[2,3] Fused Indoles. Synthesis of β-Carbolines and Azepino[4,5-*b*]indoles from 3-(2-Alkylindol-3-yl)-2-azidoacrylates [1]

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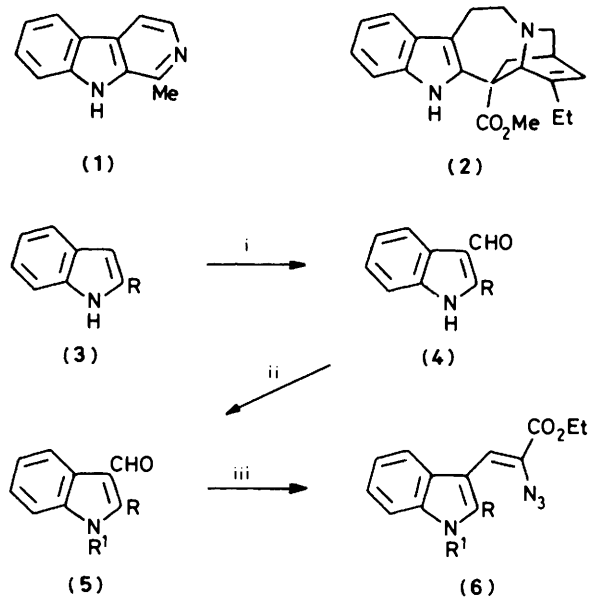
Decomposition of the azidoacrylates (**6**) derived from 2-substituted indole-3-carbaldehydes gives pharmacologically important β-carbolines [(**8**), (**11**)], azepino[4,5-*b*]indoles (**13**), or enamines (**14**) depending on the conditions. The formation of azepinoindoles, shown to proceed by cyclisation of the initially formed enamines, represents a new reaction of vinyl azides which is particularly favoured in the indole series.

Indoles containing an additional ring fused across the 2,3-positions are widely distributed in Nature. Examples in which the fused ring contains six or seven members include relatively simple β-carboline alkaloids such as harman (**1**), and the more complex catharanthine (**2**). The recent isolation of ethyl β-carboline-3-carboxylate (β-CCE) from human urine and brain tissue, and demonstration that it possesses a high affinity for benzodiazepine-binding brain proteins [2] has prompted a renewed interest in the chemistry of β-carbolines. Therefore, it was of interest to explore the possibility that, by analogy with the preparation of other fused pyridines,[3] β-carbolines could be readily prepared from azidoacrylates bearing β-(2-alkylindolyl) substituents. We now report full details of this work.



(1) (2) (3) (4) (5) (6)

Scheme 1. *Reagents:* i, Me_2NCHO, $POCl_3$; ii, $PhCH_2Br$, K_2CO_3, acetone or $MeOCH_2Cl$, NaH, DMF; iii, $EtO_2CCH_2N_3$, NaOEt, EtOH, −10 °C

Results and Discussion

The starting 2-substituted indoles (**3**) were prepared by the Madelung reaction, except for the 2-methyl derivative which is commercially available and 2-phenylindole which was prepared by the Fischer indole synthesis. Formylation using the Vilsmeier–Haack reaction proceeded in good yield, as did the *N*-alkylation of the resulting indole-3-carbaldehydes (Scheme 1, Table). Indole-3-carbaldehydes are considerably less reactive than, for instance, benzaldehyde, and therefore it was expected that condensation of these aldehydes with ethyl azidoacetate might be difficult. This was indeed the case, and only poor to moderate yields of the required azidoacrylates (**6**) were obtained from the aldehydes (**5**) by condensation with ethyl azidoacetate under the standard conditions.[3] *N*-Unsubstituted indole-3-carbaldehydes did not condense with ethyl azidoacetate and it would also appear that the reaction is sensitive to steric effects since the yields of the azides (**6**) decrease markedly as the size of the 2-substitutent increases. Similar effects have been noted previously, 2-methylindole-3-carbaldehyde being considerably less reactive towards condensation with malonic acid than the 2-unsubstituted aldehyde.[4]

Thermolysis of the azide (**6a**) in boiling toluene, with the reflux condenser open to the atmosphere, gave the expected β-carboline (**8a**) (76%), together with a trace of the enamine (**9a**) (6%). Similar thermolysis of the azide (**6b**) in xylene gave the β-carboline (**8b**) (59%) and the enamine (**9b**) (5%). However, when the thermolysis of (**6b**) was carried out under nitrogen in degassed xylene, the intermediate 1,2-dihydro-β-carboline (**7b**) could be detected in the thermolysis mixture by n.m.r. spectroscopy. Attempted separation of compound (**7b**) by chromatography resulted in isolation of the β-carboline (**8b**) (85%). Cleavage of the *N*-methoxymethyl group with hot formic acid gave β-CCE (**10**).

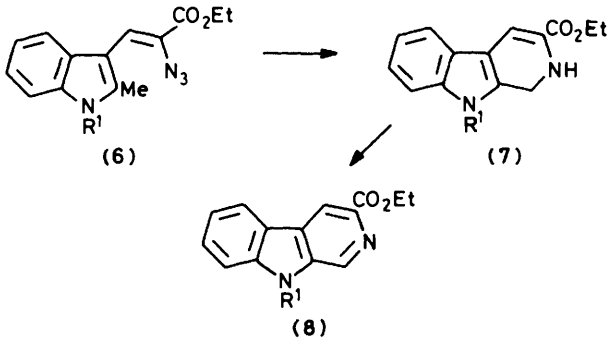
Decomposition of the 2-ethyl substituted azide (**6c**) in xylene took a different course in that two major products were formed. That the more polar compound was the expected β-carboline (**11a**) (35%) was immediately apparent from its spectral properties, and from its cleavage, under acidic conditions, to ethyl harman-3-carboxylate (**12**). The other thermolysis product, isolated in 24% yield, was assigned the 3,4,5,6-tetrahydroazepino[4,5-*b*]indole structure (**13a**).

The decomposition of the azide (**6c**) was also investigated in other solvents. Thus, it was found that in 1,2-dichlorobenzene the β-carboline (**11a**) was the only isolated product (43%),

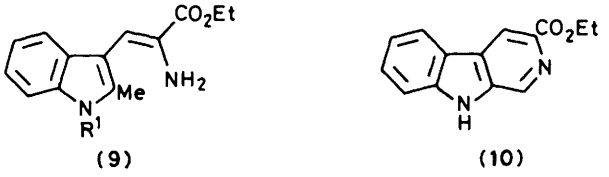
Table. Preparation of the indole-3-aldehydes (**4**), the *N*-alkyl derivatives (**5**), and the azidoacrylates (**6**)

		Product yield (%)		
R	R^1	(4)	(5)	(6)
a; Me	CH_2Ph	96	67	15
b; Me	CH_2OMe	96	78	36 (47)[a]
c; Et	CH_2OMe	70	82	24 (40)
d; Pr^n	CH_2OMe	75	73	26
e; c-Hex	CH_2OMe	79	72	4 (28
f; Pr^i	CH_2OMe	88	75	6
g; Ph	CH_2OMe	97	68	1 (4)

[a] Yield in parentheses is based on the consumed starting materials.

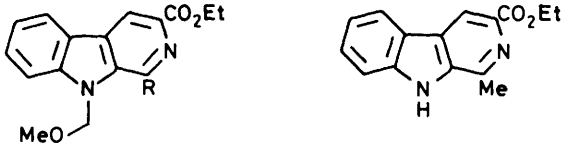


(6) (7) (8)



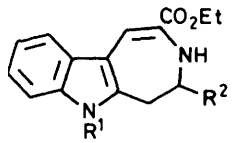
(9) (10)

a; $R^1 = CH_2Ph$ b; $R^1 = CH_2OMe$



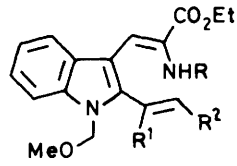
(11) (12)

a; R = Me b; R = Et



(13)

a; $R^1 = CH_2OMe$, $R^2 = H$
b; $R^1 = CH_2OMe$, $R^2 = Me$
c; $R^1 = R^2 = H$
d; $R^1 = H$, $R^2 = Me$



(14)

a; $R = R^1 = R^2 = H$
b; R = Ac, $R^1 = R^2 = H$
c; $R = R^1 = H$, $R^2 = Me$
d; R = Ac, $R^1 = H$, $R^2 = Me$
e; R = H, R^1, $R^2 = -(CH_2)_4-$
f; R = Ac, R^1, $R^2 = -(CH_2)_4-$
g; $R = R^2 = H$, $R^1 = Me$
h; R = Ac, $R^1 = Me$, $R^2 = H$

whereas the formation of the azepinoindole (**13a**) (60%) was favoured by the use of the more polar dimethylformamide (DMF) as thermolysis solvent; no (**11a**) was formed in this case. When the thermolysis was conducted at a lower temperature in refluxing benzene, a new compound was formed as the only product, the ^1H n.m.r. spectrum of which established its structure as the enamine (**14a**). The enamine, which was characterised as its *N*-acetyl derivative (**14b**), could not be purified since attempted chromatography on, or stirring with, silica gel caused cyclisation to the azepinoindole (**13a**). On being heated in solution, the enamine gave (**11a**) and/or (**13a**), depending on the solvent, the results closely paralleling those obtained from the azide itself.

The n-propylindolylazidoacrylate (**6d**) behaved similarly although the ratio of products was somewhat different. Thus, heating the azide in xylene or, better, in DMF gave the azepinoindole (**13b**) (51%), with only a trace of the β-carboline (**11b**) being detected by t.l.c. In benzene, the enamine (**14c**) was the major product, and although more stable than (**14a**) it cyclised to give compound (**13b**) when stirred over silica gel.

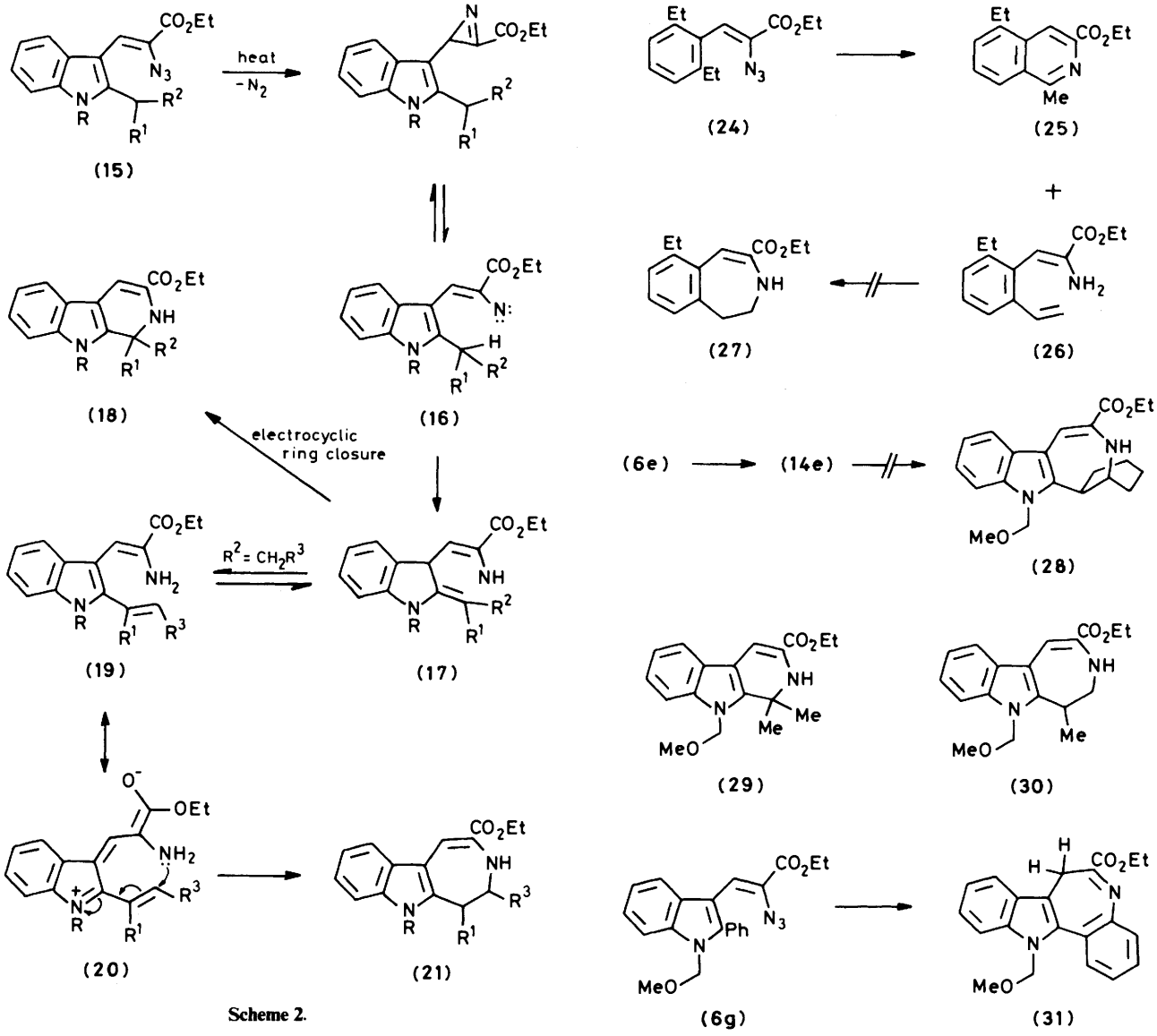
Although the formation of β-carbolines is similar to the preparation of other annelated pyridines from vinyl azides,[3] the formation of seven-membered rings represents a new type of vinyl azide reaction. In rationalising these observations, the results of Taniguchi and co-workers on the decomposition of azidoacrylates derived from benzofuran-2-carbaldehydes were considered.[5] Thermolysis of a generalised indolyl azidoacrylate (**15**) is expected to give an azirine which is in thermal equilibrium[6] with the vinylnitrene (**16**); this nitrene then undergoes a [1,6]hydrogen shift to give the imine (**17**). This imine may then undergo electrocyclic ring closure to give the dihydro-β-carboline (**18**), and hence give β-carbolines if either R^1 or R^2 is hydrogen, or a further hydrogen shift may occur to give the enamine (**19**). Since the enamines were formed only at lower temperatures, it may be assumed that they are the kinetically controlled products. At higher temperatures β-carbolines are formed by reversion to, and electrocyclic ring closure of, the imine (**17**), or the azepinoindoles (**21**) are formed by conjugate attack on the terminal carbon of the vinyl group by the NH_2 group. The fact that this type of ring closure to give a seven-membered ring has not been observed in other systems suggests that it is promoted by the particular polarisation of the 3-substituted indole system due to resonance structures such as (**20**) (Scheme 2). The observed enhanced ring closure of the enamines in the presence of a weak acid (silica gel), or in a more polar solvent (DMF), would support this mechanism.

Both of the azepinoindoles (**13a**) and (**13b**) could be deprotected to the corresponding NH compounds (**13c**) and (**13d**) by treatment with hydrochloric acid in ethanol. Attempts to reduce the azepinoindole (**13a**) to the hexahydro derivative (**22**) were not successful, although it could be dehydrogenated in a low yield to the dihydro derivative (**23**) by treatment with t-butyl hypochlorite followed by base.

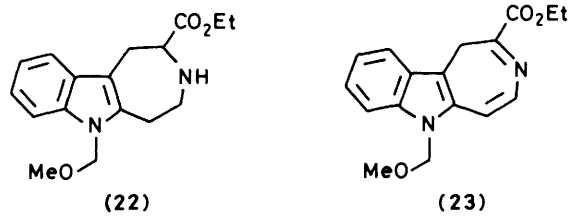
In order to investigate the generality of this azepine-forming reaction, the decomposition of the azidoacrylate (**24**), prepared from 2,6-diethylbenzaldehyde, was studied. Initial experiments showed that thermolysis of the azide (**24**) gave, amongst other products, appreciable quantities of the air sensitive ethyl 1,2-dihydro-5-ethyl-1-methylisoquinoline-3-carboxylate, so subsequent experiments were carried out with deliberate oxidation at the end of the thermolysis. Thus, thermolysis of the azide (**24**) in xylene, followed by oxidation with iodine, gave the isoquinoline (**25**) (35%) and the enamine (**26**) (19%). No trace of the benzazepine (**27**) was detected in this or any other decomposition of the azide (**24**), providing further evidence that the formation of these seven-membered rings is peculiarly favoured in the indole systems.

Tetrahydroazepino[4,5-*b*]indoles have not been prepared before, although the 1,2,3,4,5,6-hexahydro derivatives are quite well known, and indeed have been used in alkaloid synthesis.[7] The azepinoindole system occurs in alkaloids such as catharanthine (**2**), and an attempt was made to extend our method to the synthesis of compound (**28**) which possesses the ring skeleton of the alkaloid. Therefore the cyclohexyl-substituted azide (**6e**) was decomposed in benzene to give the expected enamine (**14e**), characterised as its *N*-acetyl derivatives (**14f**). However, the enamine (**14e**) proved to be thermally stable, and attempts to cyclise it to compound (**28**) under various conditions failed. Heating the enamine (**14e**), or the azide (**6e**), in refluxing DMF resulted in complex mixtures.

The failure to cyclise enamine (**14e**) prompted an investigation of the isopropyl azide (**6f**), since like the cyclohexyl derivative it would lead to an intermediate enamine which contained an α-substituent on the double bond [Scheme 2, (**19**;



Scheme 2.



$R^1 \neq H$)]. The enamines which cyclise readily bear no substituent at this position [(**19**; R^1 = H)]. Thermolysis of the azide (**6f**) in benzene gave the enamine (**14g**) as expected, whereas thermolysis in xylene resulted in the formation of the 1,2-dihydro-β-carboline (**29**). This structure was postulated on the basis of the n.m.r. spectrum, although the compound could not be obtained completely pure. Prolonged heating of the azide (**6f**) in bromobenzene gave the β-carboline (**11a**) (9%), presumably *via* the dimethyl compound (**29**), although the exact mechanism for the formation of compound (**11a**) is not known. No traces of the azepinoindole (**30**) were detected.

Thus it appears that the formation of azepinoindoles from 2-alkylindolylazidoacrylates is not a general reaction, and is only likely to proceed well when the intermediate enamines (**19**) can adopt a suitable orientation for cyclisation.

Finally, the phenyl-substituted azide (**6g**) was investigated. Thermolysis of the azide in refluxing xylene for 1 h resulted in the formation of one compound which was isolated as a yellow crystalline solid after chromatography and recrystallisation. The compound was assigned the benzazepinoindole structure (**31**) on the basis of literature precedent,[8] although this assignment was complicated by the fact that in its ^1H n.m.r. spectrum no signal is observed for the CH_2 group in the seven-membered ring. A two-proton singlet was expected by analogy with compound (**23**). The structure (**31**) was confirmed by *X*-ray crystallography,† and therefore the absence of the n.m.r. signal is presumably attributable to some rapid tautomeric equilibrium which renders the peak so broad that it is lost in the base-line.

Experimental

I.r. spectra were recorded in the range 4 000—600 cm^{-1} on a Perkin-Elmer 257 spectrophotometer, and were calibrated against polystyrene. Solid samples were run as Nujol mulls and

† Determined by Dr. D. J. Williams of this department.

liquids as thin films unless otherwise stated. ^{1}H N.m.r. spectra were recorded at 250, 90, or 60 MHz on Bruker WM250, Perkin-Elmer R32, and Varian EM360 instruments respectively. Mass spectra were obtained on a VG Micromass 7070B instrument using a direct insertion probe. Chromatography was carried out on Merck 60H silica gel using hand-bellows to apply pressure to the column, and using light petroleum containing an increasing proportion of ether as eluant, unless otherwise stated. Preparative layer chromatography (p.l.c.) was carried out on 20 × 20 cm glass plates coated to a thickness of 2 mm with Merck 60 GF_{254} silica gel. Light petroleum refers to the light petroleum fraction, b.p. 40—60 °C, and was redistilled before use. Ether refers to diethyl ether. All solvents were dried by standard procedures.

Preparation of Indole-3-carbaldehydes.—These reactions were carried out by the Vilsmeier–Haack method following the standard procedure.[9] The following compounds were prepared: 2-methylindole-3-carbaldehyde (**4a**) (96% from 2-methylindole), m.p. 199—202 °C (lit.,[10] 200—202 °C).

2-Ethylindole-3-carbaldehyde (**4c**) (70% from 2-ethylindole), m.p. 167—171 °C (Found: C, 76.5; H, 6.4; N, 8.1. $C_{11}H_{11}NO$ requires C, 76.3; H, 6.4; N, 8.1%); $\nu_{max.}$ 3 185, 1 639, 1 633, and 1 590 cm^{-1} δ [90 MHz, $(CD_3)_2SO$] 1.28 (3 H, t), 3.02 (2 H, q), 7.10 (2 H, m), 7.33 (1 H, m), 7.98 (1 H, m), and 10.02 (1 H, s); NH not observed.

2-n-Propylindole-3-carbaldehyde (**4d**) (75% from 2-n-propylindole), m.p. 154—155.5 °C (Found: C, 76.7; H, 7.0; N, 7.4. $C_{12}H_{13}NO$ requires C, 77.0; H, 7.0; N, 7.5%); $\nu_{max.}$ 3 180, 1 620, and 1 580 cm^{-1}; δ [90 MHz, $(CD_3)_2SO$] 1.0 (3 H, t), 1.83 (2 H, sextet), 3.10 (2 H, t), 7.20 (2 H, m), 7.46 (1 H, m), 8.13 (1 H, m), and 10.14 (1 H, s); NH not observed.

2-Cyclohexylindole-3-carbaldehyde (**4e**) (79% from 2-cyclohexylindole), m.p. 202—205 °C (Found: C, 79.2; H, 7.5; N, 6.2. $C_{15}H_{17}NO$ requires C, 79.3; H, 7.5; N, 6.2%); $\nu_{max.}$ 3 180, 1 622, and 1582 cm^{-1}; δ [90 MHz, $(CD_3)_2SO$] 1.2—2.1 (10 H, m), 3.3 (1 H, m), 7.18 (2 H, m), 7.43 (1 H, m), 8.08 (1 H, m), 10.18 (1 H, s), and 11.83 (1 H,br s).

2-Isopropylindole-3-carbaldehyde (**4f**) (88% from 2-isopropylindole), m.p. 179—180 °C (Found: C, 76.8; H, 7.0; N, 7.5. $C_{12}H_{13}NO$ requires C, 77.0; H, 7.0; N, 7.5%); $\nu_{max.}$ 3 200, 1 634, and 1 590 cm^{-1}; δ [90 MHz; $CDCl_3$–$(CD_3)_2SO$] 1.44 (6 H, d), 3.77 (1 H, septet), 7.25 (2 H, m), 7.44 (1 H, m), 8.26 (1 H, m), 10.27 (1 H, s), and 11.33 (1 H,br s).

2-Phenylindole-3-carbaldehyde (**4g**) (97% from 2-phenylindole), m.p. 256—258.5 °C (lit.,[10] 251—252 °C).

N-Alkylation of Indole-3-carbaldehydes.—*1-Benzyl-2-methylindole-3-carbaldehyde* (**5a**). A mixture of 2-methylindole-3-carbaldehyde (10.0 g, 0.063 mol), anhydrous potassium carbonate (52.0 g), benzyl bromide (11.83 g, 0.069 mol), and acetone (250 ml) was stirred and heated under reflux for 24 h. Filtration and evaporation gave a solid which was recrystallised from ethanol to give the *title compound* (**5a**) (10.47 g, 67%), m.p. 135 °C (Found: C, 82.0; H, 6.2; N, 5.7. $C_{17}H_{15}NO$ requires C, 81.9; H, 6.1; N, 5.6%); $\nu_{max.}$ 1 645 cm^{-1}; δ (60 MHz; $CDCl_3$) 2.63 (3 H, s), 5.33 (2 H, s), 6.83—7.5 (8 H, m), 8.40 (1 H, m), and 10.25 (1 H, s).

1-Methoxymethyl-2-methylindole-3-carbaldehyde (**5b**). Sodium hydride (50% dispersion in oil; 2.0 g, 0.042 mol) was suspended in dry dimethylformamide (20 ml). A solution of 2-methylindole-3-carbaldehyde (5.0 g, 0.031 mol) in dimethylformamide (20 ml) was added at room temperature. After being stirred for 30 min, excess of chloromethyl methyl ether (4 ml) was added, and stirring was continued overnight. The mixture was poured into water, and extracted with ether. The combined organics extracts were dried ($MgSO_4$) and evaporated. The crude product was recrystallised from ether–light petroleum to give the *title compound* (**5b**) (4.99 g, 78%), m.p. 87—90 °C (Found: C, 71.0; H, 6.4; N, 6.9. $C_{12}H_{13}NO_2$ requires C, 70.9; H, 6.45; N, 6.9%); $\nu_{max.}$ 1 640 cm^{-1}; δ (90 MHz; $CDCl_3$) 2.64 (3 H, s), 3.27 (3 H, s), 5.40 (2 H, s), 7.20—7.50 (3 H, m), 8.25 (1 H, m), and 10.10 (1 H, s). The following compounds were prepared similarly: *2-ethyl-1-methoxymethylindole-3-carbaldehyde* (**5c**) (82%), m.p. 72—74 °C (Found C, 72.0; H, 7.0; N, 6.4. $C_{13}H_{15}NO_2$ requires C, 71.9; H, 7.0; N, 6.45%); $\nu_{max.}$ 1 635 cm^{-1}; δ (90 MHz; $CDCl_3$) 1.34 (3 H, t), 3.17 (2 H, q), 3.32 (3 H, s), 5.50 (2 H, s), 7.25—7.55 (3 H, m), 8.30 (1 H, m), and 10.24 (1 H, s).

1-Methoxymethyl-2-n-propylindole-3-carbaldehyde (**5d**) (73%), m.p. 49—51 °C (Found: C, 72.5; H, 7.4; N, 6.0. $C_{14}H_{17}NO_2$ requires C, 72.7; H, 7.4; N, 6.1%); $\nu_{max.}$ 1 646 cm^{-1}; δ (90 MHz; $CDCl_3$) 1.00 (3 H, t), 1.72 (2 H, sextet), 3.08 (2 H, t), 3.28 (3 H, s), 5.42 (2 H, s), 7.20—7.50 (3 H, m), 8.23 (1 H, m), and 10.20 (1 H, s).

2-Cyclohexyl-1-methoxymethylindole-3-carbaldehyde (**5e**) (72%), m.p. 77—80 °C (Found: C, 75.4; H, 7.85; N, 5.2. $C_{17}H_{21}NO_2$ requires C, 75.2; H, 7.8; N, 5.2%), $\nu_{max.}$ 1 640 cm^{-1}; δ (90 MHz; $CDCl_3$) 1.20—2.10 (10 H, m), 3.20 (1 H, m), 3.29 (3 H, s), 5.54 (2 H, s), 7.20—7.55 (3 H, m), 8.40 (1 H, m), and 10.53 (1 H, s).

2-Isopropyl-1-methoxymethylindole-3-carbaldehyde (**5f**) (75%), m.p. 104—107 °C (Found: 72.7; H, 7.5; N, 6.0. $C_{14}H_{17}NO_2$ requires C, 72.7; H, 7.4; N, 6.1%); $\nu_{max.}$ 1 639 cm^{-1}; δ (90 MHz; $CDCl_3$) 1.54 (6 H, d), 3.32 (3 H, s), 3.63 (1 H, septet), 5.56 (2 H, s), 7.20—7.55 (3 H, m), 8.39 (1 H, m), and 10.53 (1 H, s).

1-Methoxymethyl-2-phenylindole-2-carbaldehyde (**5g**) (68%), m.p. 109—110 °C (Found: C, 76.8; H, 5.7; N, 5.25. $C_{17}H_{15}NO_2$ requires C, 77.0; H, 5.7; N, 5.3%); $\nu_{max.}$ 1 647 cm^{-1}; δ (90 MHz; $CDCl_3$) 3.21 (3 H, s), 5.33 (2 H, s), 7.20—7.60 (8 H, m), 8.40 (1 H, m), and 9.70 (1 H, s).

Condensation of Indole-3-carbaldehydes with Ethyl Azidoacetate.—*Ethyl 2-azido-3-(1-benzyl-2-methylindol-3-yl)propenoate* (**6a**). A mixture of the aldehyde (**5a**) (1.00 g, 4.02 mmol) and ethyl azidoacetate (5.18 g, 40.2 mmol) in tetrahydrofuran (7 ml) was added dropwise to a stirred solution of sodium (0.40 g, 16.08 mg atom) in ethanol (11 ml) at −15 to −5 °C. The mixture was stirred at this temperature for 6 h, and then allowed to warm to room temperature, poured into aqueous saturated ammonium chloride, and extracted with ether. The ether extracts were washed with water, dried ($MgSO_4$), evaporated, and the residue chromatographed to give the *title compound* (**6a**) (0.222 g, 15%), m.p. 90—92 °C (decomp.) (from ether–light petroleum), $\nu_{max.}$ 2 104, 1 702, and 1 615 cm^{-1}; δ (90 MHz; $CDCl_3$) 1.39 (3 H, t), 2.41 (3 H, s), 4.40 (2 H, q), 5.37 (2 H, s), 6.95—7.30 (9 H, m), and 8.05 (1 H, m); *m/z* 334 (M^+ − 26), 330, 258, 249, 243, and 91 (base).

Ethyl 2-azido-3-(1-methoxymethyl-2-methylindol-3-yl)propenoate (**6b**). The aldehyde (**5b**) (4.49 g, 22.11 mmol) was dissolved in ethyl azidoacetate (11.41 g, 88.44 mmol) and added dropwise to a stirred solution of sodium (2.035 g, 88.44 mg atom) in ethanol (50 ml) at −12 to −5 °C. Work-up as above, and chromatography, gave the *title compound* (**6b**) (2.52 g, 36%), m.p. 90 °C (decomp.) (Found: C, 61.2; H, 5.8; N, 17.7. $C_{16}H_{18}N_4O_3$ requires C, 61.1; H, 5.8; N, 17.8%); $\nu_{max.}$ 2 110, 1 700, and 1 616 cm^{-1}; δ (90 MHz; $CDCl_3$) 1.40 (3 H, t) 2.49 (3 H, s), 3.21 (3 H, s), 4.33 (2 H, q), 5.37 (2 H, s), 7.07—7.40 (3 H, m), 7.17 (1 H, s), and 7.80 (1 H, m).

The following azides were prepared similarly: *ethyl 2-azido-3-(2-ethyl-1-methoxymethylindol-3-yl)propenoate* (**6c**) (24%), oil, $\nu_{max.}$ 2 105, 1 700, and 1 615 cm^{-1}; δ (90 MHz; $CDCl_3$) 1.26 (3 H, t), 1.40 (3 H, t), 2.96 (2 H, q), 3.30 (3 H, s), 4.42 (2 H, q), 5.50 (2 H, s), 7.20—7.50 (3 H, m), 7.28 (1 H, s), and 8.02 (1 H, m).

Ethyl 2-azido-3-(1-methoxymethyl-2-n-propylindol-3-yl)pro-

penoate (**6d**) (26%), oil, $\nu_{max.}$ 2 106, 1 702, and 1 613 cm $^{-1}$; δ (90 MHz; $CDCl_3$) 0.99 (3 H, t), 1.40 (3 H, t), 1.66 (2 H, sextet), 2.90 (2 H, t), 3.28 (3 H, s), 4.42 (2 H, q), 5.47 (2 H, s), 7.20—7.50 (3 H, m), 7.30 (1 H, s), and 8.04 (1 H, m).

Ethyl 2-azido-3-(2-cyclohexyl-1-methoxymethylindol-3-yl)-propenoate (**6e**) (4%), oil, $\nu_{max.}$ 2 105, 1 697, and 1 605 cm $^{-1}$; δ (250 MHz; $CDCl_3$) 1.43 (3 H, t), 1.7—2.1 (10 H, m), 3.0 (1 H,br m), 3.29 (3 H, s), 4.41 (2 H, q), 5.50 (2 H, s), 7.22 (2 H, m), 7.42 (1 H, m), 7.48 (1 H, s), and 7.74 (1 H, m).

Ethyl 2-azido-3-(2-isopropyl-1-methoxymethylindol-3-yl)propenoate (**6f**) (6%), oil, $\nu_{max.}$ 2 120, 1710, and 1 615 cm $^{-1}$ δ (90 MHz; $CDCl_3$) 1.39 (3 H, t), 1.43 (6 H, d), 3.28 (3 H, s), 3.41 (1 H, septet), 4.41 (2 H, q), 5.52 (2 H, s), 7.20—7.55 (3 H, m), 7.46 (1 H, s), and 7.79 (1 H, m).

Ethyl 2-azido-3-(1-methoxymethyl-2-phenylindol-3-yl)propenoate (**6g**) (1%), yellow solid, $\nu_{max.}$ 2 100, 1 700, and 1 617 cm $^{-1}$; δ (90 MHz; $CDCl_3$) 1.26 (3 H, t), 3.18 (3 H, s), 4.23 (2 H, q), 5.30 (2 H, s), 6.96 (1 H, s), 7.16—7.54 (8 H, m), and 8.04 (1 H, m).

Thermolysis of the Azide (**6a**).—A solution of the azide (**6a**) (200 mg) in toluene (80 ml) was heated under reflux for 17 h. Evaporation of the solvent and chromatography of the residue gave (i) *ethyl 2-amino-3-(1-benzyl-2-methylindol-3-yl)propenoate* (**9a**) (11 mg, 6%) as an oil, $\nu_{max.}$ 3 480, 3 340, 1 722, 1 670, and 1 618 cm $^{-1}$; δ (90 MHz; $CDCl_3$) 1.37 (3 H, t), 2.33 (3 H, s), 4.37 (2 H, q), 5.38 (2 H, s), 6.73 (1 H, s), and 6.9—7.4 (9 H, m); *m/z* 334 (M^+), 187, 142, 115 (base), 114, and 86; and (ii) *ethyl 9-benzylpyrido*[3,4-b]*indole-3-carboxylate* (**8a**) (140 mg, 76%) as yellow needles, m.p. 120—121 °C (Found: C, 76.2; H, 5.5; N, 8.4. $C_{21}H_{18}N_2O_2$ requires C, 76.3; H, 5.5; N, 8.5%); $\nu_{max.}$ 1 704 cm $^{-1}$; δ (90 MHz; $CDCl_3$) 1.48 (3 H, t), 4.56 (2 H, q), 5.64 (2 H, s), 7.10—7.70 (8 H, m), 8.26 (1 H, d), and 8.92 (2 H, s). This latter signal split into two singlets at δ 8.97 and 9.20 when the spectrum was recorded in $(CD_3)_2SO$.

Thermolysis of the Azide (**6b**).—(*a*) A solution of the azide (**6b**) (500 mg) in xylene (100 ml) was heated under reflux for 1.5 h. Evaporation of the solvent, and chromatography of the residue gave (i) ethyl 2-amino-3-(1-methoxymethyl-2-methylindol-3-yl)propenoate (**9b**) (22 mg, 5%) as an oil, $\nu_{max.}$ 3 460, 3 370, and 1 700 cm^{-1}; δ (60 MHz; $CDCl_3$) 1.40 (3 H, t), 2.45 (3 H, s), 3.28 (3 H, s), 4.34 (2 H, q), 5.43 (2 H, s), 6.60 (1 H, s), and 7.0—7.8 (4 H, m); *m/z* 288 (M^+); (ii) 1-methoxymethyl-2-methylindole-3-carbaldehyde (**5b**) (59 mg. 18%); and (iii) *ethyl 9-methoxymethylpyrido*[3,4-b]*indole-3-carboxylate* (**8b**) (266 mg, 59%), as pale yellow needles, m.p. 128.5—130.5 °C (Found; C, 67.7; H, 5.7; N, 9.85. $C_{16}H_{16}N_2O_3$ requires C, 67.6; H, 5.7; N, 9.9%; $\nu_{max.}$ 1 707 cm $^{-1}$; δ (90 MHz; $CDCl_3$) 1.48 (3 H, s), 3.28 (3 H, s), 4.50 (2 H, q), 5.71 (2 H, s), 7.29 (1 H, m), 7.54 (2 H, m), 8.10 (1 H, d), 8.73 (1 H, s), and 8.96 (1 H, s).

(*b*) The azide (**6b**) (250 mg) was refluxed under nitrogen in degassed xylene (50 ml) for 1.5 h. The solvent was evaporated, and the residue examined by n.m.r. spectroscopy. In addition to signals for compound (**8b**), *ethyl 1,2-dihydro-9-methoxymethylpyrido*[3,4-b]*indole-3-carboxylate* (**7b**) was detected; δ (90 MHz; $CDCl_3$) 1.37 (3 H, t), 3.24 (3 H, s), 4.34 (2 H, q), 5.00 (2 H, s), 5.38 (2 H, s), 6.73 (1 H, s), and 7.15—7.65 (4 H, m). The ratio of (**8b**):(**7b**) was *ca.* 1 : 1. Chromatography of this mixture gave only compound (**8b**) (191 mg, 85%).

Deprotection of compound (**8b**). The β-carboline (**8b**) (85 mg) was heated under reflux in formic acid (90%; 1.5 ml) and water (0.5 ml) for 12 h. Evaporation and chromatography of the residue gave ethyl pyrido[3,4-*b*]indole-3-carboxylate (**10**) (53 mg, 75%), m.p. 224—229 °C (lit.,[2e] 231—232 °C).

Thermolysis of the Azide (**6c**).—(*a*) *In xylene.* A solution of the azide (**6c**) (145 mg) in xylene (29 ml) was heated under reflux for 20 h. Evaporation of the solvent and chromatography of the residue gave (i) *ethyl 6-methoxymethyl-3,4,5,6-tetrahydroazepino*[4,5-b]*indole-2-carboxylate* (**13a**) (32 mg, 24%) as a gum which slowly crystallised, m.p. 40—43 °C (Found: C, 67.7; H, 6.8; N, 9.1. $C_{17}H_{20}N_2O_3$ requires C, 68.0; H, 6.7; N, 9.3%); $\nu_{max.}$ 3 380, 1 690, and 1 625 cm $^{-1}$; δ (250 MHz; $CDCl_3$) 1.39 (3 H, t), 3.25 (3 H, s), 3.29 (2 H, t, *J* 5.1 Hz), 3.48 (2 H, t, *J* 5.1 Hz), 4.33 (2 H, q), 5.47 (2 H, s), 6.93 (1 H, s), 7.21 (2 H, m), 7.38 (1 H, m), and 7.73 (1 H, m); *m/z* 300 (M^+, base), 269, 255, and 181; and (ii) *ethyl 9-methoxymethyl-1-methylpyrido*[3,4-b]*indole-3-carboxylate* (**11a**) (46 mg, 35%), m.p. 105—106 °C (Found: C, 68.5; H, 6.0; N, 9.25. $C_{17}H_{18}N_2O_3$ requires C, 68.4; H, 6.1; N, 9.4%); $\nu_{max.}$ 1 704 cm $^{-1}$; δ (250 MHz; $CDCl_3$) 1.51 (3 H, t), 3.15 (3 H, s), 3.32 (3 H, s), 4.54 (2 H, q), 5.87 (2 H, s), 7.38 (1 H, m), 7.64 (2 H, m), 8.19 (1 H, d), and 8.76 (1 H, s); *m/z* 298 (M^+), 267, 253, and 226.

(*b*) *In 1,2-dichlorobenzene.* A solution of the azide (**6c**) (150 mg) in 1,2-dichlorobenzene (30 ml) was heated under reflux for 1 h. Evaporation of the solvent, and chromatography of the residue gave the β-carboline (**11a**) (57 mg, 43%).

(*c*) *In dimethylformamide.* A solution of the azide (**6c**) (550 mg) in dimethylformamide (110 ml) was heated under reflux for 2.5 h. The cooled solution was poured into water, and extracted with ether. The combined ether extracts were washed with water, dried ($MgSO_4$), and evaporated. Chromatography of the residue gave the azepinoindole (**13a**) (300 mg, 60%).

(*d*) *In benzene.* A solution of the azide (**6c**) (384 mg) in benzene (80 ml) was heated under reflux for 2 h. Evaporation of the solvent gave *ethyl 2-amino-3-(1-methoxymethyl-2-vinylindol-3-yl)propenoate* (**14a**) as a brown gum, $\nu_{max.}$ 3 480, 3 380, 1 705, 1 635, and 1 580 cm $^{-1}$; δ (250 MHz; $CDCl_3$) 1.40 (3 H, t), 3.33 (3 H, s), 3.92 (2 H,br, D_2O exch.), 4.36 (2 H, q), 5.51 (2 H, s), 5.65 (1 H, dd, *J* 12, 1.3 Hz), 5.72 (1 H, dd, *J* 18, 1.3 Hz), 6.69 (1 H, s), 6.90 (1 H, dd, *J* 18, 12 Hz), 7.30 (3 H, m), and 7.67 (1 H, m); N-*acetyl derivative* (**14b**), m.p. 150—160 °C (decomp.) (Found: C, 66.8; H, 6.4; N, 8.1. $C_{19}H_{22}N_2O_4$ requires C, 66.65; H, 6.5; N, 8.2%).

Deprotection of Compound (**11a**).—A mixture of the β-carboline (**11a**) (37 mg) and formic acid (90%; 2.5 ml) was heated under reflux for 5 h. Evaporation, followed by chromatography of the residue gave ethyl 1-methylpyrido[3,4-*b*]indole-3-carboxylate (**12**) (30 mg, 95%), m.p. 219—223 °C (lit.,[11] 248—249 °C), $\nu_{max.}$ 3 310, 1 700, 1 618, and 1 590 cm^{-1}; δ [250 MHz; $(CD_3)_2SO$] 1.38 (3 H, t), 2.83 (3 H, s), 4.38 (2 H, q), 7.31 (1 H, ddd, *J* 8, 6.7, 1.1 Hz), 7.60 (1 H, ddd, *J* 8, 6.7, 1.3 Hz), 7.66 (1 H, d, *J* 8 Hz, with additional fine splitting), 8.36 (1 H, d, *J* 8 Hz), 8.76 (1 H, s), and 12.04 (1 H,br s); *m/z* 254 (M^+), 238, 209, and 182 (base).

Deprotection of Compound (**13a**).—The azepinoindole (**13a**) (63 mg) was dissolved in a mixture of ethanol (4 ml) and hydrochloric acid (5M; 4 ml), and the resulting solution was kept at room temperature for 24 h. The solution was neutralised with solid sodium hydrogen carbonate, and extracted with ether. The ether extracts were washed with water, dried ($MgSO_4$), and evaporated. Chromatography of the residue gave *ethyl 3,4,5,6-tetrahydroazepino*[4,5-b]*indole-2-carboxylate* (**13c**) (35 mg, 65%), m.p. 152—154 °C (Found: C, 70.2; H, 6.3; N, 10.9. $C_{15}H_{16}N_2O_2$ requires C, 70.3; H, 6.3; N, 10.9%); $\nu_{max.}$ 3 380, 3 360, 1 683, and 1 630 cm $^{-1}$; δ (250 MHz; $CDCl_3$–D_2O) 1.38 (3 H, t), 3.20 (2 H, t, *J* 4.4 Hz), 3.42 (2H, t, *J* 4.4 Hz), 4.32 (2 H, q), 6.96 (1 H, s), 7.17 (2 H, m), 7.26 (1 H, m), and 7.71 (1 H, m); *m/z* 256 (M^+, base), 228, and 182.

Dehydrogenation of Compound (**13a**).—A solution of the azepinoindole (**13a**) (85 mg, 0.28 mmol) in dichloromethane (10 ml) was cooled to −22 °C, and treated with t-butyl hypochlorite (38.5 μl, 0.34 mmol). The mixture was stirred for 1 h, and then 1,8-diazabicyclo[5.4.0]undec-7-ene (50.5 μl, 0.34 mmol) was added. The mixture was warmed to room tempera-

ture, and then stirred overnight. The solution was washed with water, dried ($MgSO_4$), evaporated, and the residue chromatographed to give *ethyl* 1,6-*dihydro*-6-*methoxymethylazepino*[4,5-b]*indole*-2-*carboxylate* (**23**) (15 mg, 18%) as a yellow gum (Found: M^+ 298.1321. $C_{17}H_{18}N_2O_3$ requires M 298.1317); $\nu_{max.}$(*CHCl*$_3$) 1 715 and 1 600 cm^{-1}; δ (90 MHz; $CDCl_3$) 1.34 (3 H, t), 3.27 (3 H, s), 3.47 (2 H, s), 4.29 (2 H, q), 5.51 (2 H, s), 6.90 (1 H, d, *J* 8 Hz), 7.33 (3 H, m), 7.75 (1 H, d, *J* 8Hz), and 7.81 (1 H, m); *m/z* 298 (M^+, base), 224, and 179.

Thermolysis of the Azide (**6d**).—(*a*) *In dimethylformamide.* A solution of the azide (**6d**) (200 mg) in dimethylformamide (40 ml) was heated under reflux for 5 h. Work-up as before gave *ethyl* 6-*methoxymethyl*-4-*methyl*-3,4,5,6-*tetrahydroazepino*[4,5-b]*indole*-2-*carboxylate* (**13b**) (94 mg, 51%) as a gum, $\nu_{max.}$ 3 370 and 1 684 cm^{-1}; δ (250 MHz; $CDCl_3$) 1.39 (3 H, t), 1.44 (3 H, d, *J* 6.3 Hz), 3.06 (1 H, dd, *J* 16.8 8.2 Hz), 3.24 (3 H, s), 3.26 (1 H, dd, *J* 16.8, 2.2 Hz), 3.44 (1 H, ddq, *J* 8.2, 6.3, 2.2 Hz), 4.32 (2 H, q), 5.44 (2 H, s), 6.94 (1 H, s), 7.21 (2 H, m), 7.39 (1 H, m), and 7.73 (1 H, m). Irradiation at δ 1.44 resulted in the collapse of the signal at δ 3.44 to a dd.

(*b*) *In benzene.* A solution of the azide (**6d**) (100 mg) in benzene (20 ml) was heated under reflux for 2 h. Evaporation of the solvent and chromatography of the residue gave *ethyl* 2-*amino*-3-[1-*methoxymethyl*-2-(*prop*-2-*en*-3-*yl*)*indol*-3-*yl*]*propenoate* (**14c**) (60 mg, 65%), as a gum, δ (250 MHz) 1.40 (3 H, t), 2.01 (3 H, dd, *J* 7, 1.7 Hz), 3.32 (3 H, s), 3.89 (2 H, br), 4.35 (2 H, q), 5.50 (2 H, s), 6.22 (1 H, dq, *J* 16, 7 Hz), 6.59 (1 H, dq, *J* 16, 1.7 Hz), 6.68 (1 H, s), 7.21 (2 H, m), 7.44 (1 H, m), and 7.64 (1 H, m); N-*acetyl derivative* (**14d**), m.p. 170—176 °C (Found: C, 67.3; H, 6.8; N, 7.8. $C_{20}H_{24}N_2O_4$ requires C, 67.4; H, 6.8; N, 7.9%).

Deprotection of Compound (**13b**).—The azepinoindole (**13b**) (50 mg) was hydrolysed by the method described for compound (**13a**). Work-up gave *ethyl* 4-*methyl*-3,4,5,6-*tetrahydroazepino*[4,5-b]*indole*-2-*carboxylate* (**13d**) (15 mg, 35%) as pale yellow needles, m.p. 180—182 °C (Found: C, 71.4; H, 6.9; N, 10.0. $C_{16}H_{18}N_2O_2$ requires C, 71.1; H, 6.7; N, 10.4%); $\nu_{max.}$ 3 390, 3 360, and 1 674 cm^{-1}; δ (250 MHz; $CDCl_3$–D_2O) 1.40 (3 H, t), 1.41 (3 H, d, *J* 7 Hz), 3.13 (2 H, m), 3.45 (1 H, m), 4.32 (2 H, q), 6.95 (1 H, s), 7.15 (2 H, m), 7.25 (1 H, m), and 7.70 (1 H, m); *m/z* 270 (M^+, base), 242, and 196.

Preparation and Thermolysis of the Azide (**24**).—(*a*) 2,6-*Diethylbenzoic acid.* This was prepared (64%) by the literature procedure [12] from 2,6-diethylbromobenzene and had m.p. 89—91 °C (lit.,[12] 90—92 °C).

(*b*) 2,6-*Diethylbenzaldehyde.* 2,6-Diethylbenzoic acid (1.03 g, 5.79 mmol) in 1,2-dimethoxyethane (10 ml) was added to a suspension of an excess of lithium aluminium hydride in 1,2-dimethoxyethane (30 ml) under nitrogen. The mixture was heated under reflux overnight. Standard work-up gave 2,6-diethylbenzyl alcohol (0.85 g, 90%) as an oil which slowly solidified, m.p. 67—71 °C. The alcohol (0.85 g, 5.18 mmol) in acetone (5 ml) was treated with Jones reagent (1M in aqueous acetone; 7.8 ml), and the resulting mixture was stirred at room temperature for 20 min. Standard work-up gave 2,6-*diethylbenzaldehyde* (0.68 g, 81%) as an oil, $\nu_{max.}$ 1 688 cm^{-1}; δ (90 MHz; $CDCl_3$) 1.27 (6 H, t), 2.99 (4 H, q), 7.05—7.55 (3 H, m), and 10.53 (1 H, s); *m/z* 162 (M^+, base); 2,4-*dinitrophenylhydrazone*, m.p. 192.5—201 °C (from methanol—nitromethane) (Found: C, 59.8; H, 5.2; N, 16.5. $C_{17}H_{18}N_4O_4$ requires C, 59.6; H, 5.3; N, 16.4%).

(*c*) *Ethyl* 2-*azido*-3-(2,6-*diethylphenyl*)*propenoate* (**24**). A mixture of 2,6-diethylbenzaldehyde (0.50 g, 3.09 mmol) and ethyl azidoacetate (1.59 g, 12.3 mmol) was added to a solution of sodium (248 mg, 12.3 mg atom) in ethanol (10 ml) at −10 °C. The solution was stirred at −10 to −5 °C for 6 h, and then at 3 °C for 16 h. Standard work-up and chromatography gave the *title azide* (**24**) (*ca.* 90% pure; 0.585 g, 63%) as a colourless oil, $\nu_{max.}$ 2 115, 1 720, and 1 626 cm^{-1}; δ (90 MHz; $CDCl_3$) 1.13 (6 H, t), 1.36 (3 H, t), 2.45 (4 H, q), 4.29 (2 H, q), and 6.95—7.25 (4 H, m); the remaining *ca.* 10% of the material was the starting aldehyde.

(*d*) *Thermolysis.* A solution of the azide (**24**) (85 mg) in xylene (16 ml) was heated under reflux for 2 h. The solution was cooled and iodine (1 equiv.) was added. After being stirred for 5 min, the solution was washed with sodium thiosulphate solution, dried ($MgSO_4$), and evaporated. The residue was subjected to p.l.c., and gave (i) *ethyl* 2-*amino*-3-(2-*ethyl*-6-*vinylphenyl*)-*propenoate* (**26**) (15 mg, 19%), $\nu_{max.}$ 3 480, 3 385, and 1 710 cm^{-1}; δ (90 MHz; $CDCl_3$) 1.18 (3 H, t), 1.40 (3 H, t), 2.62 (2 H, q), 4.33 (2 H, q), 5.27 (1 H, dd, *J* 11, 1.5 Hz), 5.72 (1 H, dd, *J* 17, 1.5 Hz), 6.50 (1 H, s), 6.86 (1 H, dd, *J* 17, 11 Hz), and 7.15—7.50 (3 H, m); N-*acetyl* derivative, m.p. 110—112 °C (Found: C, 70.9; H, 7.6; N, 4.8. $C_{17}H_{21}NO_3$ requires C, 71.1; H, 7.4; N, 4.9%); and (ii) *ethyl* 5-*ethyl*-1-*methylisoquinoline*-3-*carboxylate* (**25**) (28 mg, 35%) as an oil, $\nu_{max.}$ 1 718 cm^{-1}; δ (90 MHz; $CDCl_3$) 1.41 (3 H, t), 1.51 (3 H, t), 3.06 (3 H, s), 3.18 (2 H, q), 4.56 (2 H, q), 7.61 (2 H, m), 8.02 (1 H, m), and 8.61 (1 H, s); *picrate*, m.p. 132—135 °C (from ethanol) (Found: C, 53.65; H, 4.2; N, 11.9. $C_{21}H_{20}N_4O_9$ requires C, 53.4; H, 4.3; N, 11.8%).

Thermolysis of the Azide (**6e**).—A solution of the azide (**6e**) (60 mg) in benzene (12 ml) was heated under a reflux for 3 h. Evaporation of the solvent, and chromatography of the residue gave *ethyl* 2-*amino*-3-(2-*cyclohex*-1-*enyl*-1-*methoxymethylindol*-3-*yl*)*propenoate* (**14e**), which was acetylated to give *ethyl* 2-*acetamido*-1-(2-*cyclohex*-1-*enyl*-1-*methoxymethylindol*-3-*yl*)-*propenoate* (**14f**) (28 mg, 45% from the azide), m.p. 140—151 °C (Found: C, 69.5; H, 7.1; N, 7.0. $C_{23}H_{28}N_2O_4$ requires C, 69.7; H, 7.1; N, 7.1%); $\nu_{max.}$ 3240, 1710, 1654, and 1632 cm^{-1}; δ(250 MHz; $CDCl_3$) 1.36 (3 H, t), 1.65—1.85 (4 H, m), 1.98 (3 H, br s), 2.20—2.35 (4 H, m), 3.29 (3 H, s), 4.32 (2 H, q), 5.40 (2 H, s), 6.02 (1 H, m), 6.92 (1 H, s), 7.10—7.30 (3 H, m), 7.47 (1 H, m), and 7.52 (1 H, br s); *m/z* 396 (M^+), 365, 350, 337 (base), 305, and 291.

Thermolysis of the Azide (**6f**).—(*a*) *In benzene.* A solution of the azide (**6f**) (100 mg) in benzene (20 ml) was heated under reflux for 5 h. Evaporation of the solvent gave crude *ethyl* 2-*amino*-3-(2-*isopropenyl*-1-*methoxymethylindol*-3-*yl*)*propenoate* (**14g**) which was acetylated to give *ethyl* 2-*acetamido*-3-(2-*isopropenyl*-1-*methoxymethylindol*-3-*yl*)*propenoate* (**14h**) (50 mg, 48% from the azide), m.p. 130—137 °C (Found: C, 67.2; H, 6.8; N, 7.8. $C_{20}H_{24}N_2O_4$ requires C, 67.4; H, 6.8; N, 7.9%); $\nu_{max.}$ 3 240, 3 200, 1 700, 1 653, and 1 630 cm^{-1}; δ (250 MHz; $CDCl_3$) 1.36 (3 H, t), 1.96 (3 H,br s), 2.14 (3 H,br s), 3.29 (3 H, s), 4.32 (2 H, q), 5.28 (1 H, m), 5.42 (2 H, s), 5.65 (1 H, m), 6.98 (1 H,br s), and 7.10—7.55 (5 H, m).

(*b*) *In xylene.* A solution of the azide (**6f**) (100 mg) in xylene (20 ml) was heated under reflux for 7 h. Evaporation of the solvent, and separation of the residue by p.l.c. gave impure *ethyl* 1,2-*dihydro*-1,1-*dimethyl*-9-*methoxymethylpyrido*[3,4-b]*indole*-3-*carboxylate* (**29**), $\nu_{max.}$ 3 380 and 1 700 cm^{-1}; δ (90 MHz; $CDCl_3$) 1.36 (3 H, t), 1.61 (6 H, s), 3.30 (3 H, s), 4.33 (2 H, q), 5.57 (2 H, s), 6.80 (1 H, s), and 7.1—7.8 (4 H, m).

(*c*) *In bromobenzene.* A solution of the azide (**6f**) (50 mg) in bromobenzene (10 ml) was heated under reflux for 168 h. Evaporation of the solvent, and chromatography of the residue gave ethyl 9-methoxymethyl-1-methylpyrido[3,4-*b*]indole-3-carboxylate (**11a**) (5 mg, 9%), identical with the previously prepared sample.

Thermolysis of the Azide (**6g**).—A solution of the azide (**6g**) (20 mg) in xylene (10 ml) was heated under reflux for 1

h. Evaporation of the solvent and separation of the residue by p.l.c. gave *ethyl 1,8-dihydro-8-methoxymethylbenz*[2,3]-*azepino*[4,5-b]*indole-2-carboxylate* (**31**) (10 mg, 54%), m.p. 144—148 °C (Found: C, 72.1; H, 5.7; N, 8.0. $C_{21}H_{20}N_2O_3$ requires C, 72.4; H, 5.8; N, 8.0%); $\nu_{max.}$ 1 708 cm $^{-1}$; δ [250 MHz; $(CD_3)_2CO$] 1.31 (3 H, t), 3.46 (3 H, s), 4.28 (2 H, q), 5.58 (2 H, s), 7.29 (2 H, m), 7.40—7.60 (3 H, m), 7.70 (1 H, m), 7.83 (1 H, m), and 8.21 (1 H, m); *m/z* 348 (M^+, base), 303, and 229.

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