was subsequently separated by fractional crystallisation from ethanol into a pure crystalline epimer of m.p. 228—231 °C; unfortunately, the second C-8 epimer could not be obtained analytically pure. However, subtraction of the ^{13}C resonances for the crystalline isomer from the spectrum of the oily sample enriched with the second isomer allowed the major signals of the non-crystalline epimer to be identified. Assignment of stereochemistry then followed from a

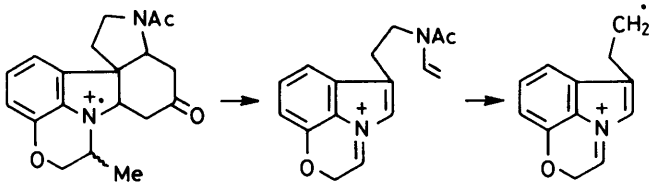
Table. ^{13}C N.m.r. spectra of C-8 epimers of (**24**) and (**25**)

	(**24a**) m.p. 228—231 °C	(**24b**) (Non-crystalline)	(**25a**) m.p. 203.5—204.5 °C	(**25b**) (Non-crystalline)
C-8a	17.06 p.p.m.	12.84 p.p.m.	16.79 p.p.m.	12.30 p.p.m.
C-8	52.11	44.96	52.66	45.13
C-9	72.37	71.62	72.92	72.16
C-6a	63.71	60.95	63.71	61.27
C-3a	72.05	66.25	72.43	66.80
C-2	47.56	46.70	47.56	46.91
C-1	37.70	36.46	37.65	36.73
C-13b	54.17	53.74	54.44	53.90

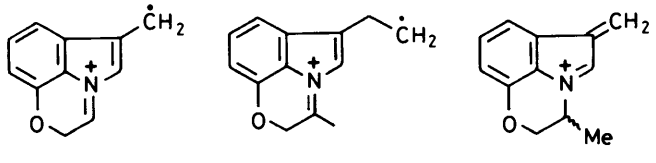
comparison of ^{13}C signals (see Table) with the corresponding ones in the spectra of the 10,11-dimethoxy derivatives (**25a**) and (**25b**), prepared as intermediates in the synthesis of obscurinervidine.[10] Since the isomer of m.p. 203.5—204.5 °C was converted into obscurinervidine it must have the stereochemistry shown in (**25a**), from which it seems almost certain that the crystalline isomer in the unmethoxylated series has the same stereochemistry, as depicted in (**24a**).



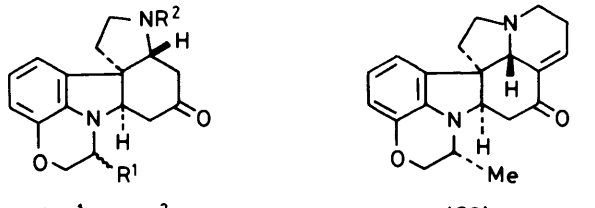
(**31**) (**32**)



(**24**)$^{+\bullet}$ (**33**) *m/z* 269 *m/z* 185



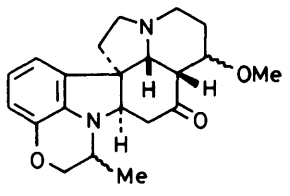
m/z 171 (**34c**) (**34a**) (**34b**) *m/z* 186



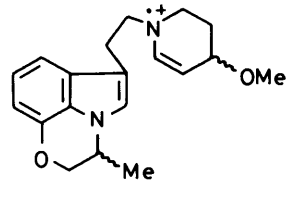
(**35**) R^1=Me, R^2=H
(**36**) R^1=Et, R^2=Ac
(**37**) R^1=Et, R^2=H

(**38**)

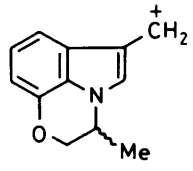
The pursuit of the model series towards the obscurinervidine ring system required removal of the *N*-acetyl group, followed by addition of ring D. Initially the *N*-acetyl group was removed from (**24**) (epimeric mixture) by treatment with triethyloxonium fluoroborate–sodium hydrogen carbonate; however, yields were variable, and it was subsequently found that hydrolysis with dilute hydrochloric acid gave consistently better yields of the secondary amino ketone (**35**). Ring D was then added by Michael addition of acrolein to (**35**), followed by cyclization with sodium methoxide in methanol. In preliminary attempts to perform this reaction a complex mixture of products was obtained, from which the desired enone (**38**) could not be isolated. Eventually a saturated ketone ($\nu_{max.}$ 1 706 cm^{-1}) was obtained which exhibited no hydroxy absorption, and was therefore not the expected β-ketol; however, it became clear from the ^1H n.m.r. spectrum, which exhibited a three-proton singlet at δ 3.21, and the mass spectrum, that this product was the



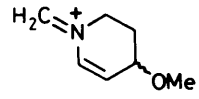
(**39**)



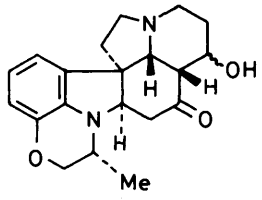
(**40**)



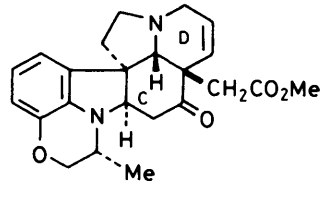
(**41**)



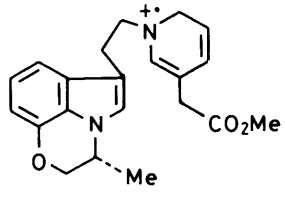
(**42**) *m/z* 126



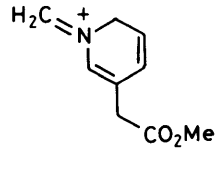
(**43**)



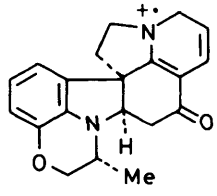
(**44**)



(**45**) *m/z* 352



(**46**) *m/z* 166

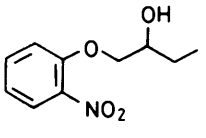


(**47**) *m/z* 320

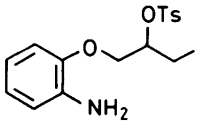
β-methoxy ketone (**39**), generated by addition of methanol to the rather strained enone (**38**). The mass spectrum of (**39**) shows the expected loss of ketene from the molecular ion to give the ion (**40**) at *m/z* 312, which fragments to give an ion at *m/z* 186 (**41**) and the base peak at *m/z* 126 (**42**). Evidently the reaction conditions employed for the formation of ring D had been too vigorous, and had allowed the addition of methanol to the enone (**38**). When milder conditions, identical with those used by Büchi[11] in the vindorosine synthesis, were employed on the pure amino ketone derived from (**24a**) the resulting product consisted of three components, which were probably the two diastereoisomeric ketols (**43**) and the enone (**38**). Without purification the product mixture was treated with mesyl chloride in pyridine, again as described by Büchi,[11] and the desired enone was subsequently isolated by chromatography of the crude product.

Completion of the obscurinervidine skeleton was achieved by alkylation of the enone (**38**) with ethyl bromoacetate–potassium t-butoxide, which gave the oxo ester (**44**) in 40% yield. That alkylation had occurred at the α-position (C-20)* to the carbonyl group was confirmed by the ketone carbonyl absorption at 1 714 cm^{-1}, and the presence of a two-proton multiplet centred on δ 5.79 in the ^1H n.m.r. spectrum. The stereochemistry of (**44**) follows from the considerable hindrance to approach by alkylating agent at the α-face of the extended enolate anion by the two carbon atoms C-5 and C-6 of the ethanamine bridge. Alkylation thus occurs on the β-face, and this is confirmed by the mass spectrum of (**44**), which reveals that the molecule suffers facile retro Diels-Alder cleavage of ring C characteristic of compounds containing a *cis* C/D ring junction; the molecule ion thus loses ketene to give an ion at *m/z* 352 (**45**), which fragments in the familiar way to ions at *m/z* 171 (**34c**) and 166 [(**46**), base peak]. An interesting, alternative fragmentation, which is not available to simple *Aspidosperma* alkaloids containing an ethyl group at C-20, and which supports very strongly the *cis* C/D stereochemistry, involves a McLafferty rearrangement; the elements of methyl acetate are thus lost from the molecular ion, to give the important ion (**47**) at *m/z* 320.

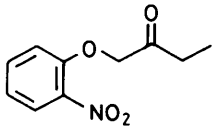
Concurrently with the above studies the synthesis of a model for obscurinervine (**1**) was being investigated, and for this purpose the benzoxazine derivative (**10**) was required. Initially it was proposed to prepare this compound *via* the nitro alcohol (**48**), obtainable by the reaction of potassium *o*-nitrophenoxide with 1,2-epoxybutane. Unfortunately, this reaction gave only 34% of (**48**), and conditions that would result in a much improved yield could not be found. Tosylation of (**48**), followed by hydrogenation of the nitro group, gave the primary amine (**49**), which when heated in DMF for 3 h, gave the benzoxazine derivative (**10**) in modest yield. In a second approach to (**10**) the nitro alcohol (**48**) was oxidised by pyridinium chlorochromate to the corresponding ketone (**50**), but the yield obtained was only 30%; hydrogenation of (**50**) then gave (**10**) in 85% yield. The third, and by far the best route to (**10**), involved reaction of potassium *o*-nitrophenoxide with 1-bromobutan-2-one to give (**50**), followed by hydrogenation–cyclization (this compound has earlier been prepared by essentially the same method,[12] but full details are not available).



(**48**)



(**49**)



(**50**)

Elaboration of (**10**) was then undertaken, advantage being taken of the experience gained with the methyl analogue (**7**). *N*-Nitrosation of (**10**) followed by reduction ($LiAlH_4$) gave the *N*-amino derivative (**11**), which was condensed with methyl pyruvate and cyclised to the pyrrolo-benzoxazine ester (**16**); hydrolysis then gave the corresponding acid (**17**). However, this particular route was not pursued beyond this point, because the Grandberg synthesis using the aminobenzoxazine (**11**) and 5-chloropentan-2-one provided a shorter and much more efficient preparation of the tryptamine analogue (**6**). Formation of the derivative (**27**) with ethoxymethylenemalonic ester, followed by Takano cyclisation with acetic anhydride–acetic acid, then afforded the pentacyclic enaminoketone (**29**), which was reduced by means of lithium and t-butyl alcohol in liquid ammonia. The product, the N_b-acetylated amino ketone (**36**) was obtained as an inseparable mixture of C-22 epimers having the desired relative configuration at positions 2, 7, and 21. Reaction of (**36**) with triethyloxonium tetrafluoroborate–sodium hydrogen carbonate then gave the parent diamino ketone (**37**).

The model series having been examined in some detail, attention was then focussed on the synthesis of obscurinervidine.[10]

Experimental

M.p.s were determined on a Kofler hot-stage apparatus and are uncorrected. U.v. absorption spectra were recorded on either a Pye-Unicam SP 800A or a PU 8800 spectrometer. I.r. spectra were recorded on either a Perkin-Elmer 297 or a 1420 spectrophotometer. N.m.r. spectra were recorded on either a Perkin-Elmer R32 instrument (^1H, 90 MHz), a Jeol FX90Q F.T. (^1H, 90 MHz and ^{13}C) or, where stated, on a Bruker 400 MHz spectrometer. Solutions in deuteriochloroform, with tetramethylsilane as internal standard, were used unless otherwise stated. Mass spectra were recorded on a Kratos MS25 instrument; accurate mass measurements were carried out on an A.E.I./Kratos MS 902/50 machine.

3-Methyl-N-nitroso-3,4-dihydro-2H-1,4-benzoxazine.—A solution of sodium nitrite (3.58 g, 55 mmol) in water (13 ml) was added dropwise to a solution of 3-methyl-3,4-dihydro-2*H*-1,4-benzoxazine[3] (**7**) (7.26 g, 51 mmol) in concentrated hydrochloric acid (7.5 ml) and crushed ice (30 g), the temperature of the solution being maintained below 5 °C. The mixture was stirred for 1 h and then extracted with benzene (4 × 40 ml). The combined organic extracts were washed with water (50 ml) and then dried ($MgSO_4$). Concentration under reduced pressure gave the *title compound* (8.60 g, 99%) as an orange oil (Found: M^+, 178.074 43. $C_9H_{10}N_2O_2$ requires *M*, 178.074 22); $\nu_{max.}$ (film) 3 110, 1 590, 1 436, 1 272, 755, and 720 cm^{-1}; δ_H 8.1—7.9 (1 H, m), 7.25—6.85 (3 H, m), 5.03 (1 H, qt, *J* 6, 1 Hz), 4.03 (2 H, dq, *J* 13, 1.0 Hz), and 1.10 (3 H, d, *J* 6.6 Hz); *m/z* (%) 178 (2), 149 (25), 148 (100), 134 (14), 133 (24), 120 (40), 106 (8), 104 (8), 79 (10), 78 (13), and 77 (18).

* In all the compounds that contain the hexacyclic ring system [*i.e.* (**38**), (**39**), (**43**), and (**44**)] the *biogenetic* numbering system is used.

N-*Amino*-3-*methyl*-3,4-*dihydro*-2H-1,4-*benzoxazine* (**8**).—(*a*) A suspension of zinc dust (13.9 g) in water (21 ml) was stirred while 3-methyl-*N*-nitroso-3,4-dihydro-2*H*-1,4-benzoxazine (9.07 g, 51 mmol) in glacial acetic acid was added dropwise, the temperature of the reaction mixture being maintained in the range 5—10 °C. After the addition was complete the solution was stirred for a further hour at room temperature and then heated to 80 °C on a steam-bath. The hot solution was filtered and the metal residue washed with 1.5M hydrochloric acid. The combined filtrates were allowed to cool and then treated with sufficient 40% aqueous sodium hydroxide to redissolve the basic zinc salts. The oily layer that separated was removed and the aqueous layer extracted with ether (2 × 100 ml). The combined organic extracts were dried ($MgSO_4$) and the solvent was removed under reduced pressure to give a dark brown oil which was chromatographed on Kieselgel G. Elution with 10% ether in benzene gave two main fractions. The first fraction contained 3-methyl-3,4-dihydro-2*H*-1,4-benzoxazine (**7**) (1.67 g, 22%) as a pale orange oil, identified by its i.r. and n.m.r. spectra. The second fraction contained the *title compound* (**8**) (5.74 g, 67%), which was obtained from benzene as colourless needles, m.p. 80—82 °C (Found: C, 65.5; H, 7.3; N, 16.75%; M^+, 164.09487. $C_9H_{12}N_2O$ requires C, 65.90; H, 7.30; N, 17.10%; *M*, 164.094 95); $\nu_{max.}$(Nujol) 3 320, 1 610, 1 580, 1 375, 1 274, and 760 cm^{-1}; δ_H 6.68—7.30 (4 H, m), 4.0—4.40 (2 H, m), 3.40 (3 H, m, two hydrogens exchange with D_2O), and 1.25 (3 H, d, *J* 7 Hz); *m*/*z* (%) 168 (100), 149 (49), 148 (8), 135 (9), 134 (10), 133 (13), 132 (12), 120 (22), 107 (6), 106 (8), 94 (36), 91 (11), and 76 (28); $\lambda_{max.}$ 220, 256, and 294 nm.

(*b*) A solution of lithium aluminium hydride (0.92 g, 24.2 mmol) in dry ether (15 ml) was added dropwise to a cooled solution of 3-methyl-*N*-nitroso-3,4-dihydro-2*H*-1,4-benzoxazine (4.28 g, 24 mmol) in dry ether (15 ml) at 0—5 °C. The reaction mixture was stirred at 10 °C for 90 min and then wet ether (20 ml) and 30% aqueous sodium hydroxide (20 ml) were added dropwise. The aqueous phase was separated and extracted with ether (3 × 30 ml) and the combined ethereal layers were washed with water (50 ml) and saturated brine (50 ml), and then dried (Na_2SO_4). Concentration under reduced pressure gave the *title compound* (**8**) (3.66 g, 93%), which was recrystallised from light petroleum (b.p. 40—60 °C) and obtained as colourless needles, m.p. 83—84 °C, identical with that obtained by method (*a*).

Methyl Pyruvate Derivative of N-*Amino*-3-*methyl*-3,4-*dihydro*-2H-1,4-*benzoxazine* (**8**).—(*a*) The aminobenzoxazine (**8**) (3.0 g, 18 mmol) and pyruvic acid (1.61 g, 18 mmol) were dissolved in ethanol (50 ml), and the mixture was stirred for 10 min. Removal of the solvent left a yellow oil to which, in benzene, an excess of diazomethane in ether was added. The reaction mixture was then gently warmed on a steam-bath and the solvent removed under reduced pressure to leave a yellow oil which crystallised on addition of a small quantity of light petroleum. The solid was recrystallised from hexane to give the *title compound* (4.2 g, 16.92 mmol, 94%) as golden rosettes, m.p. 71—72 °C (Found: C, 62.95; H, 6.4; N, 11.1%; M^+, 248.115 68. $C_{13}H_{16}N_2O_3$ requires C, 62.89; H, 6.50; N, 11.28%; *M*, 248.116 084); $\nu_{max.}$(Nujol) 1 712, 1 602, and 1 587 cm^{-1}; δ_H 6.60—7.30 (4 H, m), 3.70—4.40 (3 H, m), 3.84 (3 H, s), 2.23 (3 H, s), and 1.22 (3 H, d, *J* 7 Hz); *m*/*z* (%) 248 (45), 148 (100), 133 (24), 120 (46), 91 (11), 78 (24), and 77 (28); $\lambda_{max.}$ 219, 247, 280, and 342 nm.

(*b*) The aminobenzoxazine (**8**) (3.0 g, 18 mmol) was dissolved in ethanol (50 ml) and methyl pyruvate (1.84 g, 18 mmol) was added dropwise with stirring. The solution was stirred for 15 min after which the solvent was removed under reduced pressure to leave an amber oil. Crystallisation occurred on addition and trituration with a small quantity of light petroleum and the resulting mixture was recrystallised from hexane to give the title compound (2.61 g, 94%) as yellow plates, m.p. and mixed m.p. 71—72 °C.

Attempted Cyclisation of the Methyl Pyruvate Derivative of N-*Amino*-3-*methyl*-3,4-*dihydro*-2H-1,4-*benzoxazine with Formic Acid*.—The above prepared methyl pyruvate derivative (0.2 g, 0.8 mmol) was added to anhydrous formic acid (10 ml) and the resulting solution was heated under reflux for 1 h. The reaction mixture was then allowed to cool, and extracted with benzene (2 × 30 ml). The solvent was removed under reduced pressure to leave a yellow oil which was chromatographed on Kieselgel G (50 g). Elution with 10% ether in benzene gave two fractions. The first fraction was found to be starting material (80 mg). The second fraction was shown to be N-*formyl*-3-*methyl*-3,4-*dihydro*-2H-1,4-*benzoxazine* (52 mg, 0.3 mmol, 36%), which was obtained as a pale yellow-green oil, b.p. 141–143 °C/0.5 mmHg (Found: C, 67.45; H, 6.05; N, 7.65. $C_{10}H_{11}NO_2$ requires C, 67.78; H, 6.26; N, 7.90%); $\nu_{max.}$(film) 1 670 and 1 600 cm^{-1}; δ_H 8.82 (1 H, s), 6.80—7.50 (4 H, m), 4.70—5.10 (1 H, m), 3.90—4.50 (2 H, m), and 1.26 (3 H, d, *J* 7 Hz); *m*/*z* (%) 177 (89), 170 (25), 162 (6), 148 (5), 138 (68), 120 (7), 114 (16), 106 (12), 79 (6), and 77 (7); $\lambda_{max.}$ 222, 247, and 292 nm.

Methyl 3-*Methyl*-3,4-*dihydropyrrolo*[1,2,3-de]-2H-1,4-*benzoxazine*-5-*carboxylate* (**12**).—(*a*) The above prepared methyl pyruvate derivative (2.5 g, 10 mmol) was added to a saturated methanolic solution of hydrogen chloride (100 ml) and the mixture was heated at reflux for 45 min. After the solution had been allowed to cool it was diluted with water (100 ml) and extracted with chloroform (3 × 100 ml). The organic extract was dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by chromatography on Kieselgel G (50 g) using benzene–ether (15%) as eluant, which gave the *title compound* (**12**) (1.48 g, 64%). Recrystallisation from aqueous methanol gave colourless needles, m.p. 67—68 °C (Found: C, 67.55; H, 5.6; N, 6.15%; M^+, 231.089 54. $C_{13}H_{13}NO_3$ requires C, 67.2; H, 5.67; N, 6.06%; *M*, 231.089 837); $\nu_{max.}$(Nujol) 1 719, 1 590, 1 525, 784, and 740 cm^{-1} δ_H 7.20 (1 H, s), 6.60—7.40 (3 H, m), 5.21 (1 H, m), 4.36 (2 H, m), 3.91 (3 H, s), and 1.47 (3 H, d, *J* 8 Hz); *m*/*z* (%) 231 (100), 216 (20), 159 (27), and 157 (15); $\lambda_{max.}$ 210, 245, 285sh, 296, and 332 nm.

(*b*) A solution of the aminobenzoxazine (**8**) (5.0 g, 30 mmol) and methyl pyruvate (3.1 g, 30 mmol) in ethanol (100 ml) was stirred at room temperature for 15 min after which the solvent was removed under reduced pressure. The residue was then heated under reduced pressure (10—15 mmHg) at 130 °C. After 30 min the desired product was allowed to distil slowly from the reaction mixture. The title compound (**12**) (3.85 g, 55%) thus obtained was recrystallised from aqueous methanol and obtained as colourless needles, m.p. 67—69 °C.

3-*Methyl*-3,4-*dihydropyrrolo*[1,2,3-de]-2H-1,4-*benzoxazine*-5-*carboxylic Acid*.—The ester (**12**) (5.0 g, 21.6 mmol) was added to 2M aqueous sodium hydroxide (50 ml) and the resulting mixture was heated at reflux for 2 h. The solution was cooled to 0 °C after which concentrated hydrochloric acid was added until the mixture was acidic to litmus. The precipitate was collected, dried, and recrystallised from benzene–light petroleum (b.p. 60—80 °C) to give the *title compound* (4.6 g, 98%) as colourless prisms, m.p. 216—218 °C (Found: C, 66.35; H, 5.25; N, 6.8%; M^+, 217.073 91. $C_{12}H_{11}NO_3$ requires C, 66.35; H, 5.10; N, 6.45%; *M*, 217.073 887); $\nu_{max.}$(Nujol) 2 600br, 1 680, and 1 590 cm^{-1}; δ_H 9.00 (1 H, br s, exchanges D_2O), 6.60—7.50 (4 H, m), 5.00—5.40 (1 H, m), 4.22—4.45 (2 H, m), and 1.52 (3 H, d, *J* 8 Hz); *m*/*z* (%) 217 (100), 202 (25), 159 (37), 158 (14), 157 (13), and 130 (12); $\lambda_{max.}$ 210, 242, 282sh, 294, and 323 nm.

3-*Methyl*-3,4-*dihydropyrrolo*[1,2,3-de]-2H-1,4-*benzoxazine* (**13**).—The above prepared acid (500 mg, 2.3 mmol), sodium carbonate (120 mg, 1.15 mmol), and cupric sulphate pentahydrate (280 mg, 1.15 mmol) were added to water (25 ml). The green copper salt (650 mg, 57%) was collected and dried *in vacuo* over calcium chloride. A mixture of this copper salt (250 mg, 0.8 mmol), 3-methyl-3,4-dihydropyrrolo[1,2,3-*de*]-2*H*-1,4-benzoxazine-5-carboxylic acid (5.0 g, 23 mmol), and freshly distilled quinoline (175 ml) was heated at reflux for 5 h. The reaction mixture was cooled to room temperature, diluted with ether (150 ml), then washed with dilute hydrochloric acid (4 × 100 ml), water (100 ml), dilute aqueous sodium carbonate (2 × 100 ml), and finally water (100 ml). The ethereal layer was dried ($NaSO_4$), concentrated under reduced pressure, and the residue was purified by chromatography on Kieselgel G (200 g), using benzene–ether (10%) as eluant, which gave the *title compound* (**13**) (2.60 g, 65%) as a colourless oil (Found: C, 73.55; H, 6.35; N, 8.1. $C_{11}H_{11}NO$ requires C, 73.30; H, 6.36; N, 8.09%); $\nu_{max.}$(liq. film) 1 631, 1 585, 1 243, 1 042, 785, and 730 cm^{-1}; δ_H 7.23—6.45 (5 H, m), 4.45—3.85 (3 H, m), and 1.49 (3 H, d, *J* 6.4 Hz); *m/z* (%) 173 (100), 158 (49), 133 (12), 130 (20), 104 (28), and 77 (13).

3-*Methyl*-3,4-*dihydropyrrolo*[1,2,3-de]-2H-1,4-*benzoxazin*-6-*ylglyoxylyl Chloride*.—Oxalyl chloride (217 mg, 1.71 mmol) was added dropwise during 15 min to a stirred solution of the benzoxazine (**13**) (250 mg, 1.45 mmol) in anhydrous ether (20 ml) at 0 °C. Stirring and cooling were continued for a further hour and the yellow crystals that had been formed were collected, washed with anhydrous ether, and dried *in vacuo* overnight. The *title compound* (323 mg, 1.28 mmol, 88%) was obtained as glistening yellow plates after recrystallisation from dry benzene (Found: M^+, 263.034 01. $C_{13}H_{10}ClNO_3$ requires *M*, 263.034 916); $\nu_{max.}$(Nujol) 1 765 1 250, and 1 053 cm^{-1}; δ_H 8.21 (1 H, s), 6.80—8.00 (3 H, m), 3.90—5.80 (3 H, m), and 1.64 (3 H, d, *J* 7 Hz); *m/z* (%) 265 (0.1) 237 (6), 235 (17), 200 (100), 159 (11), 115 (4), and 103 (8); $\lambda_{max.}$ 219, 247, 255, and 272sh nm.

3-*Methyl*-3,4-*dihydropyrrolo*[1,2,3-de]-2H-1,4-*benzoxazine*-6-*glyoxylamide* (**18**).— The above prepared crude acid chloride (174 mg, 0.66 mmol) was added slowly with stirring to 1M ammonium hydroxide (25 ml) at 5 °C. After being stirred for a further 2 h at 5 °C the product was recovered and dried overnight *in vacuo*. Recrystallisation from ethanol gave the *title compound* (**18**) (126 mg, 0.52 mmol, 78%) as pale yellow crystals, m.p. 144—146 °C (Found: C, 63.75; H, 4.65; N, 11.8%; M^+, 244.084 61. $C_{13}H_{12}N_2O_3$ requires C, 63.93; H, 4.95; N, 11.47%; *M*, 244.084 786); $\nu_{max.}$(Nujol) 3 440, 3 330, 1 697, 1 620, 1 600, 1 558, 1 251, and 1 049 cm^{-1}; δ_H 8.88 (1 H, s), 6.70—7.95 (3 H, m), 7.75 (1 H, br s, partial exchange with D_2O), 4.35—4.80 (2 H, m), 3.95—4.30 (1 H, m), and 1.62 (3 H, d, *J* 7 Hz); *m/z* (%) 244 (20), 200 (100), and 159 (12); $\lambda_{max.}$ 222, 249, 256, and 275sh nm.

6-*Dimethylaminomethyl*-3-*methyl*-3,4-*dihydropyrrolo*[1,2,3-de]-2H-1,4-*benzoxazine* (**19**).—A mixture of 3-methyl-3,4-dihydropyrrolo[1,2,3-*de*]-2*H*-1,4-benzoxazine (1.0 g, 5.7 mmol) and formalin (310 mg) was added to an ice-cold solution of aqueous dimethylamine (1.0 g, 6.0 mmol) and glacial acetic acid (580 mg). The reaction mixture was stirred at room temperature for 4 h and then made alkaline to litmus by the addition of dilute aqueous potassium hydroxide. The mixture was extracted with chloroform (2 × 40 ml) and the combined organic phases were dried ($MgSO_4$). Removal of the solvent under reduced pressure gave a yellow oil which on distillation gave the *title compound* (**19**) (1.24 g, 92%), as a colourless oil, b.p. 134—138 °C/0.02 mmHg (Found: C, 73.75; H, 8.0; N, 11.95%; M^+, 230.141 320. $C_{14}H_{18}N_2O$ requires C, 73.01; H, 7.88; N, 12.16%; *M*, 230.141 905); $\nu_{max.}$(film) 3 050, 1 635, 1 590, 1 241, 1 042, 783, and 734 cm^{-1}; δ_H 6.50—7.35 (4 H, m), 3.81—4.57 (3 H, m), 3.58 (2 H, s), 2.25 (6 H, s), and 1.39 (3 H, d, *J* 7 Hz); *m/z* (%) 230 (28) and 186 (100); $\lambda_{max.}$ 230, 274, 290, and 299 nm.

6-*Dimethylaminomethyl*-3-*methyl*-3,4-*dihydropyrrolo*[1,2,3-de]-2H-1,4-*benzoxazine Methiodide*.—The benzoxazine (**19**) (0.9 g, 3.9 mmol) was added slowly to methyl iodide (10 ml) with vigorous stirring. The solution was stirred at room temperature for 3 h after which the solid precipitate was collected and washed carefully with ice-cold ether. Recrystallisation from methanol–ether gave the *methiodide* (1.38 g, 97%) as colourless prisms, m.p. 198 °C (decomp.) (Found: C, 48.85; H, 5.5; N, 7.35. $C_{15}H_{21}N_2IO$ requires C, 48.40; H, 5.69; N, 7.53%); $\nu_{max.}$(Nujol) 1 632 1 588, 1 525, 1 460, 785, and 740 cm^{-1}; δ_H(CD_3OD) 7.72 (1 H, s), 6.50—7.50 (3 H, m), 4.73 (2 H, s), 3.97—4.61 (3 H, m), 3.15 (9 H, s), and 1.53 (3 H, d, *J* 7 Hz).

3-*Methyl*-3,4-*dihydropyrrolo*[1,2,3-de]-2H-1,4-*benzoxazin*-6-*ylacetonitrile* (**20**).—To a solution of potassium cyanide (830 mg, 12.75 mmol) in water (20 ml), the above prepared methiodide (1.58 g, 4.25 mmol) was added and the resulting mixture was heated under reflux for 2.5 h during which time an oil separated from the aqueous solution. This oil was extracted with chloroform (3 × 40 ml) and the combined organic extracts were washed with water and dried (Na_2SO_4). The solvent was removed under reduced pressure leaving an orange oil which was chromatographed on Kieselgel G (200 g); elution with 10% ether in benzene gave two main fractions. The first fraction contained 5-*cyano*-3,6-*dimethyl*-3,4-*dihydropyrrolo*[1,2,3-de]-2H-1,4-*benzoxazine* (**21**) (140 mg, 16%), which was obtained as a pale yellow oil, b.p. 90—94 °C/0.05 mmHg (Found: C, 73.4; H, 5.65; N, 13.25%; M^+, 212.0944. $C_{13}H_{12}N_2O$ requires C, 73.57; H, 5.70; N, 13.20%; *M*, 212.094 958); $\nu_{max.}$(film) 2 210, 1 625, 1 581, 1 240, and 1 039 cm^{-1}; δ_H 6.86—7.50 (3 H, m), 4.30—4.81 (3 H, m), 2.49 (3 H, s), and 1.55 (3 H, d, *J* 7 Hz); *m/z* (%) 212 (100), 197 (96), 172 (14), and 171 (18); $\lambda_{max.}$ 243, 281, 289, 319, and 335sh nm.

The second fraction contained the *title compound* (**20**) (596 mg, 66%), which was obtained as a pale yellow oil, b.p. 143—147 °C/0.05 mmHg (Found: C, 73.8; H, 5.55; N, 12.95%; M^+, 212.094 62. $C_{13}H_{12}N_2O$ requires C, 73.57; H, 5.70; N, 13.20%; *M*, 212.094 958); $\nu_{max.}$(film) 2 245, 1 632, 1 588, 1 243, 1 042, 785, and 735 cm^{-1}; δ_H 6.64—7.40 (4 H, m), 3.90—4.60 (3 H, m), 3.78 (2 H, s), and 1.49 (3 H, d, *J* 8 Hz); *m/z* (%) 212 (100) and 186 (4); $\lambda_{max.}$ 231, 263sh, 274, 289, and 298 nm.

6-(2-*Aminoethyl*)-3-*methyl*-3,4-*dihydropyrrolo*[1,2,3-de]-2H,1,4-*benzoxazine* (**3**).—(*a*) The above prepared acetonitrile (**20**) (500 mg, 2.00 mmol) and cobaltous chloride hexahydrate (952 mg, 4.00 mmol) were dissolved in 99% methanol (25 ml) and sodium borohydride (760 mg, 20.0 mmol) was added. The mixture was stirred for 1 h at 20 °C after which 3M hydrochloric acid (8 ml) was added and stirring continued until all the black precipitate had dissolved. Ether extraction removed any unchanged starting material after which the aqueous layer was basified with concentrated ammonia solution. It was then extracted with chloroform (3 × 50 ml), and the combined extracts evaporated under reduced pressure to leave the *title* 3-*methyl compound* (**3**) (322 mg, 75%) as a yellow oil (Found: M^+, 216.126 256. $C_{13}H_{16}N_2O$ requires *M*, 216.1260); $\nu_{max.}$(film) 3 350br, 2 920, 1 630, 1 585, 1 240, and 1 042 cm^{-1}; δ_H 6.50—7.40 (4 H, m), 3.85—4.60 (3 H, m), 2.60—3.20 (4 H, m), 1.35 (3 H, d, *J* 8 Hz), and 1.32 (2 H, br s, exchanges with D_2O); *m/z* (%) 216 (34) and 186 (100); $\lambda_{max.}$ 231, 265sh, 275, 290, and 310 nm.

(*b*) A solution of the above prepared acetonitrile (**20**) (370 mg, 1.74 mmol) in dry ether (5 ml) was added dropwise to a solution of lithium aluminium hydride (76 mg, 2.0 mmol) in dry ether (10 ml), at 0 °C. After 1 h the reaction was quenched by the addition of water (4 ml) and 6M sulphuric acid (6 ml). The aqueous phase

was separated and extracted with ether (3 × 15 ml), after which it was adjusted to pH 10 by the addition of 2M aqueous potassium hydroxide. The aqueous phase was then extracted with ethyl acetate (4 × 20 ml), and the combined organic extracts were washed with saturated brine (30 ml), and dried (Na_2SO_4). Removal of the solvent under reduced pressure gave the title compound (**3**) as a yellow oil (340 mg, 90%), identical (i.r. and n.m.r. spectra) with that prepared by procedure (*a*).

3-*Methyl*-6-[2-(3-*oxobut*-1-*enylamino*)*ethyl*]-3,4-*dihydropyrrolo*[1,2,3-de]-2H-1,4-*benzoxazine* (**22**).—Triethylamine (2.22 g, 22 mmol) was slowly added to a solution of the above prepared benzoxazine (**3**) (945 mg, 4.4 mmol) in absolute ethanol, cooled to 0 °C. After 20 min 1-chlorobut-1-en-3-one[13] (919 mg, 8.8 mmol) was added dropwise. After a further 6 h at 0—5 °C the reaction mixture was concentrated under reduced pressure. The residue was taken up in dichloromethane (30 ml), washed with water (3 × 20 ml), dried (Na_2SO_4), and concentrated under reduced pressure to give the *title compound* (**22**) (824 mg, 66%) as an orange oil (Found: M^+, 284.152 30. $C_{17}H_{20}N_2O_2$ requires *M*, 284.152 469); $\nu_{max.}$(liq. film) 3 250br, 1 635, 780, and 735 cm^{-1}; δ_H 7.31—6.37 (5 H, m), 4.96 (1 H, d, *J* 8 Hz), 4.3 (3 H, m), 3.46 (2 H, t, *J* 6 Hz), 3.00 (2 H, t, *J* 6 Hz), 2.07 (3 H, s), and 1.45 (3 H, d, *J* 6.5 Hz); *m*/*z* (%) 284 (M^+, 17), 199 (15), 186 (100), 145 (6), 128 (3), and 117 (4).

6-[2-(N-*Acetyl*-N-3-*oxobut*-1-*enylamino*)*ethyl*]-3-*methyl*-3,4-*dihydropyrrolo*[1,2,3-de]-2H-1,4-*benzoxazine* (**23**).—The above prepared benzoxazine (**22**) (345 mg, 1.18 mmol), in dry tetrahydrofuran was added to a suspension of sodium hydride (50% dispersion; 58 mg, 1.18 mmol) in dry tetrahydrofuran (20 ml) at −5 °C, under an atmosphere of nitrogen. The mixture was stirred at −5 °C for 30 min after which acetyl chloride (112 mg, 1.43 mmol) was added dropwise. The mixture was stirred at 0 °C for 1 h and then concentrated under reduced pressure. The residue was taken up in dichloromethane (30 ml) and the solution was washed with water (2 × 20 ml), dried (Na_2SO_4), and concentrated under reduced pressure. The residue was purified by chromatography on Kieselgel G (40 g) using ethyl acetate–light petroleum (b.p. 60—80 °C) (10%) as eluant. Recrystallisation from dichloromethane–hexane then gave the *title compound* (**23**) [300 mg, 49% from tryptamine derivative (**3**)] as colourless prisms, m.p. 126—126.5 °C (Found: C, 70.1; H, 6.75; N, 8.65%; M^+, 326.162 76. $C_{19}H_{22}N_2O_3$ requires C, 69.9; H, 6.8; N, 8.6%; *M*, 326.163 032); $\nu_{max.}$(Nujol) 1 684, 1 649, 1 610, 1 583, 1 240, 1 005, 783, and 735 cm^{-1}; δ_H 8.01 (1 H, d, *J* 13.66 Hz), 7.19 (1 H, d, *J* 7.3 Hz), 6.98 (1 H, t, *J* 7.3 Hz), 6.95 (1 H, s), 6.63 (1 H, d, *J* 7.3 Hz), 5.69 (1 H, d, *J* 13.66 Hz), 4.35 (3 H, m), 3.89 (2 H, t, *J* 8.6), 2.97 (2 H, t, *J* 8.6 Hz), 2.26 (3 H, s), 2.18 (3 H, s), and 1.46 (3 H, d, *J* 6.4 Hz); δ_C 196.81 (C-5′), 170.28 (C-7′), 143.24 (C-9a), 140.91 (C-3′), 127.31 (C-6a), 125.47 (C-9b), 121.24 (C-9), 120.37 (C-8), 112.36 (C-6), 111.33 (C-7), 108.35 (C-4′), 105.01 (C-5), 71.18 (C-2), 49.03 (C-3), 44.64 (C-2′), 28.33 (C-6′), 23.18 (C-1′), 21.94 (C-8′), and 16.25 (C-3a); *m*/*z* (%) 326 (M^+, 15), 199 (82), 186 (100), 145 (8), 117 (4), and 43 (60); $\lambda_{max.}$ 223, 279, and 300 nm.

3-*Acetyl*-8-*methyl*-2,3,3a,4,6,6a,8,9-*octahydro*[1,4]*oxazino*-[2,3,4-jk]*pyrrolo*-[2,3-d]-*carbazol*-5(1H)-*one* (**24**).—The above prepared benzoxazine (**23**) (100 mg, 0.31 mmol) was added to freshly distilled boron trifluoride–diethyl ether (25 ml) at 90 °C. After 10 min the mixture was poured into ice-cold saturated aqueous sodium carbonate (50 ml) and the mixture extracted with dichloromethane (4 × 50 ml). The combined organic phases were washed with 0.5M potassium hydroxide solution (50 ml) and water (3 × 50 ml), dried (Na_2SO_4), and concentrated under reduced pressure. The residue, consisting of at least six components (t.l.c. analysis), was purified by chromatography on Kieselgel G (30 g) using ethyl acetate as eluant, which gave the title compound (**24**) (5—10 mg, 5—10%), as a yellow solid, m.p. 223—225 °C (Found: M^+, 326.163 00. $C_{19}H_{22}N_2O_3$ requires *M*, 326.163 032); δ_H 6.8—6.55 (3 H, m), 4.4—3.60 (7 H, m), 3.4—2.2 (6 H, m), 2.10 (3 H, s), and 1.23 (3 H, d, *J* 6.6 Hz); *m*/*z* (%) 326 (M^+, 40), 269 (7), 240 (16), 212 (2), 199 (18), 186 (27), 170 (2), 87 (4), 56 (22), and 43 (100); $\lambda_{max.}$(EtOH) 215, 252, and 293 nm.

4-*Isopropylideneamino*-3-*methyl*-3,4-*dihydro*-2H,1,4-*benzoxazine* (**9**).—A solution of aminobenzoxazine (**8**) (3.0 g, 18.3 mmol), acetone (6 ml), and toluene-*p*-sulphonic acid (10 mg) in ethanol (30 ml) was heated at 60 °C for 2 h. The solvent was removed under reduced pressure, and the oily residue was distilled to give the *title compound* (**9**) (3.5 g, 95%) as a clear yellow oil, b.p. 120—124 °C/12 mmHg (Kugelrohr) (Found: M^+, 204.126 21. $C_{12}H_{16}N_2O$ requires *M*, 204.126 256); $\nu_{max.}$(liq. film) 3 080—2 820, 1 645, 1 603, 1 588, 1 495, 1 270, 1 247, 1 057, and 745 cm^{-1}; δ_H 6.75 (3 H, m), 6.36 (1 H, m), 4.15 (2 H, m), 3.43 (1 H, m), 2.12 (3 H, s), 1.98 (3 H, s), and 1.03 (3 H, d, *J* 5.85 Hz); *m*/*z* (%) 204 (M^+, 85), 189 (9), 148 (100), 133 (34), 120 (57), 106 (10), 91 (10), 77 (21), 65 (10), 56 (16), and 42 (11).

3,3′-*Dimethyl*-7,7′-*bi*-(3,4-*dihydro*-2H-1,4-*benzoxazyl*) (**30**).—The above prepared benzoxazine (**9**) (0.5 g, 2.45 mmol) was added to polyphosphoric acid (15 g) at 60 °C with stirring. The reaction mixture was heated at 150 °C for 3 h after which it was cooled, dissolved in dilute aqueous sodium hydrogen carbonate, and extracted with dichloromethane (4 × 30 ml). The combined organic layers were washed with water (2 × 25 ml), dried (Na_2SO_4), and concentrated under reduced pressure. Purification of the residue by chromatography on Kieselgel G (70 g), using benzene–ether (5%) as eluant, gave the *title compound* (**30**) (0.12 g, 33%), which was recrystallised from light petroleum (b.p. 60—80 °C) and obtained as colourless prisms, m.p. 68—69.5 °C (Found: M^+, 296.152 67. $C_{18}H_{20}N_2O_2$ requires *M*, 296.152 469); $\nu_{max.}$(Nujol) 3 360, 1 618, 1 571, 1 500, 1 290, 1 205, 1 020, 810, and 765 cm^{-1}; δ_H 7.07 (2 H, s), 7.00 (2 H, dd, *J* 5.5, 1.5 Hz), 6.70 (2 H, dd, *J* 5.5, 1.5 Hz), 4.27 (2 H, dd, *J* 10, 2.6 Hz), 3.7 (4 H, m), 3.63 (2 H, br s, exchanges with D_2O), and 1.16 (6 H, d, *J* 6.0 Hz); δ_C 143.78 (C-8a), 132.08 (C-4a), 119.35 (C-8), 115.61 and 114.36 (C-5 and C-6), 70.81 (C-2), 45.23 (C-3), and 17.77 (CH_3); *m*/*z* (%) 296 (M^+, 100), 281 (15), 253 (4), 222 (3), 211 (3), 148 (5), 133 (7), 69 (2), and 42 (4); $\lambda_{max.}$(EtOH) 218.5, 292, and 314 nm.

5-*Hydroxymethyl*-3-*methyl*-3,4-*dihydropyrrolo*[1,2,3-de]-2H-1,4-*benzoxazine* (**15**).—A solution of the ester (**12**) (1.0 g, 4.33 mmol) in dry ether (50 ml) was added dropwise to a stirred suspension of lithium aluminium hydride (90 mg, 2.38 mmol) in dry ether (500 ml), cooled to 0 °C. The mixture was then allowed to warm to room temperature, and stirred for a further 2 h. Wet ether (25 ml) was added, followed by 30% aqueous sodium hydroxide (30 ml). The precipitate was removed by filtration through a Celite pad and the filtrate was extracted with ether (2 × 30 ml). The combined ethereal layers were washed with 2M aqueous hydrochloric acid solution (25 ml) and water (2 × 50 ml), dried (Na_2SO_4), and concentrated under reduced pressure to give the *title compound* (**15**) (95%, 0.88 g) as colourless prisms, m.p. 89.5—91 °C (Found: M^+, 203.094 66. $C_{12}H_{13}NO_2$ requires *M*, 203.094 623); $\nu_{max.}$(Nujol) 3 260br, 1 631, 1 586, 1 497, 1 330, 1 304, 1 224, 1 006, 965, 798, 786, and 735 cm^{-1}; δ_H 6.90 (3 H, m), 6.26 (1 H, s), 4.61 (2 H, s), 4.45 (1 H, m), 4.13 (2 H, d, *J* 2.8 Hz), 2.50 (1 H, br s, exchanges with D_2O), and 1.33 (3 H, d, *J* 7.2 Hz); *m*/*z* (%) 203 (M^+, 100), 188 (28), 170 (23), 161 (6), 145 (7), 130 (5), 117 (9), 104 (8), 89 (9), and 77 (10); $\lambda_{max.}$(EtOH) 222, 266, and 292sh nm.

3,5-*Dimethyl*-3,4-*dihydropyrrolo*[1,2,3-de]-2H-1,4-*benzoxazine* (**14**).—(a) A solution of the ester (**12**) (200 mg, 0.87 mmol) in

tetrahydrofuran (10 ml) was added to a solution of lithium aluminium hydride (164 mg, 4.3 mmol) in tetrahydrofuran (25 ml). The mixture was stirred for 4 h at room temperature after which anhydrous aluminium chloride (230 mg, 1.73 mmol) was added and the mixture was heated at reflux for 48 h. It was then cooled and 30% aqueous sodium hydroxide (10 ml) was added. After filtration the aqueous phase was separated and extracted with tetrahydrofuran (2 × 25 ml). The combined organic phases were washed with water (2 × 25 ml), dried (Na_2SO_4), and concentrated under reduced pressure. The residue was purified by chromatography on Kieselgel G (25 g), using benzene as eluant, which gave the title compound (**14**) (458 mg, 57%) as a pale yellow oil, which proved to be unstable to distillation.

(b) A solution of the ester (**12**) (690 mg, 3.0 mmol) in dry toluene (10 ml) was added to sodium bis(2-methoxyethoxy)-aluminium hydride (2.1 ml, 15 mmol) in dry toluene. The reaction mixture was heated at reflux for 7 days and then cooled to 0 °C. 30% Aqueous sodium hydroxide (10 ml) was added and the solution was filtered. The aqueous phase was separated and extracted with toluene (2 × 25 ml). The combined organic phases were washed with 2M hydrochloric acid (2 × 15 ml) and water (20 ml), dried (Na_2SO_4), and then concentrated under reduced pressure. Purification of the residue by chromatography on Kieselgel G (50 g), using benzene as eluant, gave the *title compound* (**14**) (460 mg, 82%), as a clear, pale yellow oil (Found: M^+ 187.099 46. $C_{12}H_{13}NO$ requires M, 187.099 708); $\nu_{max.}$(liq. film) 3 060, 2 980, 2 913, 2 872, 1 635, 1 589, 1 540, 1 500, 1 460, 1 245, 1 145, 1 092, 790, 734, and 683 cm^{-1}; δ_H 7.04 (1 H, d, J 7.2 Hz), 6.84 (1 H, t, J 7.2 Hz), 6.54 (1 H, d, J 7.2 Hz), 6.10 (1 H, s), 4.2 (3 H, m), 2.30 (3 H, s), and 1.27 (3 H, d, J 10 Hz); m/z (%) 187 (M^+, 100), 172 (69), 144 (18), 130 (3), 117 (10), 89 (6), 77 (5), 63 (4), and 51 (4); $\lambda_{max.}$(EtOH) 225, 272, 284, 290, and 295 nm.

6-(2-*Aminoethyl*)-3,5-*dimethyl*-3,4-*dihydropyrrolo*[1,2,3-de]-2H-1,4-*benzoxazine* (**5**).—To the aminobenzoxazine (**8**) (46.85 g, 0.285 mol) in methanol (600 ml) and water (40 ml) 5-chloropentan-2-one (37.9 g, 0.314 mol) was added dropwise with stirring. The mixture was heated at reflux for 15 h, after which the solvent was removed under reduced pressure. The residue was taken up in 2M hydrochloric acid (100 ml) and filtered hot through a pad of activated charcoal. The filtrate was cooled, made alkaline by the addition of 2M aqueous sodium hydroxide and extracted with benzene (5 × 250 ml). The combined organic layers were washed with water (2 × 300 ml), dried (Na_2SO_4), and then concentrated under reduced pressure. Distillation of the residue gave the *title compound* (**5**) (45.5 g, 69%) as a clear, pale yellow oil, b.p. 130—135 °C/0.2 mmHg (Found: C, 72.7; H, 7.9; N, 12.2%; M^+, 230.141 95. $C_{14}H_{18}N_2O$ requires C, 73.0; H, 7.88; N, 12.16%; M, 230.141 905); $\nu_{max.}$(liq. film) 3 390, 3 310, 3 085—2 900, 1 647, 1 600, 1 511, 1 356, 1 257, 1 140, 791, and 747 cm^{-1}; δ_H 7.05 (1 H, d, J 7.5 Hz), 6.86 (1 H, t, J 7.5 Hz), 6.54 (1 H, d, J 7.5 Hz), 4.16 (3 H, m), 2.84 (4 H, m), 2.28 (3 H, s), 1.26 (3 H, d, J 6.5 Hz), and 1.2 (2 H, br s, exchanges with D_2O); m/z (%) 230 (M^+, 22), 200 (100), 186 (3), 172 (2), 159 (6), 143 (2), and 131 (4); $\lambda_{max.}$($\log_{10}$ ε) (MeOH) 223 (4.46), 270 (3.83), 281 (3.81), and 294 nm (3.77).

6-[2-(2,2-*Diethoxycarbonylvinylamino*)*ethyl*]-3,5-*dimethyl*-3,4-*dihydropyrrolo*[1,2,3-de]-2H-1,4-*benzoxazine* (**26**).—A solution of the above prepared benzoxazine (**5**) (2.0 g, 8.7 mmol) and diethyl ethoxymethylenemalonate (1.80 g, 8.7 mmol) in ethanol (100 ml) was heated at reflux for 16 h. Concentration under reduced pressure then gave the *title compound* (**26**) (3.4 g, 98%) as a clear, pale yellow oil (Found: M^+, 400.199 83. $C_{22}H_{28}N_2O_5$ requires M, 400.199 809); $\nu_{max.}$($CHCl_3$) 3 300br, 3 003, 2 960, 2 900, 1 703, 1 695, 1 666, 1 645, 1 618, 1 510, 1 390, 1 355, and 1 086 cm^{-1}; δ_H 9.14 (1 H, br), 7.59 (1 H, d, J 13 Hz), 7.06 (1 H, dd, J 1, 7.5 Hz), 6.93 (1 H, t, J 7.5 Hz), 6.60 (1 H, dd, J 1, 7.5 Hz), 4.31 (3 H, m), 4.15 (4 H, m), 3.56 (2 H, m, J 7 Hz), 2.97 (2 H, t, J 7 Hz), 2.26 (3 H, s), and 1.3 (9 H, m); m/z (%) 400 (M^+, 13), 355 (2), 200 (100), and 159 (5); $\lambda_{max.}$($\log_{10}$ ε) (MeOH) 222 (4.55), 275.5 (4.33), and 350 nm (3.06).

3-*Acetyl*-2,3,3a,4,8,9-*hexahydro*-8-*methyl*[1,4]*oxazino*[2,3,4-jk]*pyrrolo*[2,3-d]*carbazol*-5-(1H)-*one* (**28**).—A stirred solution of the above prepared pyrrolobenzoxazine (**26**) (6.0 g, 15.0 mmol), glacial acetic acid (50 ml), and acetic anhydride (75 ml) was heated at reflux for 70 h. The solution was cooled, diluted to twice its volume with water and then adjusted to pH 12 by the addition of 2M aqueous sodium hydroxide. The mixture was stirred for 20 min and then extracted with chloroform (4 × 125 ml). The combined organic extracts were washed with 2M aqueous sodium hydroxide (2 × 75 ml), water (50 ml), 2M hydrochloric acid solution (2 × 75 ml), and then again with water (2 × 75 ml). The organic layer was dried (Na_2SO_4), evaporated under reduced pressure and the residue purified by chromatography on Kieselgel *G* (200 g) using chloroform–ethanol (0—3%) as eluant to give the *title compound* (**28**) (2.18—2.40 g, 45—49%), as a pale yellow oil, b.p. 205—210 °C/0.25 mmHg (Kugelrohr) (Found: M^+, 324.1472. $C_{19}H_{20}N_2O_3$ requires M, 324.147 283); $\nu_{max.}$ ($CHCl_3$) 3 060—2 900, 1 651, 1 615, 1 605, 1 500, 1 490, 1 382, and 1 131 cm^{-1}; δ_H 6.82 (3 H, m), 5.50, 5.49, 5.40, 5.38 (1 H, 4 s), 4.77 (1 H, m), 4.6—2.0 (9 H, m), 2.20, 2.16 (3 H, 2 s), and 1.50 and 1.33 (3 H, 2d, J 6.4 Hz); δ_C 193.24, 192.86, 192.43, 192.00 (C-5), 168.97, 168.59, 167.89, 167.61 (C-1′ or 6a), 166.80, 166.59 (C-6a or 1′), 142.00, 141.83 (C-10), 134.46, 134.30, 133.76, 133.65 (C-10a), 129.91, 128.34, 128.23 (C-13a), 123.41, 123.08, 122.65 (C-12), 115.61, 115.50, 115.34, 115.17, 115.01, 114.74 (C-11 and C-13), 97.46, 97.35, 97.08 (C-6), 69.78 (C-9), 60.78, 58.02 (C-3a), 54.88, 53.47 (C-13b), 48.16, 48.05 (C-8), 44.86, 43.39 (C-2), 40.36, 40.20, 39.65, 38.68, 38.51 (C-4 and C-1), 22.21, 21.99 (C-2′), and 16.09 and 12.35 (C-8a); m/z (%) 324 (M^+, 53), 282 (44), 239 (76), and 226 (100); $\lambda_{max.}$($\log_{10}$ ε) (MeOH) 208 (4.27), 237 (3.88), 288 (3.65), and 345 nm (4.15).

3-*Acetyl*-8-*methyl*-2,3,3a,4,6,6a,8,9-*octahydro*[1,4]*oxazino*-[2,3,4-jk]*pyrrolo*[2,3-d]*carbazol*-5(1H)-*one* (**24**).—Liquid ammonia (75 ml) was distilled through a potassium hydroxide drying tower and condensed into a receiving flask containing a solution of the pentacyclic enamino ketone (**28**) (2.4 g, 7.42 mmol) in tetrahydrofuran (7 ml). t-Butyl alcohol (550 mg, 7.42 mmol) was then added, followed by the slow addition of lithium metal (104 mg, 14.8 mmol). The mixture was then stirred at −33 °C for 45 min after which the ammonia was allowed to evaporate. Water (50 ml) and chloroform (100 ml) were added to the residue. The aqueous phase was separated and extracted with chloroform (3 × 50 ml) and the combined organic extracts were washed with saturated brine, dried (Na_2SO_4), and then concentrated under reduced pressure to give the title compound (**24**) (2.18—2.3 g, 90—95%) as a yellow foam. Recrystallisation from ethanol separated the two diastereo-isomers giving a colourless, crystalline solid and a yellow oil.

Diastereoisomer I (**24a**) formed colourless prisms, m.p. 228—231 °C (Found: C, 69.7; H, 6.65; N, 8.35%; M^+, 326.162 93. $C_{19}H_{22}N_2O_3$ requires C, 69.92; H, 6.79; N, 8.68%; M, 326.163 032); $\nu_{max.}$(Nujol) 1 711, 1 645, 1 617, 1 208, 1 189, 780, and 741 cm^{-1}; δ_H($CDCl_3$; 400 MHz) 6.75 (1 H, t, J 8 Hz, 12-H), 6.68 (1 H, d, J 8 Hz, 13-H), 6.66 (1 H, d, J 8 Hz, 11-H), 4.20 (1 H, t, J 3.5 Hz, 6a-H), 4.07 (1 H, dd, J 3, 11 Hz, 9-H), 3.97 (1 H, dd, J 8.5, 11 Hz, 9-H), 3.85 (1 H, t, J 11 Hz, 2-H), 3.80 (1 H, t, J 3 Hz, 3a-H), 3.71 (1 H, m, 2-H), 3.36 (1 H, dd, J 3.5, 18 Hz, 6-H), 3.06 (1 H, ddq, J 3, 6.4, 8.5 Hz, 8-H), 2.95 (1 H, dd, J 3, 17.5 Hz, 4-H), 2.62 (1 H, m, 1-H), 2.58 (1 H, dd, J 3, 17.5 Hz, 4-H), 2.54 (1 H, dd,

J 3.5, 18 Hz, 6-H), 2.12 (1 H, m, 1-H), 2.09 (3 H, s, COMe), and 1.21 (3 H, d, *J* 6.4 Hz, 8a-H); δ_C 207.98 (C-5), 167.00 (C-1'), 143.18 (C-10), 137.60 (C-10a), 131.05 (C-13a), 121.73 (C-12), 114.20 (C-13), 114.20 (C-11), 72.37 (C-9), 72.05 (C-3a), 63.71 (C-6a), 54.17 (C-13b), 52.11 (C-8), 47.56 (C-2), 43.23, 38.73, 37.70 (C-1, C-4, C-6), 23.40 (C-2'), 17.06 (C-8a); *m/z* (%) 326 (M^+, 100), 311 (8), 269 (33), 240 (70), 212 (18), 199 (67), 186 (80), 170 (7.9), 145 (10), 115 (9), 87 (13), and 56 (16); $\lambda_{max.}$($\log_{10}$ ε) (MeOH) 212.5 (4.52), 247.5 (3.75), and 292 nm (3.45).

Diastereoisomer II (**24b**) was obtained as a pale yellow oil; δ_H ($CDCl_3$; 400 MHz) 6.875 (1 H, m), 6.68 (1 H, m), 6.605 (1 H, m), 4.365 (1 H, dd, *J* 4.2, 9.0 Hz, 3a-H), 4.25 (1 H, dd, *J* 3.1, 11.0 Hz, 9-H), 4.1 (2 H, m), 4.035 (1 H, dd, *J* 6.2, 11.0 Hz, 9-H), 3.925 (1 H, dd, *J* 3.8, 8.0 Hz, 6-H), 3.75 (1 H, dd, *J* 6.0, 8.0 Hz, 6-H), 3.316 (1 H, ddq, *J* 3.1, 6.2, 6.2 Hz, 8-H), 2.952 (1 H, dd, *J* 4.2, 17.6 Hz, 4-H), 2.597 (1 H, dd, *J* 9.0, 17.6 Hz, 4-H), 2.51 (2 H, m), 2.146 (3 H, s, $COCH_3$), 1.479 (1 H, dd, *J* 5.4, 6.4 Hz, 1-H), and 1.138 (3 H, d, *J* 6.2 Hz, 8a-H); δ_C 207.49 (C-5), 169.67 (C-1'), 142.48 (C-10), 135.11 (C-10a), 132.51 (C-13a), 120.16 (C-12), 114.74 (C-13), 114.04 (C-11), 71.62 (C-9), 66.25 (C-3a), 60.95 (C-6a), 53.74 (C-13b), 46.70 (C-2), 44.96 (C-8), 40.57, 38.25, 36.45 (C-1, C-4, C-6), 22.91 (C-2'), and 12.84 (C-8a). The u.v., i.r., and mass spectra were essentially identical with those of (**24a**).

Hexacyclic Methoxy Ketone (**39**).—A solution of the pentacyclic amino ketone (**24a**) and (**24b**) (0.5 g, 1.53 mmol) in 2M hydrochloric acid (50 ml) was heated at reflux for 16 h, after which it was cooled to room temperature. The reaction mixture was washed with chloroform (2 × 50 ml) and then adjusted to pH 12 by the addition of 2M aqueous sodium hydroxide. The mixture was extracted with chloroform (3 × 75 ml) and the combined organic layers were washed with water (2 × 50 ml), dried (Na_2SO_4), and concentrated under reduced pressure. The residue was purified by chromatography on Kieselgel G (30 g) using as eluant dichloromethane–methanol (2%)/concentrated ammonia solution (1%) (prepared by shaking the mixture vigorously and then discarding the excess aqueous phase), which gave the pentacyclic amine (**35**) as a clear yellow oil. This amine was taken up in dry methanol (13 ml) containing sodium methoxide (from 15 mg of sodium) and stirred at room temperature for 15 min. Freshly distilled acrolein (0.25 g, 4.46 mmol) was then added after which stirring was continued for 48 h. The reaction mixture was diluted with water (20 ml) and then extracted with dichloromethane (4 × 40 ml). The combined organic extracts were washed with water (75 ml), dried (Na_2SO_4), and concentrated under reduced pressure. The residue was purified by chromatography on Kieselgel G (60 g) using dichloromethane–methanol (2%) as eluant, which gave the *hexacyclic methoxide* (**39**) (44—65 mg, 8—12%) as a colourless oil (Found: M^+, 354.194 22. $C_{21}H_{26}N_2O_3$ requires *M*, 354.194 331); $\nu_{max.}$($CHCl_3$) 3 050, 3 000, 2 970, 2 935, 2 810, 1 706, 1 620, 1 486, 1 100, 1 051, and 1 030 cm^{-1}; δ_H 6.71 (3 H, m), 4.01 (3 H, m), 3.46 (1 H, apparent t, *J* 3 Hz), 3.21 (3 H, s, OMe), 3.3—1.4 (13 H, m), and 1.18 (3 H, d, *J* 6.4 Hz, 24-H); δ_C 209.87 (C-17), 143.03 (C-12), 137.49 (C-13), 135.65 (C-8), 121.67 (C-10), 114.69 (C-11), 113.17 (C-9), 73.89 (C-2 or C-21), 73.68 (C-15), 72.48 (C-23), 68.80 (C-21 or C-2), 55.96 (OCH_3), 54.55 (C-5), 52.60 (C-7), 52.33 (C-22), 48.38 (C-20), 47.35 (C-3), 40.41 (C-6), 38.14 (C-16), 26.49 (C-14), and 16.96 (C-24); *m/z* (%) 354 (M^+, 17), 312 (1), 200 (5) 186 (8), 168 (10), 148 (7), 126 [100, $\underline{CH{=}CHCH(OMe)CH_2CH_2\overset{+}{N}{=}}$]; $\lambda_{max.}$(MeOH) 213.5, 247, and 290 nm.

Hexacyclic Enone (**38**).—To a solution of the pentacyclic amine (**35**) (350 mg, 1.23 mmol) in dry methanol (50 ml) and dry benzene (5 ml) acrolein (102 mg, 1.82 mmol) was added followed, after 10 min, by a solution of sodium metal (28.3 mg, 1.23 mmol) in dry methanol (5 ml). The solution was stirred at 0 °C for 30 min after which acrolein (29 mg, 0.52 mmol) was added. The mixture was heated at reflux for 2 h and then cooled to 0 °C. The solution was neutralised by the addition of 2M hydrochloric acid and then concentrated under reduced pressure. The residue was extracted with chloroform (4 × 50 ml) and the combined organic extracts were washed with saturated aqueous sodium hydrogen carbonate, dried (Na_2SO_4), and concentrated under reduced pressure. The residue was taken up in dry pyridine (30 ml) and cooled to 0 °C. Methanesulphonyl chloride (340 mg, 3.0 mmol) was added and the solution was kept at 0 °C for 1 h; it was then stirred at room temperature for 48 h. Concentration under reduced pressure gave a red viscous oil which was taken up in chloroform (100 ml), washed with saturated aqueous sodium hydrogen carbonate, dried (Na_2SO_4) and concentrated under reduced pressure. The residue was purified by chromatography on Kieselgel G (50 g) using dichloromethane–methanol (0—2%) as eluant, to give the *hexacyclic enone* (**38**) (107 mg, 27%). This was recrystallised from acetone–hexane and obtained as pale yellow prisms, m.p. 199.5—201 °C (Found: C, 74.2; H, 6.8; N, 8.4%; M^+, 322.168 14. $C_{20}H_{22}N_2O_2$ requires C, 74.5; H, 6.88; N, 8.69%; *M*, 322.168 118); $\nu_{max.}$($CHCl_3$) 3 060—2 760, 1 691, 1 626, 1 604sh, 1 486, 1 345, 1 050, 1 020, and 843 cm^{-1}; δ_H 7.05—6.85 (2 H, m, 15-H + Ar-H), 6.75—6.55 (2 H, m, Ar-H), 4.32—3.67 (4 H, m), 3.3—1.90 (11 H, m), and 1.12 (3 H, d, *J* 6.4 Hz); δ_C 197.68 (C-17), 142.80 (C-12), 137.71 (C-13), 135.33 (C-15), 134.14 (C-8 and C-20), 120.43 (C-10), 114.96 (C-11), 113.28 (C-9), 71.83 (C-23), 67.45, 63.87 (C-2 & C-21), 55.64 (C-7), 47.62 (C-3 or C-5), 45.51 (C-22), 43.18 (C-5 or C-3), 39.38 (C-6), 37.16 (C-16), 19.66 (C-14), and 14.90 (C-24); *m/z* (%) 322 (M^+, 100), 307 (6), 265 (8), 200 (31), 186 (18), 174 (25), 149 (15), 138 (13), 107 (10), and 69 (7); $\lambda_{max.}$($\log_{10}$ ε) (MeOH) 216 (4.48), 238 (4.05), and 295.5 nm (3.45).

Hexacyclic Oxo Ester (**44**).—A solution of the hexacyclic enone (**38**) (25 mg, 0.078 mmol) in dimethylformamide (2 ml) was added to a solution of potassium t-butoxide (18 mg, 0.16 mmol) in t-butyl alcohol (4 ml) and dimethylformamide (1 ml) at 0 °C. The solution was stirred at 0 °C for 30 min and then at room temperature for 1 h. Freshly distilled methyl bromoacetate (83 mg, 0.543 mmol) was added to the reaction mixture, which was then stirred for 2 h. Water (5 ml) was added and the solvents were removed under reduced pressure. The residue was taken up in chloroform (15 ml), and the solution washed with water (15 ml), dried (Na_2SO_4), and concentrated under reduced pressure. The residue was purified by chromatography on Kieselgel G (25 g) using dichloromethane as eluant to give the *hexacyclic oxo ester* (**44**) (12.3 mg, 40%) as a pale yellow oil (Found: M^+, 394.189 06. $C_{23}H_{26}N_2O_4$ requires *M*, 394.189 245); $\nu_{max.}$ 3 100—2 720, 1 735, 1 714, 1 626, 1 605, 1 490, 1 336, 1 293, and 1 082 cm^{-1}; δ_H 6.8—6.55 (3 H, m), 5.79 (2 H, m), 4.14 (3 H, m), 3.80 (1 H, dd, *J* 4.1, 3.8 Hz), 3.46 (3 H, s), 3.4 (3 H, m), 2.86—1.0 (8 H, m), and 1.12 (3 H, d, *J* 6.6 Hz); *m/z* (%) 394 (M^+, 49), 352 (8), 320 (11), 200 (31), 186 (19), 179 (100), 173 (15), 165 (29), 151 (29), 149 (26), and 106 (18); $\lambda_{max.}$(MeOH) 217, 249.5, and 291 nm.

1-(*o-Nitrophenoxy*)*butan-2-ol* (**48**).—1,2-Epoxybutane (17.1 g, 0.24 mol) was added to a suspension of the potassium salt of *o*-nitrophenol (10.0 g, 47.4 mmol) in absolute ethanol (100 ml), and the mixture was heated at reflux for 24 h; it was then cooled and diluted with water (50 ml). The volatile components were removed under reduced pressure, and the residual aqueous phase was extracted with ether (4 × 30 ml). The combined ethereal layers were washed with 2M aqueous sodium hydroxide (3 × 30 ml), dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by chromatography on Kieselgel G (150 g) using chloroform as eluant, which gave the

title compound (**48**) (3.08 g, 34%) as an unstable yellow oil, b.p. 150—156 °C/1 mmHg (Kugelrohr); $\nu_{max.}$(liq. film) 3 400br, 1 610, 1 585, 1 525, 1 355, 1 282, 1 259, 770, and 750 cm^{-1}; δ_H 7.95—6.75 (4 H, m), 4.0 (3 H, m), 2.95 (1 H, br s, exchanges with D_2O), 1.55 (2 H, m), and 0.95 (3 H, t, *J* 7.5 Hz).

1-(o-*Nitrophenoxy*)-2-(p-*tolylsulphonyloxy*)*butane*.—Toluene-*p*-sulphonyl chloride (0.56 g, 2.9 mmol) was added to a solution of the butanol (**48**) (0.30 g, 1.4 mmol) in dry pyridine (5 ml), cooled to 0 °C. After 48 h at 0 °C the mixture was poured onto 30 g of ice–water. The resulting precipitate was filtered off, washed with 0.5M hydrochloric acid and then with water. After being dried *in vacuo* over silica gel, the colourless solid was recrystallised from light petroleum (b.p. 40—60 °C)–dichloromethane to give the *title compound* (0.48 g, 92%) as colourless prisms, m.p. 93—93.5 °C (Found: 56.15; H, 5.4; N, 3.55; S, 9.05%; M^+, 365.094 23. $C_{17}H_{19}NO_6S$ requires C, 55.9; H, 5.5; N, 3.8; S, 8.8; M, 365.093 30); $\nu_{max.}$(Nujol) 1 612, 1 585, 1 521, 1 280, 1 190, 1 177, 1 156, 910, 840, 820, 750, and 660 cm^{-1}; δ_H 7.86—6.96 (8 H, m), 4.74 (1 H, quin, *J* 5.5 Hz), 4.35 (2 H, m, *J* 5.5 Hz), 2.41 (3 H, s), 1.84 (2 H, m), and 0.86 (3 H, t, *J* 7.3 Hz); *m/z* (%) 365 (M^+, 11), 227 (8), 194 (8), 173 (13), 155 (100), 123 (25), 106 (7), 91 (64), 78 (6), and 55 (22).

1-(o-*Aminophenoxy*)-2-(p-*tolylsulphonyloxy*)*butane* (**49**).—1-(*o*-Nitrophenoxy)-2-(*p*-tolylsulphonyloxy)butane (0.47 g, 1.3 mmol) in ethyl acetate (35 ml) was hydrogenated at 10 atm and 60 °C for 4 h using 5% palladium on carbon (70 mg) as catalyst. The mixture was filtered through a Celite pad and the filtrate concentrated under reduced pressure to give the *title compound* (**49**) (0.39 g, 90%), which was recrystallised from ethanol and obtained as yellow prisms, m.p. 103—104 °C (Found: C, 61.15; H, 6.5; N, 4.15; S, 9.6%; M^+, 335.119 36. $C_{17}H_{21}NO_4S$ requires C, 60.9; H, 6.27; N, 4.18; S, 9.55%; *M*, 335.119 121); $\nu_{max.}$(Nujol) 3 455, 3 370, 1 624, 1 596, 1 510, 1 230, 1 176, 926, 823, 770, 750, and 670 cm^{-1}; δ_H 7.84 (2 H, d, *J* 9 Hz), 7.31 (2 H, d, *J* 9 Hz), 6.9—6.6 (4 H, m), 4.89 (1 H, m), 4.05 (2 H, d, *J* 6 Hz), 3.8 (2 H, br s, exchanges with D_2O), 2.43 (3 H, s), 1.80 (2 H, m), and 0.92 (3 H, t, *J* 7.5 Hz); *m/z* (%) 335 (M^+, 3), 163 (52), 134 (100, $o\text{-}H_2NC_6H_4OCH{=}CH_2]^{+\bullet}$), 109 (31, $o\text{-}HOC_6H_4NH_2]^{+\bullet}$), 91 (10), 80 (13), 65 (5), and 55 (8); $\lambda_{max.}$ ($\log_{10}$ ε) (MeOH) 204 (4.45), 224 (4.21), and 283 nm (3.45).

1-(o-*Nitrophenoxy*)*butan*-2-*one* (**50**).—(*a*) A solution of pyridinium chlorochromate (0.82 g, 3.8 mmol) in dry dichloromethane (5 ml) was added dropwise to a vigorously stirred solution of the butanol (**48**) (0.35 g, 1.66 mmol) in dry dichloromethane (3 ml). The reaction mixture was stirred for 3 h at room temperature after which ether (40 ml) was added and the mixture was filtered through a pad of Florisil. The filtrate was dried ($MgSO_4$) and then concentrated under reduced pressure to give an oily residue which was purified by chromatography on Kieselgel G (50 g) using chloroform as eluant. The *title compound* (**50**) (0.10 g, 30%) was recrystallised from light petroleum (b.p. 40—60 °C) and obtained as colourless prisms, m.p. 53.7—54.4 °C.

(*b*) 1-Bromobutan-2-one (30.0 g, 0.198 mol) was added dropwise to a stirred suspension of the potassium salt of *o*-nitrophenol (35.0 g, 0.198 mol) in dry acetone (160 ml), cooled to 0 °C. The mixture was heated at reflux for 3 h and then cooled and filtered. The filtrate was concentrated under reduced pressure to give an orange-brown solid which on recrystallisation from light petroleum (b.p. 60—80 °C)–dichloromethane afforded the *title butanone* (**50**) (31.0 g, 75%) as colourless prisms, m.p. 54—54.5 °C.

The spectral data on the compounds obtained by these two methods were identical (Found: C, 57.1; H, 5.35; N, 6.95%; M^+, 209.068 58. $C_{10}H_{11}NO_4$ requires C, 57.4; H, 5.25; N, 6.70%; *M*, 209.068 802); $\nu_{max.}$(Nujol) 1 722, 1 610, 1 585, 1 515, 1 250, 1 150, 860, and 750 cm^{-1}; δ_H 7.92 (1 H, dd, *J* 1.5, 8 Hz), 7.54 (1 H, dt, *J* 8.4, 1.5 Hz), 7.00 (2 H, m), 4.65 (2 H, s), 2.74 (2 H, q, *J* 7.3 Hz), and 1.12 (3 H, t, *J* 7.3 Hz); *m/z* (%) 209 (M^+, 2), 167 (1), 123 (49), 106 (7), 92 (3), 78 (7), 64 (5), 57 (100), 51 (6), and 43 (2); $\lambda_{max.}$ ($\log_{10}$ ε) (MeOH) 210 (4.18), 252 (3.52), and 313 nm (3.35).

3-*Ethyl*-3,4-*dihydro*-2H-1,4-*benzoxazine* (**10**).—(*a*) A solution of the butane (**49**) (0.40 g, 1.19 mmol) in dimethylformamide (15 ml) was heated at reflux for 3 h and then cooled. Concentration under reduced pressure gave an oily residue which was purified by chromatography on Kieselgel G (20 g), using chloroform as eluant, to give the *title compound* (**10**) (0.12 g, 38%) as a yellow oil, b.p. 112—114 °C/0.1 mmHg.

(*b*) 1-(*o*-Nitrophenoxy)butan-2-one was hydrogenated over 5% palladium on carbon catalyst at 30 atm and 90 °C. Work-up by the normal procedure gave the title compound (**10**) (85%) as a yellow oil, b.p. 100—102 °C/0.065 mmHg (Kugelrohr).

All spectral data obtained on the products obtained by these two methods were identical (Found: C, 73.6; H, 8.35; N, 8.55%; M^+, 163.099 96. $C_{10}H_{13}NO$ requires C, 73.6; H, 8.05; N, 8.6%; *M*, 163.099 708); $\nu_{max.}$(liq. film) 3 370, 2 963, 2 930, 2 872, 1 609, 1 590, 1 500, 1 310, 1 275, 1 210, 1 055, and 745 cm^{-1}; δ_H 6.69 (4 H, m), 4.21 (1 H, dd, *J* 10.5, 2.7 Hz), 3.82 (1 H, dd, *J* 10.5, 7.5 Hz), 3.7 (1 H, br s, exchanges with D_2O), 3.27 (1 H, ddt, *J* 7.5, 2.7, 2.2 Hz), 1.49 (2 H, qd, *J* 2.2, 6.34 Hz), 0.995 (3 H, t, *J* 6.34 Hz); δ_C 143.83 (C-8a), 133.70 (C-4a), 121.24 (C-6), 118.20 (C-7), 116.31 (C-8), 115.33 (C-5), 68.91 (C-2), 50.87 (C-3), 25.19 (CH_2CH_3), and 9.75 (CH_3); *m/z* (%) 163 (M^+, 35), 140 (12), 134 (100), 120 (4), 106 (28), 79 (12), 65 (10), and 58 (27); $\lambda_{max.}$($\log_{10}$ ε) (MeOH) 206.5 (4.41), 243 (3.77), and 292 nm (3.53).

3-*Ethyl*-N-*nitroso*-3,4-*dihydro*-2H-1,4-*benzoxazine*.—Reaction of the benzoxazine (**10**) with sodium nitrite in aqueous acid was carried out according to the procedure used to prepare the 3-methyl analogue (see above), and gave the *title compound* (90%) as a yellow oil (Found: M^+, 192.0919. $C_{10}H_{12}N_2O_2$ requires *M*, 192.089 872); $\nu_{max.}$(liq. film) 2 938, 2 900, 2 842, 1 577, 1 470, 1 465, 1 425, 1 290, 1 209, 1 134, 1 090, 1 058, 1 026, and 737 cm^{-1}; δ_H 8.22 (1 H, m), 7.2 (3 H, m), 5.10 (1 H, tdd, *J* 1.8 3.0, 8.0 Hz), 4.45 (1 H, dd, *J* 12.0, 1.8 Hz), 3.96 (1 H, dd, *J* 12.0, 3.0 Hz), 1.57 (2 H, qd, *J* 7.8, 8.0 Hz), and 0.88 (3 H, t, *J* 7.8 Hz); *m/z* (%) 193 (M^+, 0.2), 162 (54), 146 (10), 134 (100), 120 (19), 106 (34), 78 (26), 65 (19), and 52 (30).

N-*Amino*-3-*ethyl*-3,4-*dihydro*-2H-1,4-*benzoxazine* (**11**).—Reduction of the above prepared *N*-nitrosobenzoxazine with lithium aluminium hydride by means of the same procedure as was used in the 3-methyl series gave the *title compound* (**11**) (95%) as an orange oil (Found: M^+, 178.110 33. $C_{10}H_{14}N_2O$ requires *M*, 178.110 607); $\nu_{max.}$(liq. film) 3 450br, 2 970, 2 937, 2 880, 1 608, 1 586, 1 500, 1 275, 1 220, and 750 cm^{-1}; δ_H 7.05—6.50 (4 H, m), 4.10 (2 H, m), 3.45 (2 H, br s, exchanges with D_2O), 2.08 (1 H, m), 2.0—1.2 (2 H, m), and 0.90 (3 H, t, *J* 7.0 Hz); *m/z* (%) 178 (M^+, 69), 163 (24), 149 (100), 134 (69), 120 (34), 106 (23), 94 (14), 78 (25), 65 (21), and 51 (24); $\lambda_{max.}$(EtOH) 222, 256, and 293 nm.

Methyl-3-*Ethyl*-3,4-*dihydropyrrolo*[1,2,3-de]-2H-1,4-*benzoxazine*-5-*carboxylate* (**16**).—Methyl pyruvate (2.0 g, 20.0 mmol) was added with stirring to the *N*-aminobenzoxazine (**11**) (3.0 g, 16.8 mmol) in ethanol (25 ml). After 1 h the solvent was removed under reduced pressure to leave an oil which was slowly heated to 130 °C under reduced pressure. The desired product was then allowed to distil slowly from the reaction mixture. The crude material was purified by chromatography on Kieselgel G (75 g) using benzene–ether (5%) as eluant, which gave the *title compound* (**16**) (55%). Recrystallisation from aqueous ethanol

gave colourless prisms, m.p. 51—51.5 °C (Found: C, 68.6; H, 6.15; N, 5.7%; M^+, 245.105 26. $C_{14}H_{15}NO_3$ requires C, 68.55; H, 6.15; N, 5.7%; M, 245.105 186); $\nu_{max.}$(Nujol) 1 720, 1 630, 1 590, 1 525, 1 220, 1 150, 1 080, 889, 816, 782, 740, and 733 cm^{-1}; δ_H 7.35 (1 H, s), 740 (1 H, d, J 7.8 Hz), 7.17 (1 H, t, J 7.8 Hz), 6.89 (1 H, d, J 7.8 Hz), 5.08 (1 H, m), 4.68 (1 H, dd, J 12, 1.2 Hz), 4.35 (1 H, dd, J 12, 2.2 Hz), 3.93 (3 H, s), 1.84 (2 H, m), and 0.95 (3 H, t, J 7.2 Hz); m/z (%) 254 (M^+, 100), 216 (88), 201 (13), 184 (23), 157 (42), 144 (5), 130 (10), 102 (13), 76 (10), and 55 (7); $\lambda_{max.}$($\log_{10}$ ε) (MeOH) 203 (4.32), 238 (4.48), 284sh (4.15), 293 (4.25), and 314 nm (3.76).

3-*Ethyl*-3,4-*dihydropyrrolo*[1,2,3-de]-2H-1,4-*benzoxazine*-5-*carboxylic Acid* (**17**).—Hydrolysis of the ester (**16**) employing the same conditions as used for the 3-methyl series gave the *title compound* (**17**) (100%), which was recrystallised from aqueous ethanol and obtained as colourless prisms, m.p. 154—156 °C (Found: M^+, 231.0947. $C_{13}H_{13}NO_3$ requires M, 231.089 537); $\nu_{max.}$(Nujol) 3 000—2 300, 1 775, 1 590, 1 540, 1 260, 1 155, 907, 828, 780, and 740 cm^{-1}; δ_H 10.47 (1 H, br s, exchanges with D_2O), 7.51 (1 H, s), 7.10 (3 H, m), 4.53 (1 H, m), 3.99 (1 H, dd, J 11.5, 0.9 Hz), 3.65 (1 H, dd, J 11.5, 2.3 Hz), 1.55 (2 H, m), 0.65 (3 H, t, J 7.4 Hz); m/z (%) 231 (M^+, 93), 202 (100), 157 (34), 130 (25), 102 (16), 76 (14), 63 (6), and 55 (13); $\lambda_{max.}$($\log_{10}$ ε) (EtOH) 228 (5.57), 269sh (5.23), 279.5 (5.32), and 304 nm (4.85).

6-(2-*Aminoethyl*)-3-*ethyl*-5-*methyl*-3,4-*dihydropyrrolo*[1,2,3-de]-2H-1,4-*benzoxazine* (**6**).—Reaction of the benzoxazine (**11**) with 5-chloropentan-2-one in aqueous methanol according to the procedure used in the 3-methyl series gave the *title compound* (**6**) (69%) as an orange oil (Found: M^+, 244.157 87. $C_{15}H_{20}N_2O$ requires M, 244.157 555); $\nu_{max.}$(liq. film) 3 360, 3 290, 3 195, 2 960, 2 930, 2 870, 1 662, 1 597, 1 497, 1 469, 1 242, 1 120, 1 040, 988, 780, 759, and 735 cm^{-1}; δ_H 7.17 (1 H, m), 6.92 (1 H, t, J 8 Hz), 6.56 (1 H, d, J 8 Hz), 4.50 (1 H, m), 4.15 (2 H, m), 2.90 (4 H, m), 2.36 (3 H, s), 1.71 (2 H, m), 1.47 (2 H, br s, exchanges with D_2O), and 0.96 (3 H, t, J 8.5 Hz); m/z (%) 244 (M^+, 23), 214 (100), 184 (4), 172 (7), 160 (19), 142 (4), 131 (4), 115 (4), 78 (7), and 55 (9); $\lambda_{max.}$(EtOH) 222, 271, 281, and 293 nm.

6-[2-(2,2-*Diethoxycarbonylvinylamino*)*ethyl*]-3-*ethyl*-5-*methyl*-3,4-*dihydropyrrolo*[1,2,3-de]-2H-1,4-*benzoxazine* (**27**).—Reaction of the pyrrolobenzoxazine (**6**) with diethyl ethoxymethylenemalonate in ethanol employing the procedure used for the 3-methyl series gave the *title compound* (**27**) (97.5%) as a clear yellow oil (found: M^+, 414.216 19. $C_{23}H_{30}N_2O_5$ requires M, 414.215 458); $\nu_{max.}$(liq. film) 3 360, 3 280, 3 195, 2 976, 2 935, 2 900, 2 875, 1 708, 1 683, 1 658, 1 644, 1 610, 1 500, 1 240, 1 200, 1 100, 1 070, 1 040, 803, 781, and 734 cm^{-1}; δ_H 9.19 (1 H, m), 7.70 (1 H, d, J 13.5 Hz), 7.00 (2 H, m), 6.59 (1 H, dd, J 6.4, 1.9 Hz), 4.56 (1 H, apparent d, J 10 Hz), 4.43—3.97 (6 H, m), 3.58 (2 H, dt, J 6.4 Hz), 2.96 (2 H, apparent t, J 6.4 Hz), 2.26 (3 H, s), 1.72 (2 H, m), 1.30 (3 H, t, J 7.3 Hz), 1.19 (3 H, t, J 7.3 Hz), and 0.97 (3 H, t, J 7.3 Hz); m/z (%) 414 (M^+, 8), 214 (100), 160 (6), 83 (2), 69 (4), and 55 (18); $\lambda_{max.}$(EtOH) 223, 274, and 348 nm.

3-*Acetyl*-8-*ethyl*-2,3,3a,4,8,9-*hexahydro*[1,4]*oxazino*[2,3,4-jk]-*pyrrolo*[2,3-d]*carbazol*-5(1H)-*one* (**29**).—Reaction of the pyrrolobenzoxazine (**27**) in acetic acid and acetic anhydride employing the method used in the methyl series (see above) gave the *title compound* (**29**) (45%) as a pale yellow oil, b.p. 220—221 °C/0.25 mmHg (Kugelrohr) (Found: M^+, 338.162 71. $C_{20}H_{22}N_2O_3$ requires M, 338.163 032); $\nu_{max.}$(liq. film) 3 440br, 2 965, 2 935, 2 880, 1 640, 1 630, 1 585, 1 480, 1 365, 1 230, 1 050, 864, 815, and 742 cm^{-1}; δ_H 6.85—6.56 (3 H, m), 5.44, 5.43, 5.32, 5.30 (1 H, 4 s), 4.74 (1 H, dd, J, 7.2, 16 Hz), 4.5—4.2 (2 H, m), 4.15—3.7 (4 H, m), 3.3—2.86 (1 H, m), 2.65—2.1 (3 H, m), 2.16, 2.13 (3 H, 2 s), 1.84 (2 H, m), and 1.01 (3 H, t, J 7.4 Hz); δ_C 193.08, 192.81, 192.21, 191.89 (C-5), 168.86, 168.48, 168.32, 168.10 (C-1'), 166.59, 166.37 (C-6a), 142.04 (C-10), 134.24, 134.08, 133.48, 133.38 (C-10a), 130.29, 130.13, 128.88, 128.72 (C-13a), 123.41, 123.03, 122.87, 122.49 (C-12), 115.99, 115.39, 115.28, 114.85, 114.74 (C-11 and C-13), 97.40, 97.19, 96.48, 96.27 (C-6), 67.88, 66.15 (C-9), 60.84, 60.57, 57.97, 57.69 (C-3a), 55.37, 55.04, 53.85 (C-13b), 53.74, 53.65, 53.20 (C-8), 44.86, 44.75 (C-2), 40.90, 40.68, 39.17, 38.95 (C-1 and C-4), 25.03, 19.12 (C-8a), 22.26, 22.05 (C-2'), 10.23, and 10.13 (C-8b); m/z (%) 338 (M^+, 10), 296 (9), 253 (17), 240 (15), 115 (2), 69 (6), 55 (22), and 43 (100); $\lambda_{max.}$(EtOH) 209, 237, 289, and 344 nm.

3-*Acetyl*-2,3,3a,4,6,6a,8,9-*octahydro*-8-*ethyl*[1,4]*oxazino*[2,3,4-jk]*pyrrolo*[2,3-d]*carbazol*-5(1H)-*one* (**36**).—Reduction of the pentacyclic enamino ketone (**29**) by means of lithium in liquid ammonia with added t-butyl alcohol, employing the same method as used for the methyl series, gave the *title compound* (**36**) (95%), which was recrystallised from ethanol and obtained as colourless prisms as a 1:1 mixture of diastereoisomers, m.p. 155.5—156 °C (Found: C, 70.4; H, 7.15; N, 8.15%; M^+, 340.178 01. $C_{20}H_{24}N_2O_3$ requires C, 70.55; H, 7.10; N, 8.2%; M, 340.178 682); $\nu_{max.}$($CHCl_3$) 2 950, 2 920, 2 870, 2 850, 1 711, 1 640, 1 620, 1 485, 1 305, 1 200, 1 055, 1 045, and 755 cm^{-1}; δ_H 6.69 (3 H, m), 4.4—3.95 (4 H, m), 3.9—3.50 (3 H, m), 3.3—2.2 (5 H, m), 2.13, 2.07 (3 H, 2 s), 1.6 (3 H, m), and 0.985, 0.945 (3 H, 2 t, J 7.3 Hz); δ_C 207.92, 207.43 (C-5), 169.84, 168.67 (C-1'), 142.91, 142.59 (C-10), 138.04, 135.44 (C-10a), 133.29, 131.10 (C-13a), 120.97, 119.78 (C-12), 114.74, 114.25, 114.04 (C-11 and C-13), 71.67, 65.98 (C-3a), 69.40, 68.75 (C-9), 63.65, 60.89 (C-6a), 57.75, 50.71 (C-8), 54.01, 53.69 (C-13b), 47.46, 46.54 (C-2), 42.91, 40.57, 38.79, 38.19 (C-4 and C-1), 37.54, 36.40 (C-6), 24.10, 19.94 (C-8a), 23.29, 22.86 (C-2'), and 9.70 and 9.10 (C-8b); m/z (%) 340 (M^+, 100), 311 (68), 298 (4), 283 (14), 269 (15), 254 (34), 226 (15), 213 (34), 200 (51), 184 (19), 146 (14), 86 (18), 56 (35), and 43 (86); $\lambda_{max.}$($\log_{10}$ ε) (MeOH) 213 (4.48), 248 (3.70), and 291 nm (3.39).

8-*Ethyl*-2,3,3a,4,6,6a,8,9-*octahydro*[1,4]*oxazino*[2,3,4-jk]*pyrrolo*[2,3-d]*carbazol*-5(1H)-*one* (**37**).—Sodium hydrogen carbonate (757 mg, 9.0 mmol) followed by triethyloxonium tetrafluoroborate (855 mg, 4.5 mmol) were added to a solution of the pentacyclic *N*-acetylamino ketone (**36**) (510 mg, 1.5 mmol) in dichloromethane (25 ml) and the resulting solution was stirred at room temperature for 48 h. Dilute aqueous sodium hydrogen carbonate (10 ml) was then added, and the aqueous phase was separated and extracted with chloroform (3 × 15 ml). The combined organic extracts were washed with water and then extracted with 2M hydrochloric acid (3 × 25 ml). The combined aqueous acid extracts were basified by means of 2M sodium hydroxide, and extracted with chloroform (3 × 40 ml). The chloroform solution was washed with water (30 ml) and saturated brine (30 ml), dried (Na_2SO_4), and evaporated under reduced pressure. Chromatography of the residue on Kieselgel G (60 g), using as eluant dichloromethane–methanol (2%)/1% conc. ammonia (prepared by shaking the components vigorously, and then discarding the aqueous phase), gave the *title compound* (**37**) (362 mg, 81%) as a yellow oil (Found: M^+, 298.168 40. $C_{18}H_{22}N_2O_2$ requires M, 298.168 118); $\nu_{max.}$ ($CHCl_3$) 1 714, 1 620, 1 486, 1 405, and 1 058 cm^{-1}; δ_H 6.85—6.45 (3 H, m), 4.4—1.2 (16 H, m), and 0.9 (3 H, t, J 6 Hz); m/z (%) 298 (M^+, 41), 269 (7), 213 (18), 200 (100), 83 (67), 69 (31), and 55 (62).

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References

1 K. S. Brown and C. Djerassi, *J. Am. Chem. Soc.*, 1964, **86**, 2451.
2 For a summary see J. E. Saxton, in 'The Monoterpenoid Indole Alkaloids,' ed. J. E. Saxton, Wiley-Interscience, New York, 1983, ch. VIII.
3 G. Barker, G. P. Ellis, and D. A. Wilson, *J. Chem. Soc. C*, 1971, 2079.
4 G. Büchi, K. E. Matsumoto, and H. Nishimura, *J. Am. Chem. Soc.*, 1971, **93**, 3299; M. Ando, G. Büchi, and T. Ohnuma, *ibid.*, 1975, **97**, 6880.
5 S. Takano, K. Shishido, M. Sato, K. Yuta, and K. Ogasawara, *J. Chem. Soc., Chem. Commun.*, 1978, 943.
6 R. Fusco and F. Sannicolo, *Tetrahedron*, 1980, **36**, 161.
7 B. Robinson, 'The Fischer Indole Synthesis,' Wiley, New York, 1982, p. 752.
8 I. I. Grandberg, *Khim. Geterosikl. Soedin.*, 1974, **10**, 579, and references cited therein.
9 D. H. R. Barton and C. H. Robinson, *J. Chem. Soc.*, 1954, 3045; G. Stork and S. D. Darling, *J. Am. Chem. Soc.*, 1964, **86**, 1761.
10 J. P. Brennan and J. E. Saxton, *Tetrahedron Lett.*, 1985, **26**, 1769.
11 We are greatly indebted to Dr. G. Büchi for experimental details (hitherto unpublished) of these procedures (personal communication).
12 J. B. Dickey and J. G. McNally, U.S.P. 2 448 869, Sept. 7, 1948 (*Chem. Abstr.*, 1949, **43**, 2782).
13 C. C. Price and J. A. Pappalardo, *J. Am. Chem. Soc.*, 1950, **72**, 2613.

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