Regioselective Claisen Rearrangements in Indoles[1]

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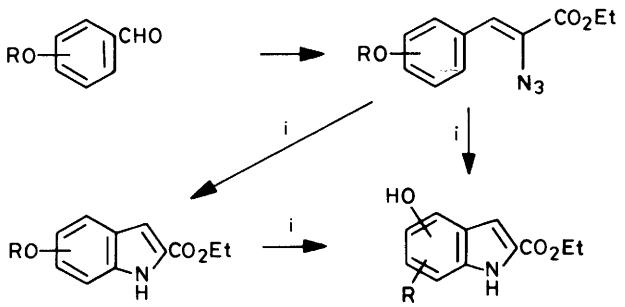
The Claisen rearrangement of several ethyl allyloxyindole-2-carboxylates is described. These indoles are readily prepared by the thermolysis of azidocinnamates in toluene, which undergo concomitant ring closure and Claisen rearrangement when heated in bromobenzene. Rearrangement of the 6-allyloxy derivatives (**10**) and (**17**) proceeds regioselectively to give the corresponding 7-allyl-6-hydroxyindoles. The method has been used to prepare 7-(1,1-dimethylallyl)-, 7-(3-methylbut-2-enyl)-, and 7-linalylindoles in synthetically useful reactions.

Since its discovery in 1912, the Claisen rearrangement of vinyl and aryl allyl ethers has been extensively studied and exploited in organic synthesis.[2,3] Regioselectivity in the aromatic Claisen rearrangements, recently the subject of renewed interest,[4,5] has been known for many years. Indeed the well known thermal rearrangement of 2-allyloxynaphthalene to give exclusively 1-allyl-2-naphthol was described in Claisen's original paper.[6] Similar regioselectivity has been observed in the rearrangements of heteroaromatic allyl ethers, and although Claisen rearrangements in the benzene ring of coumarins have been reported,[7] little if anything is known about rearrangements in the benzene ring of nitrogen-containing heterocycles (quinolines, isoquinolines, *etc.*). In particular there is only one report of Claisen rearrangements in the benzene ring of indoles, in which 5-allyloxyindole and ethyl 5-allyloxyindole-2-carboxylate gave the corresponding 4-allyl-5-hydroxyindoles regioselectively on heating.[8] The Claisen rearrangement of several allyloxyindole-2-carboxylates has now been studied with particular regard to the regioselectivity of the rearrangement of the 6-allyloxy isomers, and full details of this work are reported here.

Results and Discussion

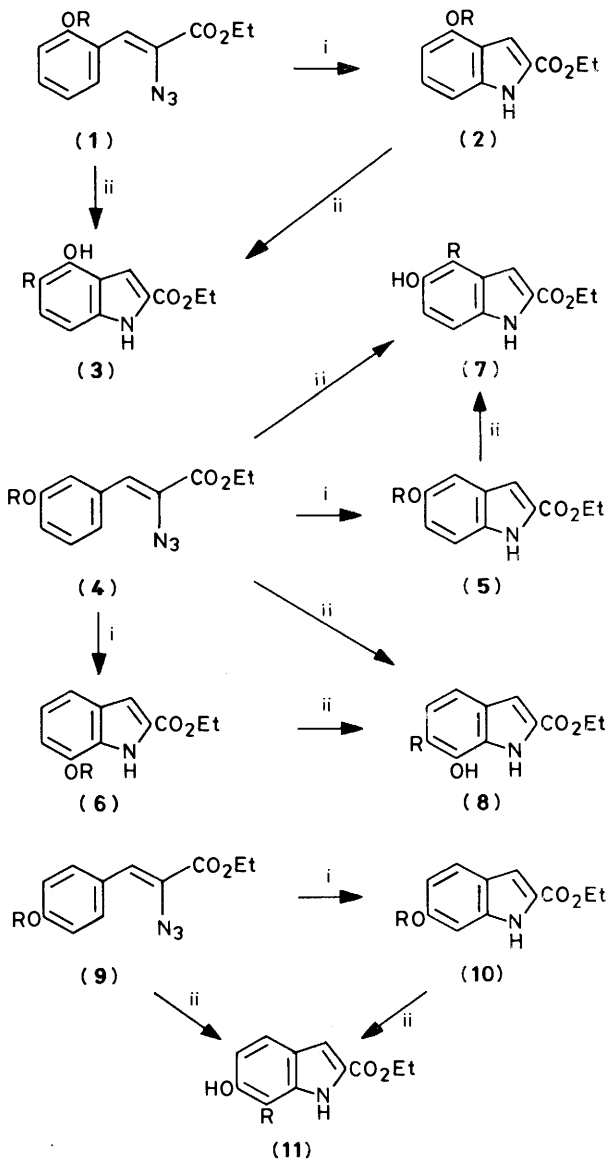
Allyloxyindole-2-carboxylates were considered to be attractive substrates for study since some of our,[9] and other,[10] earlier work on the decomposition of azidocinnamates suggested that they could be readily prepared in two steps from the corresponding allyloxybenzaldehydes (Scheme 1). Additionally,



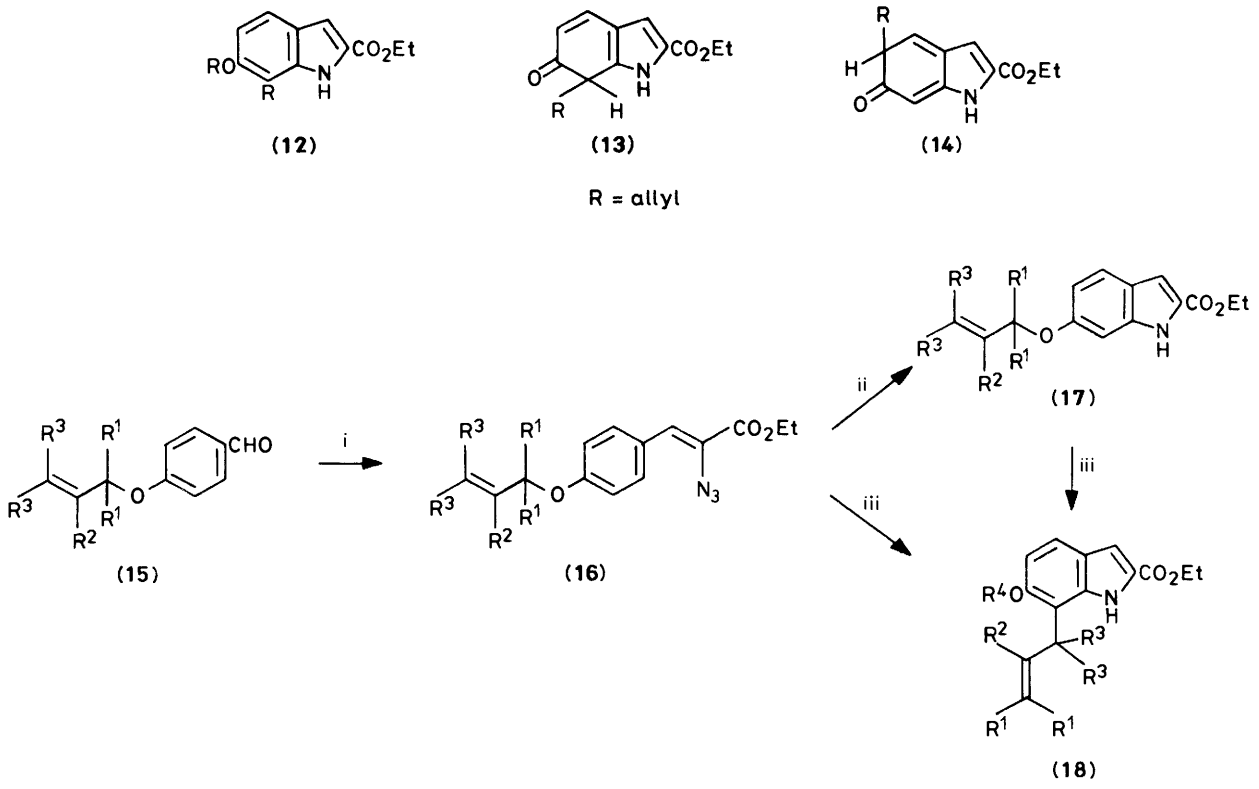
Scheme 1. R = Allyl. *Conditions:* i, heat

since the indole ring closure occurs under neutral, thermal conditions, it seemed possible that both indolisation and Claisen rearrangement might be effected in a single step simply by heating the azidocinnamates (Scheme 1). Therefore, initially, these possibilities were investigated using the known allyl ethers of 2-, 3-, and 4-hydroxybenzaldehyde as the starting materials.

Condensation of the appropriate aldehyde with ethyl azidoacetate in ethanol in the presence of sodium ethoxide gave the azidocinnamates (**1**), (**4**), and (**9**) in yields of 69, 78, and 70% respectively. Thermolysis of the azide (**1**) in boiling toluene gave the required 4-allyloxyindole-2-carboxylate (**2**) (77%). The Claisen rearrangement of compound (**2**) occurred readily in



Scheme 2. R = Allyl. *Reagents:* i, toluene, reflux; ii, bromobenzene, reflux



Scheme 3. *Reagents:* i, $N_3CH_2CO_2Et$, NaOEt, EtOH, −10 °C; ii, toluene, reflux; iii, PhBr, reflux, or see text

boiling bromobenzene (156 °C) to give the 5-allyl-4-hydroxyindole (**3**) (76%). When the azide (**1**) was heated in boiling bromobenzene, concomitant indole formation and Claisen rearrangement occurred to give the indole (**3**) (77%) (Scheme 2).

Thermolysis of the 3-substituted azide (**4**) in toluene gave both possible indoles (**5**) and (**6**) in the ratio 3:2 (45% combined). Little is known about the cyclisation of the nitrenes derived from these *meta*-substituted azidocinnamates, thermolysis of the corresponding 3-methoxy substituted azide giving an unspecified mixture of both possible indoles.[10] Claisen rearrangement of the 5-allyloxyindole (**5**) proceeded regioselectively to give the 4-allylindole (**7**) (93%) as previously reported,[8] and rearrangement of compound (**6**) gave the hydroxyindole (**8**) (62%) as expected. When the azide (**4**) was heated in bromobenzene, concomitant indolisation and Claisen rearrangement again occurred to give a mixture of the indoles (**7**) and (**8**) (75% combined) (Scheme 2). The ratio of (**7**) to (**8**) was 3:2, confirming the apparent preference for cyclisation *para* to the oxygen substituent.

Claisen rearrangement of the 6-allyloxyindole (**10**), prepared (87%) by thermolysis of the azide (**9**), occurred readily in boiling bromobenzene to give the 7-allyl-6-hydroxyindole (**11**) (71%) (Scheme 2). No products resulting from rearrangement to the 5-position were isolated. That rearrangement had occurred selectively to the 7-position was immediately clear from the n.m.r. spectrum of the product which showed the vicinal protons 4-H and 5-H as two doublets (*J* 9 Hz). The indole (**11**) could also be prepared (78%) directly from the azide (**9**) simply by heating the latter in bromobenzene.

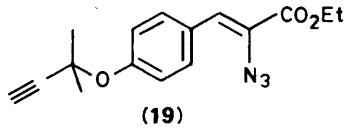
The fact that rearrangement to the 5-position is strongly disfavoured was further demonstrated when the allyl ether (**12**), prepared from the hydroxyindole (**11**), was recovered unchanged after being heated in bromobenzene. Prolonged heating caused a slow decomposition from which no products were isolated. Thus, in exact parallel with 2-allyloxynaphthalene, the Claisen rearrangement of the 6-allyloxyindole (**10**) proceeds regioselectively. The transition state leading to intermediate (**13**), which retains some aromatic stabilisation, is clearly favoured over that leading to intermediate (**14**).

Similar regioselectivity was observed in the Claisen rearrangement of other 6-allyloxyindole-2-carboxylates, prepared from the corresponding 4-allyloxybenzaldehydes (**15**) *via* the azidocinnamates (**16**). Thus, the thermolysis of the azides (**16a**) and (**16b**) in bromobenzene resulted in concomitant indolisation and Claisen rearrangement to give the corresponding 7-(2-methylallyl)- and 7-(3-methylbut-2-enyl)-indoles (**18a**) (65%) and (**18b**) (61%) (Scheme 3). Subsequently it was found that Claisen rearrangement of the 1,1-dimethylallyl derivative occurred at lower temperature, and the unrearranged indole (**17b**) could not be isolated even after refluxing of the azide (**16b**) in toluene for a short time, conditions which readily allowed the isolation of the corresponding 6-(2-methylallyloxy)indole (**17a**) from the azide (**16a**).

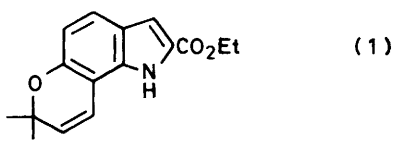
Claisen rearrangements of ethers which bear γ-alkyl substituents are often complicated by further rearrangements of the initial phenolic product, the so-called abnormal Claisen rearrangement.[2] However, these subsequent rearrangements can be prevented if an efficient trapping agent is employed to intercept the initial phenolic product, and so prevent the participation of the phenolic hydrogen in further sigmatropic processes. Butyric anhydride has been reported to be effective in intercepting the initial 'normal' Claisen product,[11] but more recently acetic anhydride has been employed.[12,13] The use of acetic anhydride to intercept the initial phenolic Claisen

rearrangement product was first reported by Fieser *et al.*[14] In order to prevent the formation of the products resulting from the abnormal Claisen rearrangement, the rearrangement of the indole (**17c**), prepared in 60% yield from the azide (**16c**), was carried out differently; thus, the indole (**17c**) was heated in acetic anhydride–*N*,*N*-dimethylaniline (1:1 v/v) to give the required 'normal' Claisen rearrangement product (**18c**) (89% as its *O*-acetate).

A reaction which is related to the abnormal Claisen rearrangement, since it also involves further sigmatropic rearrangement of the initial phenolic products, is the formation of chromenes by the thermal rearrangement of 1,1-dimethylprop-2-ynyl aryl ethers.[2] On this basis, it was expected that thermolysis of the azide (**19**), prepared from the appropriate known benzaldehyde, would give the pyrano[2,3-*g*]indole (**20**) by sequential indolisation and regioselective rearrangement [equation (1)]. In the event, both reactions occurred readily,



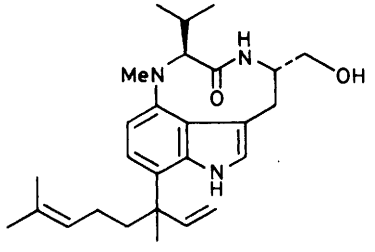
(**19**)



(**20**) (1)

and simply refluxing the azide (**19**) in toluene for 3 h gave the pyranoindole (**20**) in high yield (94%). The intermediate, unrearranged 1,1-dimethylprop-2-ynyloxyindole was not isolated.

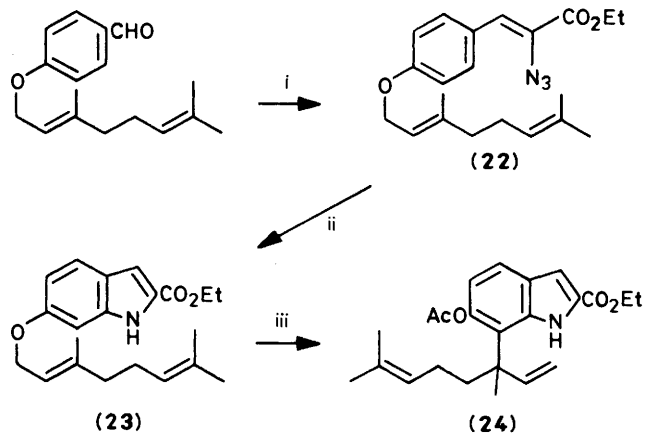
Finally in order to extend the scope of the indolisation–Claisen rearrangement sequence, and in connection with synthetic studies on lyngbyatoxin A (**21**), a highly toxic marine indole alkaloid,[15] the conversion of 4-geranyloxybenzaldehyde,[16] into the indole (**24**) was investigated (Scheme 4).



(**21**)

Condensation of the aldehyde with ethyl azidoacetate under the usual conditions gave the azidocinnamate (**22**), which on thermolysis in toluene gave the 6-geranyloxyindole (**23**) (63%). In a separate experiment, the azide was converted into the indole (**23**) which, without further purification, was heated in acetic anhydride–*N*,*N*-dimethylaniline to give the required 7-linalylindole (**24**) (32% overall from 4-geranyloxybenzaldehyde). The introduction of the 7-linalyl substituent would be a key step in any synthesis of lyngbyatoxin A, and therefore the regioselective Claisen rearrangement of an appropriate 6-geranyloxyindole derivative offers one possible approach.

Since, in principle, the additional 2- and 6-substituents may be removed if necessary, the regioselective Claisen rearrangement provides a useful route to a range of 7-allylindoles.



(**22**) (**23**) (**24**)

Scheme 4. *Reagents:* i, $EtO_2CCH_2N_3$, NaOEt, EtOH, −10 °C; ii, toluene, reflux; iii, $PhNMe_2$–Ac_2O (1:1), reflux

Experimental

I.r. spectra were recorded for liquids as thin films and for solids as Nujol mulls on a Perkin-Elmer 298 spectrophotometer, and calibrated against polystyrene. ^1H N.m.r. spectra were recorded at 90 MHz on a Perkin-Elmer R32 spectrometer or at 250 MHz on a Bruker WM250 instrument in deuteriochloroform solution using tetramethylsilane as internal standard. Mass spectra were obtained using a VG Micromass 7070B spectrometer operating at 70 eV using a direct insertion probe. Column chromatography was carried out on silica gel 60 (70—230 mesh, Merck) using light petroleum (b.p. 60—80 °C) containing an increasing proportion of ether as eluant. All solvents were dried by standard procedures. Ether refers to diethyl ether.

Preparation of Azides.—The following procedure is typical. Sodium (0.69 g, 30 mg-atom) was dissolved in ethanol (20 ml), and the stirred solution was cooled to −10 °C. A mixture of 2-allyloxybenzaldehyde (1.208 g, 7.45 mmol), ethyl azidoacetate (4.2 ml, *ca.* 30 mmol), and ethanol (2 ml) was added dropwise during 1.5 h and the reaction temperature kept between −10 and −5 °C. After being stirred for a further 1.5 h at −10 °C, the reaction mixture was allowed to warm up to room temperature, and then poured into water (150 ml). The resulting pale yellow precipitate was filtered off, washed with water, and dried to give *ethyl 2-azido-3-(2-allyloxyphenyl)propenoate* (**1**) (1.410 g, 69%), m.p. 85.5—87 °C (from ether–hexane) (Found: C, 61.4; H, 5.45; N, 15.3. $C_{14}H_{15}N_3O_3$ requires C, 61.5; H, 5.5; N, 15.4%), $\nu_{max.}$ 2 125 and 1 700 cm^{-1}; δ (90 MHz) 1.41 (3 H, t), 4.37 (2 H, q), 4.58 (2 H, m), 5.35 (2 H, m), 6.05 (1 H, m), 6.8—7.4 (3 H, m), 7.45 (1 H, s), and 8.15 (1 H, m).

The following azides were prepared similarly. *Ethyl 2-azido-3-(3-allyloxyphenyl)propenoate* (**4**) (78%), m.p. 44—45 °C (from hexane) (Found: C, 61.6; H, 5.5; N, 15.2%), $\nu_{max.}$ 2 105, 1 705, and 1 692 cm^{-1}; δ (90 MHz) 1.42 (3 H, t), 4.38 (2 H, q), 4.58 (2 H, m), 5.35 (2 H, m), 6.05 (1 H, m), 6.90 (2 H, m), and 7.35 (3 H, m). *Ethyl 2-azido-3-(4-allyloxyphenyl)propenoate* (**9**) (70%), m.p. 26—28 °C (purified by chromatography) (Found: C, 61.35; H, 5.5; N, 15.0%), $\nu_{max.}$ 2 130, 1 715, and 1 605 cm^{-1}; δ (90 MHz) 1.40 (3 H, t), 4.36 (2 H, q), 4.57 (2 H, m), 5.40 (2 H, m), 6.05 (1 H, m), 6.94 (3 H, s + d), and 7.76 (2 H, d, *J* 8 Hz). *Ethyl 2-azido-3-[4-(2-methylallyloxy)phenyl]propenoate* (**16a**) (78%), m.p. 42—44 °C (from hexane) (Found: C, 62.6; H, 6.05; N, 14.6. $C_{15}H_{17}N_3O_3$ requires C, 62.7; H, 6.0; N, 14.6%), $\nu_{max.}$ 2 130, 1 702, and 1 601 cm^{-1}; δ (90 MHz) 1.42 (3 H, t), 1.88 (3 H, s), 4.40 (2 H, q), 4.52 (2 H, s), 5.10 (2 H, m), 6.93 (1 H, s), 6.96 (2 H, d, *J* 8 Hz), and 7.80 (2 H, d, *J* 8 Hz). *Ethyl 2-azido-3-[4-(1,1-dimethylallyloxy)phenyl]propenoate* (**16b**) (68%) as an oil, $\nu_{max.}$ 2 120, 1 710, and 1 600 cm^{-1}; δ (90 MHz) 1.43 (3 H, t), 1.56 (6 H,

s), 4.41 (2 H, q), 5.22 (2 H, AB of ABX), 6.16 (1 H, m, X of ABX), 6.91 (1 H, s), 7.02 (2 H, d, *J* 8 Hz), and 7.72 (2 H, d, *J* 8 Hz); *m/z* 301 (M^+), 273, 205, 159, 132, and 69 (base). *Ethyl 2-azido-3-[4-(3-methylbut-2-enyloxy)phenyl]propenoate* (**16c**) (75%), m.p. 50—53 °C (from hexane) (Found: C, 63.9; H, 6.4; N, 13.9. $C_{16}H_{19}N_3O_3$ requires C, 63.8; H, 6.4; N, 13.9%), $\nu_{max.}$ 2 120, 1 690, and 1 600 cm^{-1}; δ (90 MHz) 1.41 (3 H, t), 1.79 (3 H, s), 1.84 (3 H, s), 4.37 (2 H, q), 4.56 (2 H, m), 5.52 (1 H, t with additional fine splitting), 6.88 (1 H, s), 6.91 (2 H, d, *J* 8.5 Hz), and 7.76 (2 H, d, *J* 8.5 Hz). *Ethyl 2-azido-3-[4-(1,1-dimethylprop-2-ynyl)oxyphenyl]propenoate* (**19**) (81%) as an oil, $\nu_{max.}$ 3 300, 2 130, 1 710, and 1 602 cm^{-1}; δ (90 MHz) 1.39 (3 H, t), 1.70 (6 H, s), 2.63 (1 H, s), 4.37 (2 H, q), 6.88 (1 H, s), 7.20 (2 H, d, *J* 8 Hz), and 7.74 (2 H, d, *J* 8 Hz); *m/z* 299 (M^+), 271, 256, and 205 (base). *Ethyl 2-azido-3-(4-geranyloxyphenyl)propenoate* (**22**) (60%) as an oil, $\nu_{max.}$ 2 120, 1 750, and 1 600 cm^{-1}; δ (90 MHz) 1.32 (3 H, t), 1.55 (3 H, s), 1.62 (3 H, s), 1.68 (3 H, s), 2.04 (4 H, m), 4.28 (2 H, q), 4.50 (2 H, m), 5.05 (1 H, m), 5.42 (1 H, br t), 6.80 (1 H, s), 6.83 (2 H, d, *J* 8 Hz), and 7.67 (2 H, d, *J* 8 Hz).

Preparation of Indole-2-carboxylates by Thermolysis of Azides.—Ethyl 4-allyloxyindole-2-carboxylate (**2**). The azide (**1**) (305 mg) was heated in refluxing toluene (20 ml) for 3 h. Evaporation of the toluene left a brownish solid which was triturated with hexane to give crystals of the *title compound* (**2**) (210 mg, 77%), m.p. 157.5—158.5 °C (from chloroform–hexane) (Found: C, 68.6; H, 6.1; N, 5.7. $C_{14}H_{15}NO_3$ requires C, 68.6; H, 6.2; N, 5.7%), $\nu_{max.}$ 3 300 and 1 692 cm^{-1}; δ (250 MHz) 1.40 (3 H, t), 4.40 (2 H, q), 4.68 (2 H, m), 5.40 (2 H, m), 6.14 (1 H, m), 6.50 (1 H, d, *J* 8.75 Hz), 7.02 (1 H, d, *J* 8.75 Hz), 7.21 (1 H, t), 7.39 (1 H, m), and 8.92 (1 H, br).

Ethyl 5- and 7-allyloxyindole-2-carboxylates (**5**) *and* (**6**). The azide (**4**) (282 mg) was heated in refluxing toluene (25 ml) for 4 h. Evaporation of the toluene left a yellow oil which was chromatographed to give (i) the *7-allyloxy isomer* (**6**) (45 mg, 18%) as a colourless oil, $\nu_{max.}$ 3 320 and 1 700 cm^{-1}; δ (250 MHz) 1.40 (3 H, t), 4.38 (2 H, q), 4.66 (2 H, dt), 5.40 (2 H, AB of ABX), 6.10 (1 H, X of ABX), 6.68 (1 H, d, *J* 8.75 Hz), 7.02 (1 H, t), 7.19 (1 H, d, *J* 2.5 Hz), 7.26 (1 H, d, *J* 8.75 Hz), and 9.18 (1 H, br); *m/z* 245 (M^+), 204, and 158 (base); *picrate*, m.p. 91.5—92 °C (from aqueous ethanol) (Found: C, 50.7; H, 3.7; N, 11.7. $C_{20}H_{18}N_4O_{10}$ requires C, 50.6; H, 3.8; N, 11.8%); and (ii) the 5-allyloxy isomer (**5**) (68 mg, 27%), m.p. 108—110 °C (lit.,[8] m.p. 106 °C).

Ethyl 6-allyloxyindole-2-carboxylate (**10**). The azide (**9**) (233.5 mg) was refluxed in toluene (25 ml) for 3 h. The toluene was evaporated to leave a yellow crystalline solid, which was recrystallised from hexane to give pale yellow crystals of the *title compound* (183 mg, 87%), m.p. 94—95 °C (Found: C, 68.9; H, 6.2; N, 5.8. $C_{14}H_{15}NO_3$ requires C, 68.6; H, 6.2; N, 5.7%), $\nu_{max.}$ 3 315 and 1 680 cm^{-1}; δ (250 MHz) 1.41 (3 H, t), 4.39 (2 H, q), 4.58 (2 H, dt), 5.4 (2 H, m), 6.1 (1 H, m), 6.86 (2 H, m), 7.16 (1 H, m), 7.55 (1 H, *ca.* d), and 8.81 (1 H, br).

Ethyl 6-(2-methylallyloxy)indole-2-carboxylate (**17a**). The azide (**16a**) (552 mg) was refluxed in toluene (25 ml) for 3 h. Evaporation of the toluene left a yellow solid which was recrystallised from chloroform–hexane to give colourless needles of the *title compound* (**17a**) (248 mg, 50%), m.p. 119—120 °C (Found: C, 69.4; H, 6.6; N, 5.3. $C_{15}H_{17}NO_3$ requires C, 69.5; H, 6.6; N, 5.4%); $\nu_{max.}$ 3 320 and 1 679 cm^{-1}; δ (250 MHz) 1.41 (3 H, t), 1.85 (3 H, s), 4.38 (2 H, q), 4.47 (2 H, s), 5.01 (1 H, s, with extra fine coupling), 5.13 (1 H, s, with extra fine coupling), 6.85 (2 H, m, simplified by irradiation at δ 7.55), 7.16 (1 H, d), 7.55 (1 H, d), and 8.78 (1 H, br).

Ethyl 6-(3-methylbut-2-enyloxy)indole-2-carboxylate (**17c**). The azide (**16c**) (852 mg) was refluxed in toluene (50 ml) for 2 h. Evaporation of the toluene left a yellow crystalline solid which was recrystallised from dichloromethane–hexane to give colourless needles of the *title compound* (**17c**) (460 mg, 60%), m.p. 141—143 °C (Found: C, 70.3; H, 7.1; N, 5.2. $C_{16}H_{19}NO_3$ requires C, 70.3; H, 7.0; N, 5.1%); $\nu_{max.}$ 3 300 and 1 680 cm^{-1}; δ (250 MHz) 1.40 (3 H, t), 1.76 (3 H, s), 1.81 (3 H, s), 4.37 (2 H, q), 4.56 (2 H, d), 5.54 (1 H, m), 6.83 (2 H, s + d), 7.16 (1 H, d), 7.54 (1 H, d), and 8.78 (1 H, br).

Ethyl 6-geranyloxyindole-2-carboxylate (**23**). The azide (**22**) (554 mg) was refluxed in toluene (20 ml) for 2 h. The toluene was evaporated to leave a yellow solid which was recrystallised from hexane to give the *title compound* (**23**) (323 mg, 63%) as colourless needles, m.p. 110—112 °C (Found: C, 74.1; H, 8.0; N, 4.1. $C_{21}H_{27}NO_3$ requires C, 73.9; H, 8.0; N, 4.1%); $\nu_{max.}$ 3 300 and 1 680 cm^{-1}; δ (250 MHz) 1.40 (3 H, t), 1.61 (3 H, s), 1.66 (3 H, s), 1.76 (3 H, s), 2.10 (4 H, m), 4.38 (2 H, q), 4.57 (2 H, m), 5.10 (1 H, m), 5.54 (1 H, t), 6.84 (2 H, m), 7.16 (1 H, d), 7.54 (1 H, d), and 8.74 (1 H, br); *m/z* 341 (M^+), 296, 205 (base), and 159.

Claisen Rearrangements of Allyloxyindoles.—Ethyl 5-allyl-4-hydroxyindole-2-carboxylate (**3**). The indole (**2**) (49 mg) was refluxed in bromobenzene (15 ml) under nitrogen for 18 h. Evaporation of the solvent left a colourless solid which was recrystallised from chloroform–hexane to give crystals of the *title compound* (**3**) (37.5 mg, 76%); data given later.

Ethyl 4-allyl-5-hydroxyindole-2-carboxylate (**7**). The indole (**5**) (75 mg) was heated in refluxing bromobenzene (15 ml) for 22 h. Evaporation of the solvent and recrystallisation of the residue from chloroform–hexane gave colourless crystals of the title compound (**7**) (69.8 mg, 93%), m.p. 169—172 °C (lit.,[8] m.p. 169 °C).

Ethyl 6-allyl-7-hydroxyindole-2-carboxylate (**8**). The indole (**6**) (44.4 mg) was refluxed in bromobenzene (15 ml) for 19.5 h. The solvent was evaporated to leave a beige solid which was recrystallised from chloroform–hexane to give the *title compound* (**8**) (27.4 mg, 62%) as pinkish needles, m.p. 178—180 °C (Found: C, 68.6; H, 6.2; N, 5.7. $C_{14}H_{15}NO_3$ requires C, 68.6; H, 6.2; N, 5.7%); $\nu_{max.}$ 3 390br, 3 340, and 1 664 cm^{-1}; δ (250 MHz) 1.45 (3 H, t), 3.56 (2 H, br d), 4.45 (2 H, q), 5.20 (2 H, m), 6.06 (1 H, m), 6.33 (1 H, br), 6.91 (1 H, d, *J* 8.7 Hz), 7.21 (1 H, d, *J* 2.5 Hz), 7.22 (1 H, d, *J* 8.7 Hz), and 9.76 (1 H, br).

Ethyl 7-allyl-6-hydroxyindole-2-carboxylate (**11**). The indole (**10**) (97 mg) was heated in refluxing bromobenzene (15 ml) for 24 h. Evaporation of the solvent, and trituration of the solid residue with hexane gave buff crystals of the *title compound* (**11**) (69.3 mg, 71%); data given later.

Ethyl 6-acetoxy-7-(1,1-dimethylallyl)indole-2-carboxylate (**18c**). The indole (**17c**) (197.8 mg) was heated in a refluxing mixture of acetic anhydride (5 ml) and *N,N*-dimethylaniline (5 ml) under nitrogen for 17 h. After being cooled, the reaction mixture was poured into ice–water (50 ml), stirred for 10 min, and then extracted with ether (100 ml). The ether extracts were washed successively with 5% hydrochloric acid (3 × 20 ml), water, saturated sodium hydrogen carbonate solution (3 × 20 ml), dried ($MgSO_4$), and evaporated to a yellow oil. Chromatography gave the *title compound* (**18c**) (203.8 mg, 89%) as a colourless oil, b.p. 160 °C at 0.5 mmHg (Kugelrohr) (Found: C, 68.85; H, 6.8; N, 4.7. $C_{18}H_{21}NO_4$ requires C, 68.55; H, 6.7; N, 4.4%); $\nu_{max.}$ 3 440, 1 760, and 1 705 cm^{-1}; δ (250 MHz) 1.40 (3 H, t), 1.60 (6 H, s), 2.31 (3 H, s), 4.38 (2 H, q), 5.34 (2 H, AB of ABX), 6.44 (1 H, X of ABX), 6.75 (1 H, d), 7.14 (1 H, d), 7.54 (1 H, d), and 9.58 (1 H, br); *m/z* 315 (M^+), 273 (base), 258, 227, 212, and 199.

Ethyl 6-acetoxy-7-linalylindole-2-carboxylate (**24**). The azide (**22**) (527 mg) was refluxed in toluene (25 ml) for 3 h. The solvent was evaporated to give the indole (**23**) as a pale yellow crystalline solid. Without further purification, the indole (**23**) was dissolved in a mixture of acetic anhydride (10 ml) and *N,N*-dimethylaniline (10 ml) and heated under reflux under nitrogen for 19.5 h. Aqueous work-up as described above gave a yellow

oil which was chromatographed to give the *title compound* (**24**) (290 mg, 53% from the azide) as a pale yellow oil, b.p. 170 °C at 0.5 mmHg (Kugelrohr) (Found: C, 72.4; H, 7.75; N, 3.75. $C_{23}H_{29}NO_4$ requires C, 72.0; H, 7.7; N, 3.65%); $\nu_{max.}$ 3 435, 1 760, and 1 710 cm^{-1}; δ (250 MHz) 1.39 (3 H, t), 1.44 (3 H, s), 1.60 (3 H, s), 1.63 (3 H, s), 1.8—2.0 (4 H, m), 2.31 (3 H, s), 4.37 (2 H, q), 5.04 (1 H, m), 5.37 (2 H, AB of ABX), 6.50 (1 H, X of ABX), 6.76 (1 H, d, *J* 8.4 Hz), 7.12 (1 H, d, *J* 1.75 Hz), 7.53 (1 H, d, *J* 8.4 Hz, with additional fine coupling), and 9.59 (1 H, br); *m/z* 383 (M^+), 341, 273, 258, 212 (base), and 205.

Preparation and Attempted Claisen Rearrangement of Ethyl 7-Allyl-6-allyloxyindole-2-carboxylate (**12**).—The hydroxyindole (**11**) (756 mg, 3.09 mmol), anhydrous potassium carbonate (0.89 g), and allyl bromide (0.9 ml) were heated together in refluxing acetone (30 ml) for 23 h. The mixture was filtered and evaporated to a yellow oil, which rapidly crystallised. Recrystallisation from hexane gave pale yellow crystals of *ethyl 7-allyl-6-allyloxyindole-2-carboxylate* (**12**) (660 mg, 75%), m.p. 76—77 °C (Found: C, 71.8; H, 6.6; N, 4.9. $C_{17}H_{19}NO_3$ requires C, 71.6; H, 6.7; N, 4.9%); $\nu_{max.}$ 3 355, 1 688, and 1 628 cm^{-1}; δ (250 MHz) 1.40 (3 H, t), 3.68 (2 H, m), 4.38 (2 H, q), 4.61 (2 H, 2 × t), 5.1—5.4 (4 H, m), 6.05 (2 H, m), 6.89 (1 H, d), 7.16 (1 H, d), 7.50 (1 H, d), and 8.74 (1 H, br).

The above indole (**12**) (97 mg) was refluxed for 69 h in bromobenzene (10 ml). Although the solution had darkened it consisted only of starting material (t.l.c.). Similarly, the indole (**12**) was largely unchanged after being heated for 39 h in refluxing 1,2-dichlorobenzene.

Concomitant Indolisation and Claisen Rearrangement.—Ethyl 5-allyl-4-hydroxyindole-2-carboxylate (**3**). The azide (**1**) (249 mg) was heated in refluxing bromobenzene (15 ml) for 18 h. The solvent was evaporated and the residue triturated with hexane to give the *title compound* (172 mg, 77%), m.p. 140—141 °C (from chloroform–hexane) (Found: C, 68.7; H, 6.2; N, 5.7. $C_{14}H_{15}NO_3$ requires C, 68.6; H, 6.2; N, 5.7%); $\nu_{max.}$ 3 330br and 1 695 cm^{-1}; δ (250 MHz) 1.40 (3 H, t), 3.50 (2 H, d), 4.40 (2 H, q), 5.18 (2 H, m), 5.50 (1 H, br s), 6.06 (1 H, m), 6.94 (1 H, *ca.* d), 7.06 (1 H, d), 7.30 (1 H, d), and 8.88 (1 H, br).

Ethyl 4-allyl-5-hydroxyindole-2-carboxylate (**7**) *and ethyl 6-allyl-7-hydroxyindole-2-carboxylate* (**8**). The azide (**4**) (363 mg) was refluxed in bromobenzene (20 ml) for 20 h. Evaporation of the solvent and chromatography of the residue gave (i) the *6-allyl-7-hydroxy isomer* (**8**) (102 mg, 31%), identical with the previously prepared sample, and (ii) the 4-allyl-5-hydroxy isomer (**7**) (143 mg, 44%).

Ethyl 7-allyl-6-hydroxyindole-2-carboxylate (**11**). The azide (**9**) (256 mg) was heated in refluxing bromobenzene (25 ml) for 21.5 h. Evaporation of the solvent and trituration of the residue with toluene–hexane gave buff crystals of the *title compound* (**11**) (179 mg, 78%), m.p. 150—152 °C (from chloroform–hexane) (Found: C, 68.2; H, 6.1; N, 5.6. $C_{14}H_{15}NO_3$ requires C, 68.6; H, 6.2; N, 5.7%); $\nu_{max.}$ 3 460, 3 280, and 1 682 cm^{-1}; δ (250 MHz) 1.40 (3 H, t), 3.64 (2 H, 2 × t), 4.38 (2 H, q), 5.04 (1 H, br s), 5.20 (2 H, m), 6.05 (1 H, m), 6.73 (2 H, d, *J* 9 Hz), 7.16 (1 H, d), 7.44 (1 H, d, *J* 9 Hz), and 8.74 (1 H, br); *m/z* 245 (M^+), 199, and 171 (base).

Ethyl 6-hydroxy-7-(2-methylallyl)indole-2-carboxylate (**18a**). The azide (**16a**) (550 mg) was refluxed in bromobenzene (25 ml) for 18 h. Evaporation of the solvent left a brown oil which crystallised on trituration with hexane. Recrystallisation from dichloromethane–hexane gave the *title compound* (**18a**) (324 mg, 65%) as pinkish needles, m.p. 111—112 °C (Found: C, 69.6; H, 6.6; N, 5.4. $C_{15}H_{17}NO_3$ requires C, 69.5; H, 6.6; N, 5.4%); $\nu_{max.}$ 3 360br and 1 678 cm^{-1}; δ (250 MHz) 1.40 (3 H, t), 1.78 (3 H, s), 3.60 (2 H, s), 4.38 (2 H, q), 4.92 (2 H, br d), 5.07 (1 H, s exch. D_2O), 6.74 (1 H, d, *J* 8.75 Hz), 7.14 (1 H, d, *J* 2.5 Hz), 7.44 (1 H, d, *J* 8.75 Hz), and 8.74 (1 H, br).

Ethyl 6-hydroxy-7-(3-methylbut-2-enyl)indole-2-carboxylate (**18b**). The azide (**16b**) (430 mg) was refluxed in bromobenzene (20 ml) for 16 h. Evaporation of the solvent left an oily solid which was purified by chromatography and recrystallisation to give the *title compound* (**18b**) (237 mg, 61%), m.p. 132—133.5 °C (from ethyl acetate–hexane) (Found: C, 70.2; H, 7.0; N, 5.1. $C_{16}H_{19}NO_3$ requires C, 70.3; H, 7.0; N, 5.1%); $\nu_{max.}$ 3 470, 3 280, and 1 676 cm^{-1}; δ (250 MHz) 1.40 (3 H, t), 1.79 (3 H, d), 1.88 (3 H, s), 3.56 (2 H, d), 4.39 (2 H, q), 5.24 (1 H, s, exch. D_2O), 5.35 (1 H, m), 6.72 (1 H, d), 7.15 (1 H, d), 7.40 (1 H, d), and 8.74 (1 H, br).

Heating the azide (**16b**) (590 mg) in refluxing toluene (25 ml) for 3 h gave the indole (**18b**) (293 mg, 55%).

Ethyl 1,7-dihydro-7,7-dimethylpyrano[2,3-g]indole-2-carboxylate (**20**). The azide (**19**) (166 mg) was refluxed in toluene (20 ml) for 3 h. The solvent was evaporated to leave a pale yellow solid which was recrystallised from dichloromethane–hexane to give the *title compound* (**20**) (141 mg, 94%), m.p. 175—176.5 °C (Found: C, 71.0; H, 6.4; N, 5.2. $C_{16}H_{17}NO_3$ requires C, 70.8; H, 6.3; N, 5.2%); $\nu_{max.}$ 3 340, 1 685, and 1 646 cm^{-1}; δ (250 MHz) 1.40 (3 H, t), 1.44 (6 H, s), 4.41 (2 H, q), 5.63 (1 H, d), 6.71 (2 H, m), 7.16 (1 H, d), 7.42 (1 H, d), and 9.26 (1 H, br).

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Received 2nd *November* 1983; *Paper* 3/1947