Vinyl Azides in Heterocyclic Synthesis. Part 6.[1] Synthesis of Isoquinolines by Intramolecular Aza-Wittig Reaction[2]

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Azidocinnamates containing *ortho*-carbonyl substituents are versatile intermediates for heterocyclic synthesis. Isoquinolines (**8**) and (**9**) are formed under mild neutral conditions by intramolecular aza-Wittig reactions of iminophosphoranes, readily derived from azides (**1**) and (**2**), respectively, with triethyl phosphite. The azafluoranthene (**10**) can also be prepared from the azide (**3**) *via* the isolable iminophosphoranes (**11**) and (**12**). Thermolysis of the azides (**1**) in toluene or xylene gives the 4-substituted indoles (**13**) in varying yield (Table 2). Similarly the indoles (**14**) and (**19**) are formed from the azides (**3**) and (**6a** and **b**) respectively.

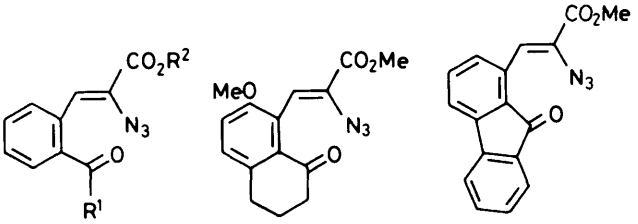
Compounds containing the isoquinoline nucleus are widely distributed in Nature—more than 1 000 isoquinoline alkaloids have now been identified[3]—and since the isolation of isoquinoline itself in 1885 enormous effort has been devoted to the synthesis of this bicyclic aromatic system.[4,5] However, the most widely used methods of isoquinoline synthesis, such as the classic Bischler-Napieralski, Pictet-Spengler, and Pomeranz-Fritsch reactions, require relatively harsh acid or dehydrating conditions to effect ring closure, and since they usually involve electrophilic attack on a benzene ring, the reaction is greatly facilitated by the presence of electron-donating substituents. Indeed, in the absence of such substituents, ring closure often fails completely or proceeds in low yield under forcing conditions.[6] Surprisingly few attempts to solve the 'activation' problem in isoquinoline synthesis have been reported, although recently the methylthio group has been proposed as an easily removable activating group which allowed the preparation of isoquinolines lacking substituents in the carbocylic ring.[6]

An alternative approach is to use a ring closure method which does not involve electrophilic attack on a benzene ring, and one such method, developed independently by Woodward[7] and by Miller,[8] involves ozonolysis of an indene to give a homophthalaldehyde derivative which on treatment with aqueous ammonia gives the fully aromatic isoquinoline directly. Although this simple but elegant approach can be used to prepare isoquinolines containing electron-withdrawing substituents, its generality is somewhat limited by the availability of the starting indenes. We now report the full details of a new isoquinoline synthesis based on the intramolecular aza-Wittig reaction, which enables ring closure to occur under mild, neutral conditions. Although a few examples of this reaction are known,[9] it has not been applied to the synthesis of isoquinolines before.[2]

Results and Discussion

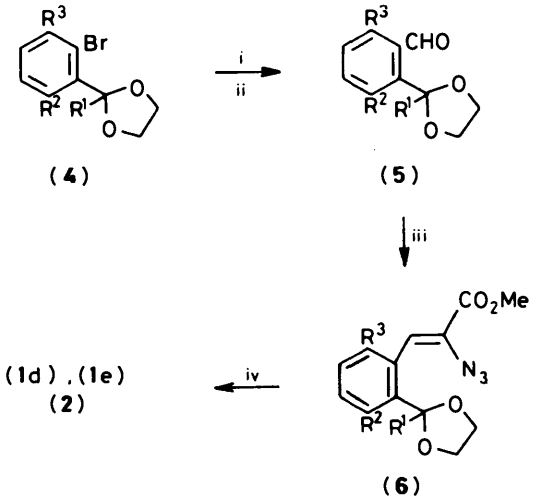
The substrates for the intramolecular aza-Wittig reaction were the azidocinnamates (**1a**—**e**), (**2**), and (**3**) containing *ortho*-carbonyl substituents. Provided that the group R^1 contained no α-C–H bonds, the azides could be prepared directly by condensation of the appropriate benzaldehyde with methyl or ethyl azidoacetate under basic conditions. Thus the azides (**1a**) and (**1b**) were obtained from 2-formylbenzophenone[10] and commercially available 2-formylbenzoic acid respectively, and the azide (**3**) was prepared from 9-oxofluorene-1-carbaldehyde.[11] Esterification of the acid (**1b**) with ethanol containing hydrogen chloride gave the ester (**1c**).

Attempted condensation of 2-acetylbenzaldehyde with ethyl azidoacetate, however, gave none of the required azidocinnamate. Instead the aldehyde underwent self-condensation in the basic medium, and therefore an alternative route which incorporated a carbonyl protecting group was developed (Scheme 1). Thus 2-bromoacetophenone and 2-bromobenzaldehyde were converted into the corresponding dioxolanes (**4a**) and (**4b**), which underwent rapid metal-halogen exchange on treatment with butyl-lithium in tetrahydrofuran (THF) at −78 °C. Quenching of the lithio species with dimethyl-



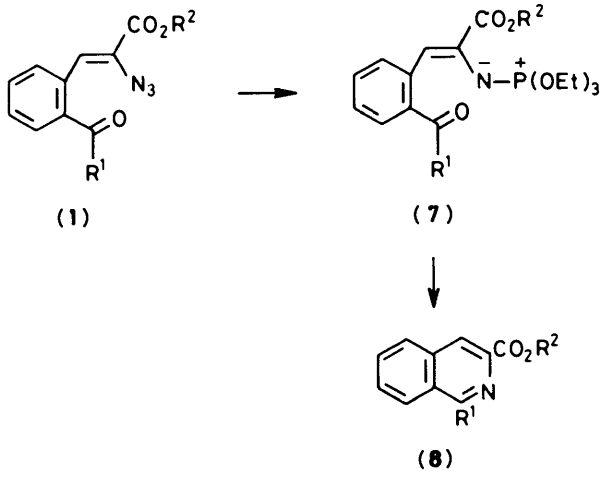
(1) (2) (3)

a; R^1 = Ph, R^2 = Et
b; R^1 = OH, R^2 = Et
c; R^1 = OEt, R^2 = Et
d; R^1 = H, R^2 = Me
e; R^1 = R^2 = Me



(4) (5) (6)

Scheme 1. [For (**4**)—(**6**): **a**, R^1 = R^2 = R^3 = H; **b**, R^1 = Me, R^2 = R^3 = H; **c**, R^1R^2 = $(CH_2)_3$, R^3 = OMe]. *Reagents:* i, BuLi, THF −78 °C; ii, DMF then aq. work-up; iii, $MeO_2CCH_2N_3$, NaOMe, MeOH; iv, dil. HCl, THF



(1) (7) (8)

Table 1. Reaction of azidocinnamates (**1**) with triethyl phosphite to give the isoquinolines (**8**)

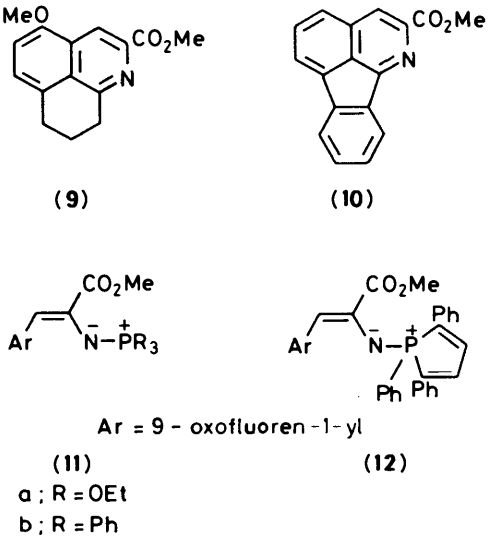
(1), (7), (8)	R^1	R^2	Yield of (8) (%)
a	Ph	Et	94
b	OH	Et	74[a]
c	OEt	Et	90
d	H	Me	91
e	Me	Me	93

[a] Exists as the isoquinolone.

formamide (DMF) gave, on aqueous work-up, the benzaldehydes (**5a**) and (**5b**), which were condensed with methyl azidoacetate to give the azides (**6a**) and (**6b**). The azide (**6c**) was prepared by a similar sequence from 8-bromo-7-methoxy-1,2,3,4-tetrahydronaphthalen-1-one.[12] The azides (**6**) could be deprotected by treatment with acidic aqueous THF at room temperature to give the required azidocinnamates (**1d**), (**1e**), and (**2**). Interestingly, attempted acid catalysed exchanged dioxolanation[13] (acetone/TsOH/room temperature) on the protected aldehyde (**6a**) gave only a poor yield of the azide (**1d**), the major product being the isoquinolone (**18**). The formation of the isoquinolone (**18**) was unexpected, and a subsequent experiment showed that it was not a primary product but was derived from the azidocinnamate (**1d**), since treatment of (**1d**) under the same acidic conditions resulted in its almost quantitative conversion into the isoquinolone (**18**). The mechanism of isoquinolone formation is discussed later.

Treatment of the azidocinnamate (**1a**) with triethyl phosphite (TEP) in cyclohexane gave ethyl 1-phenylisoquinoline-3-carboxylate (**8a**) (94%) as the sole product. The aldehyde (**1d**) and the ketone (**1e**) behaved similarly on reaction with TEP, and gave the corresponding isoquinolines (**8d**) and (**8e**) in high yield (Table 1). The reaction is assumed to proceed by initial Staudinger reaction[14] to give the iminophosphoranes (**7**), which were not detected, intramolecular attack on the carbonyl group presumably being very rapid. That the intramolecular aza-Wittig reaction is particularly favoured in these systems was further demonstrated by the fact that even less reactive ester and carboxylic acid carbonyl groups both readily participate. Thus the acid (**1b**) and the ester (**1c**) cyclised on treatment with TEP to give isoquinolone (**8b**), and the 1-ethoxyisoquinoline (**1c**) respectively (Table 1).

The scope of the reaction is not limited to simple bicyclic isoquinolines. Thus the azide (**2**) gave the tricyclic isoquinoline (**9**) on treatment with TEP in benzene. In this case an orange intermediate, presumably the iminophosphorane, was detected by t.l.c. but was rapidly converted into (**9**) on work-up. Attempts to extend the reaction to the preparation of the tetracyclic azafluoranthene (**10**) were initially unsuccessful. Reaction of the azide (**3**) with TEP gave the isolable iminophosphorane (**11a**), and with triphenylphosphine gave the analogous ylide (**11b**). Although the ylides (**11**) were recovered after heating in xylene, they were both converted into the desired azafluoranthene (**10**) on melt pyrolysis (300—350 °C) albeit in low yield (10 and 19% respectively). The yield of (**10**) was improved by the use of 1,2,5-triphenylphosphole in place of TEP or triphenylphosphine. Thus, the iminophosphole (**12**), prepared from the azide (**3**) and 1,2,5-triphenylphosphole, gave the azafluoranthene (**10**) (34%) on melt pyrolysis (300 °C, 2 min). Such iminophospholes from 1,2,5-triphenylphosphole are known to decompose faster than the corresponding iminophosphoranes derived from triphenylphosphine.[15] Clearly intramolecular attack on the carbonyl by iminophosphoranes derived from the azide (**3**) is disfavoured, presumably by the additional steric constraint imposed by the rigid fluorenone system, and therefore the ring closure to the azafluoranthene (**10**) requires more forcing conditions. In contrast, the electronically similar, but more flexible, benzophenone derivative (**1a**) cyclises readily at 35 °C.



(9) (10)

Ar = 9-oxofluoren-1-yl

(11) (12)

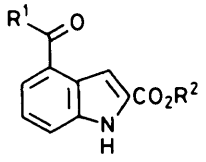
a; R = OEt

b; R = Ph

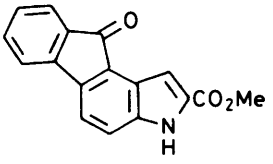
Thus, in the absence of severe steric strain, the intramolecular aza-Wittig reaction of iminophosphoranes derived from azidocinnamates bearing *ortho*-carbonyl substituents constitutes a new isoquinoline synthesis in which the ring-closure step occurs under exceptionally mild neutral conditions. The azidocinnamates can be conveniently prepared from *ortho*-bromo aryl aldehydes and ketones, and although the method necessarily gives isoquinolines bearing an ester at the 3-position, the synthetic versatility of the ester substituent ensures that this is not a serious limitation.

In order to extend the versatility of the 3-aryl-2-azidopropenoates (**1**) in heterocyclic synthesis, a study of their thermal reactions was undertaken, since, in principle, thermolysis of azides of this type should lead to 4-acylindoles, compounds of considerable synthetic importance.[16] In the event, the thermolysis of azidocinnamates containing *ortho*-carbonyl substituents was not straightforward, and 4-substituted indoles were obtained in varying yields. Thus heating the azide (**1a**) in boiling toluene gave ethyl 4-benzoylindole-2-carboxylate (**13a**) in only 10% yield as the only identifiable product. On the other hand, the azide (**1c**) gave diethyl indole-2,4-dicarboxylate (**13c**) in good yield (79%) on heating in toluene, and the azide (**3**) gave the tetracyclic indole (**14**) in 76%

yield. The indole-4-carboxylic acid (**13b**) was only formed in *ca.* 6% yield on heating the azide (**1b**), the major product being the aziridinobenzopyran (**15**). Formation of the latter is rationalised by intramolecular nucleophilic attack by the carboxylate in the intermediate azirine (**16**). The structure of the aziridinobenzopyran (**15**) was confirmed by its conversion into the isocoumarin (**17a**) on treatment with nitrosyl chloride and triethylamine. *N*-Nitrosoaziridines are known to extrude N_2O readily.[17] The structure of (**17a**) was further confirmed by conversion into the known corresponding methyl ester (**17b**) and carboxylic acid (**17c**).

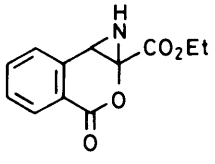


(**13**)

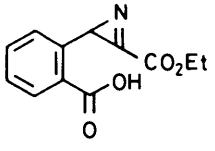


(**14**)

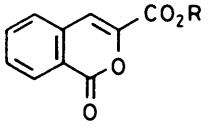
a; R^1 = Ph, R^2 = Et
b; R^1 = OH, R^2 = Et
c; R^1 = OEt, R^2 = Et
d; R^1 = H, R^2 = Me
e; R^1 = R^2 = Me



(**15**)



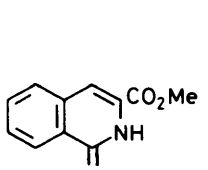
(**16**)



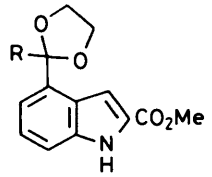
(**17**)

a; R = Et : b; R = Me: c; R = H

Thermolysis of the azidocinnamate (**1d**) gave the expected 4-formylindole-2-carboxylate (**13d**), although the yield was only 28%. The major product (32%) was identified as the isoquinolone (**18**), a compound that had previously been isolated from acid treatment of the azide (**1d**) (q.v.). Although the formation of the isoquinolone (**18**) was unexpected, a similar reaction has been reported by French workers in the thiophene series.[18] Mechanistically, the isoquinolone (**18**) is formally the result of a nitrene insertion into the aldehydic C–H bond, although in the acid-mediated reaction which occurs at room temperature a nitrene intermediate is unlikely to be involved. In the latter case the reaction presumably involves nucleophilic attack by the azide on the protonated aldehyde. Thermolysis of the *o*-acetyl-azidocinnamate (**1e**) gave a complex mixture from which the only isolable product (22%) was the expected 4-acetylindole (**13e**).

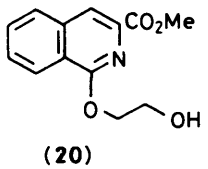


(**18**)

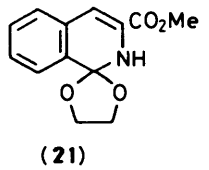


(**19**)

a, R = H ; b, R = Me

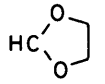
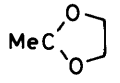


(**20**)



(**21**)

Table 2. Formation of 4-substituted indoles

Azide	X	R	Indole	Yield (%)
(**1a**)	Bz	Et	(**13a**)	10[a]
(**1b**)	CO_2H	Et	(**13b**)	6[a]
(**1c**)	CO_2Et	Et	(**13c**)	79
(**1d**)	CHO	Me	(**13d**)	28
(**1e**)	Ac	Me	(**13e**)	22
(**6a**)		Me	(**19a**)	53
(**6b**)		Me	(**19b**)	100

[a] Not isolated pure or characterised.

Thermolysis of the protected carbonyl azides (**6a**) and (**6b**) was also investigated. As with the thermolysis of the unprotected aldehyde (**1d**), the azide (**6a**) gave two products on heating in xylene. The major product (53%) was the desired 4-substituted indole (**19a**), whilst the minor product was identified as the isoquinoline (**20**), presumably formed *via* the insertion product (**21**). The protected azidoketone (**6b**), which contains no reactive benzylic hydrogen for insertion, gave the 4-substituted indole (**19b**) in quantitative yield. The formation of 4-substituted indoles from the *ortho*-substituted azidocinnamates is summarised in Table 2.

In summary, azidocinnamates containing *ortho*-carbonyl groups are versatile intermediates for heterocyclic synthesis, giving isoquinolines on treatment with tervalent phosphorus reagents and 4-functionalised indoles on thermolysis.

Experimental

For general points see ref. 19.

Preparation of Azidocinnamates.—Benzaldehydes were condensed with methyl or ethyl azidoacetate according to the general method previously described.[19] The following azides were prepared:

Ethyl 2-azido-3-(o-benzoylphenyl)propenoate (**1a**). This formed a yellow oil (35%), $\nu_{max.}$(neat) 2 120, 1 710, and 1 690 cm^{-1}; δ (90 MHz; $CDCl_3$) 1.20 (3 H, t), 4.15 (2 H, q), 7.00 (1 H, s), and 7.20—8.20 (9 H, m); *m/z* 293 (M^+ − 28), 254, 209 (base), and 194.

Ethyl 2-azido-3-(o-carboxyphenyl)propenoate (**1b**). This formed colourless needles (59%), m.p. 118—120 °C, $\nu_{max.}$($CHCl_3$) 3 450—2 450br, 2 125, 1 710, and 1 620 cm^{-1}; δ (90 MHz; $CDCl_3$), 1.40 (3 H, t), 4.43 (2 H, q), 7.30—8.25 (5 H, m),

and 11.91 (1 H, br); *m/z* 233 (M^+ − 28), 217, 189, 160, 143, 134, and 132 (base).

Methyl 2-azido-3-(9-oxofluoren-1-yl)propenoate (**3**). This formed bright yellow *needles* (50%), m.p. 125 °C (decomp.) (Found: C, 66.7; H, 3.6; N, 13.5. $C_{17}H_{11}N_3O_3$ requires C, 66.9; H, 3.6; N, 13.8%); $\nu_{max.}$(Nujol) 2 140, 2 120, 1 710, and 1 610 cm^{-1}; δ (250 MHz; $CDCl_3$) 3.98 (3 H, s), 7.27—7.34 (1 H, m), 7.44—7.54 (4 H, m), 7.63 (1 H, m), 8.17 (1 H, m), and 8.21 (1 H, s); *m/z* 305 (M^+), 291, 277, and 245 (base).

Ethyl 2-azido-3-(o-ethoxycarbonylphenyl)propenoate (**1c**). A solution of the azide (**1b**) (1.2 g) in ethanol (50 ml) was cooled to 0 °C and saturated with hydrogen chloride gas. The mixture was left at room temperature for 50 h, neutralised with solid sodium hydrogen carbonate, filtered, and the filtrate evaporated. The residue was dissolved in ether (50 ml), and the solution washed with saturated aqueous sodium carbonate, dried, evaporated, and the residue chromatographed to give the title compound (**1c**) (0.93 g, 70%) as a colourless oil, $\nu_{max.}$(neat) 2 125, 1 715, and 1 685 cm^{-1}; δ (90 MHz; $CDCl_3$) 1.56 (6 H, t), 4.48 (4 H, 2 × q), 7.26—7.65 (2 H, m), 7.68 (1 H, s), and 7.85—8.05 (2 H, m); *m/z* 279 (M^+).

o-(1,3-*Dioxolan-2-yl*)*benzaldehyde* (**5a**). Butyl-lithium (1.6M; 2.05 ml, 3.28 mmol) was added to a solution of the bromide (**4a**)[20] (500 mg, 2.18 mmol) in dry THF (10 ml) at −100 °C under nitrogen. The mixture was stirred for 15 min, and then quenched with dry DMF (480 mg, 6.6 mmol). The mixture was allowed to reach room temperature, poured into dilute hydrochloric acid, and extracted with ether (3 × 20 ml). The combined ether extracts were dried (K_2CO_3), evaporated, and the residue distilled to give the title compound (**5a**) (0.34 g, 86%), b.p. 95 °C at 0.35 mmHg (lit.,[21] 81 °C at 0.1 mmHg).

Methyl 2-azido-3-[o-(1,3-dioxolan-2-yl)phenyl]propenoate (**6a**). This was prepared (63%) by condensation of the aldehyde (**5a**) with methyl azidoacetate using the general method,[19] m.p. 73—74 °C (Found: C, 56.6; H, 4.8; N, 15.2. $C_{13}H_{13}N_3O_4$ requires C, 56.7; H, 4.7; N, 15.3%); $\nu_{max.}$(neat) 2 140, 1 720, and 1 620 cm^{-1}; δ (250 MHz; $CDCl_3$) 3.91 (3 H, s), 4.02—4.17 (4 H, m), 5.96 (1 H, s), 7.38 (2 H, m), 7.39 (1 H, s), 7.58 (1 H, dd, *J* 8, 2 Hz), and 7.98 (1 H, m); *m/z* 247 (M^+ − 28), 203, 162, 143, 116, 105, 89, 73, 59, and 45.

Methyl 2-azido-3-(o-formylphenyl)propenoate (**1d**). (a) Toluene-*p*-sulphonic acid (10 mg) was added to a solution of the azide (**6a**) (100 mg) in acetone (5 ml), and the solution was stirred at room temperature for 20.5 h. Ether (20 ml) was added, and the mixture was washed with aqueous sodium hydrogen carbonate, dried (K_2CO_3), evaporated, and the residue chromatographed to give (i) the azide (**1d**) (16 mg, 19%), data given below, and (ii) methyl 1-oxo-1,2-dihydroisoquinoline-3-carboxylate (**18**) (24 mg, 33%), m.p. 162—163 °C (lit.,[22] 159—160 °C).

In a separate experiment, a mixture of the azide (**1d**) (100 mg) and toluene-*p*-sulphonic acid (20 mg) in acetone (5 ml) was stirred at room temperature for 2 days to give the isoquinolone (**18**) (87 mg, 99%).

(b) Hydrochloric acid (6M; 6 drops) was added to a solution of the azide (**6a**) (500 mg) in THF–water (1:1; 100 ml), and the mixture stirred at room temperature for 22 h. Work-up as described above gave the *title compound* (**1d**) (316 mg, 75%), m.p. 95—97 °C (Found: C, 56.9; H, 3.9; N, 18.1. $C_{11}H_9N_3O_3$ requires C, 57.1; H, 3.9; N, 18.2%); $\nu_{max.}$(Nujol) 2 140, 1 710, 1 695, and 1 600 cm^{-1}; δ (250 MHz; $CDCl_3$) 3.94 (3 H, s), 7.52—7.63 (2 H, m), 7.71 (1 H, s), 7.87—7.94 (2 H, m), and 10.15 (1 H, s); *m/z* 203 (M^+ − 28) and 118 (base).

o-(2-*Methyl*-1,3-*dioxolan-2-yl*)*benzaldehyde* (**5b**). This was prepared from the bromide (**4b**)[23] using the method described for (**5a**) in 96% yield, b.p. 50 °C at 0.25 mmHg (Kugelrohr) (Found: C, 68.95; H, 6.5. $C_{11}H_{12}O_3$ requires C, 68.75; H, 6.25%); $\nu_{max.}$(neat) 1 690 cm^{-1}; δ (60 MHz; $CDCl_3$) 1.77 (3 H, s), 3.50—4.19 (4 H, m), 7.13—7.98 (4 H, m), and 10.67 (1 H, s); *m/z* 193 (M^+ + 1).

Methyl 2-azido-3-[o-(2-methyl-1,3-dioxolan-2-yl)phenyl]propenoate (**6b**). This was prepared from the aldehyde (**5b**) using the method described above in 36% yield, m.p. 67—68 °C (Found: C, 58.4; H, 5.2; N, 14.4. $C_{14}H_{15}N_3O_4$ requires C, 58.1; H, 5.2; N, 14.5%); $\nu_{max.}$(Nujol) 2 120, 1 715, and 1 610 cm^{-1}; δ (60 MHz; $CDCl_3$) 1.8 (3 H, s), 3.9 (3 H, s), 3.5—4.2 (4 H, m), 7.1—7.6 (4 H, m), and 7.7 (1 H, s); *m/z* 261 (M^+ − 28) and 246 (base).

Methyl 3-(o-Acetylphenyl)-2-azidopropenoate (**1e**). This was prepared by acid hydrolysis of the dioxolane (**6b**) using the method described above in 62% yield, m.p. 111—115 °C (decomp.) (Found: C, 59.0; H, 4.5; N, 17.15. $C_{12}H_{11}N_3O_3$ requires C, 58.8; H, 4.5; N, 17.1%); $\nu_{max.}$(Nujol) 2 110, 1 710, and 1 670 cm^{-1}; δ (60 MHz; $CDCl_3$) 2.6 (3 H, s), 3.9 (3 H, s), 7.35 (1 H, s), and 7.2—7.9 (4 H, m); *m/z* 217 (M^+ − 28), 143, 132 (base), and 103.

8-*Bromo-7-methoxy-3,4-dihydronaphthalen-1*(2H)-*one ethylene acetal* (**4c**). A mixture of the 8-bromo-7-methoxy-1,2,3,4-tetrahydronaphthalen-1-one[12] (2.63 g), ethylene glycol (5 ml), toluene-*p*-sulphonic acid (50 mg), and benzene (40 ml) was heated under reflux for 24 h. After being cooled, the mixture was diluted with ether, washed with aqueous sodium hydroxide (10%; 2 × 40 ml) and water (2 × 30 ml), dried, and evaporated to give the *title compound* (**4c**) as a pale yellow oil which crystallised with time, m.p. 90—91 °C (from cyclohexane) (Found: C, 52.5; H, 5.0. $C_{13}H_{15}BrO_3$ requires C, 52.2; H, 5.0%); $\nu_{max.}$(neat) 1 600, 1 560, 1 475, 1 440, 1 400, 1 340, 1 290, 1 220, and 1 140 cm^{-1}; δ (60 MHz; $CDCl_3$) 1.7—2.1 (4 H, m), 2.7 (2 H, br t, *J* 6 Hz), 3.75 (3 H, s), 4.2 (4 H, m), and 6.85 (2 H, AB, *J* 8.5 Hz); *m/z* 300/298 (M^+).

8-*Formyl-7-methoxy-3,4-dihydronaphthalen-1*(2H)-*one ethylene acetal* (**5c**). Prepared from the bromide (**4c**) using the method described for (**5a**) in 63% yield, b.p. 135 °C at 0.35 mmHg (Kugelrohr) (Found: C, 67.9; H, 6.4. $C_{14}H_{16}O_4$ requires C, 67.7; H, 6.45%); $\nu_{max.}$(neat) 1 710 cm^{-1}; δ (60 MHz; $CDCl_3$) 1.70—2.00 (4 H, m), 2.45—2.85 (2 H, m), 3.70 (3 H, s), 4.00 (4 H, s), 6.90 (2 H, AB, *J* 8.5 Hz), and 10.25 (1 H, s); *m/z* 248 (M^+).

Methyl 2-azido-3-[1-(1,3-dioxolan-2-yl)-7-methoxy-1,2,3,4-tetrahydronaphthalen-8-yl]propenoate (**6c**). This was prepared by condensation of the aldehyde (**5c**) with methyl azidoacetate using the general method,[19] as a pale yellow gum (40%), $\nu_{max.}$(neat) 2 130, 1 720, and 1 635 cm^{-1}; δ (60 MHz; $CDCl_3$) 1.7—2.0 (4 H, m), 2.6—2.9 (2 H, m), 3.75 (3 H, s), 3.85 (3 H, s), 4.0 (4 H, s), 6.95 (2 H, AB, *J* 8.5 Hz), and 7.30 (1 H, s); *m/z* 317 (M^+ − 28), 287, 257, 232, 199 (base), 176, 154, and 119.

Methyl 2-azido-3-(7-methoxy-1-oxo-1,2,3,4-tetrahydronaphthalen-8-yl)propenoate (**2**). This was prepared by hydrolysis of the ethylene acetal (**6c**) using the method described above in 73% yield, m.p. 100 °C (decomp.) (Found: C, 60.0; H, 5.0; N, 14.0. $C_{15}H_{15}N_3O_4$ requires C, 59.8; H, 5.0; N, 13.95%); $\nu_{max.}$(Nujol) 2 120, 1 720, 1 710, and 1 630 cm^{-1}; δ (60 MHz; $CDCl_3$) 1.9—2.4 (2 H, m), 2.5—3.1 (4 H, m), 3.80 (3 H, s), 3.85 (3 H, s), 7.1 (2 H, AB, *J* 8.5 Hz), and 7.35 (1 H, s); *m/z* 188 (M^+ − 113, base).

Reactions of Azidocinnamates with Phosphorus(III) *Reagents: Intramolecular Aza-Wittig Reactions.*—(i) A solution of TEP (53 mg, 0.32 mmol) in cyclohexane (1 ml) was added to a stirred solution of the azidocinnamate (**1a**) (103 mg, 0.32 mmol) in cyclohexane (2 ml) at room temperature. A gas was evolved immediately. After 30 min, more TEP (106 mg, 0.64 mmol) was added and the mixture was heated at 35 °C until t.l.c. indicated that all the azide (**1a**) had been consumed (1.3 h). The solvent was evaporated, and light petroleum was added to the residue whereupon ethyl 1-phenylisoquinoline-3-carboxylate (**8a**) crystallised in two crops (59 mg + 28 mg, 94%), m.p. 100—101 °C (lit.,[19] 100—101 °C).

(ii) A solution of the azidocinnamate (**1b**) (49 mg, 0.19 mmol) and TEP (34 mg, 0.21 mmol) in THF (2.5 ml) was stirred at room temperature for 16 h. Evaporation of the solvent and chromatography of the residue gave ethyl 1-oxo-1,2-dihydroisoquinoline-3-carboxylate (**8b**) (31 mg, 74%), m.p. 146.5—148.5 °C (lit.,[24] 147—148 °C).

(iii) A solution of the azidocinnamate (**1c**) (253 mg, 0.875 mmol) and TEP (290 mg, 1.75 mmol) in benzene (20 ml) was heated at 50—60 °C for 30 min. Evaporation of the solvent and crystallisation of the residue from chloroform–light petroleum gave *ethyl 1-ethoxyisoquinoline-3-carboxylate* (**8c**) (192 mg, 90%) as colourless needles, m.p. 93—94 °C (Found: C, 68.4; H, 6.15; N, 5.7. $C_{14}H_{15}NO_3$ requires C, 68.6; H, 6.2; N, 5.7%); $\nu_{max.}$(CCl_4) 1 735, 1 715, 1 617, and 1 570 cm^{-1}; δ (90 MHz; CCl_4) 1.43 (3 H, t), 1.53 (3 H, t), 4.42 (2 H, q), 4.72 (2 H, q), 7.55—7.95 (3 H, m), 8.04 (1 H, s), and 8.20—8.37 (1 H, m); *m/z* 245 (M^+), 230, and 217 (base).

(iv) A solution of the azidocinnamate (**1d**) (100 mg, 0.43 mmol) and TEP (79 mg, 0.48 mmol) in benzene (10 ml) was stirred at room temperature for 21 h. The mixture was diluted with ether (50 ml), washed with water, dried, and evaporated to give methyl isoquinoline-3-carboxylate (**8d**) (74 mg, 91%), m.p. 88—89 °C (lit.,[25] 86—88 °C).

(v) A solution of the azidocinnamate (**1e**) (100 mg, 0.41 mmol) and TEP (102 mg, 0.61 mmol) in benzene (7 ml) was stirred at room temperature for 4.5 h. Evaporation of the solvent and purification of the residue by chromatography gave *methyl 1-methylisoquinoline-3-carboxylate* (**8e**) (77 mg, 93%), m.p. 104—105 °C (Found: C, 71.8; H, 5.4; N, 6.95. $C_{12}H_{11}NO_2$ requires C, 71.6; H, 5.5; N, 7.0%); $\nu_{max.}$(Nujol) 1 730 cm^{-1}; δ (90 MHz; $CDCl_3$) 3.05 (3 H, s), 4.08 (3 H, s), 7.65—8.20 (4 H, m), and 8.40 (1 H, s); *m/z* 201 (M^+), 171, 143 (base), and 115.

(vi) A solution of the azidocinnamate (**2**) (100 mg, 0.33 mmol) and TEP (83 mg, 0.5 mmol) in benzene (12 ml) was stirred at room temperature for 16 h. T.l.c. indicated that all the azide had been consumed to give two products, one of which exhibited the characteristic blue fluorescence of isoquinolines when viewed under u.v. light. The solution was heated for 1 h at 75 °C, cooled, diluted with ether (50 ml), and washed with water. Magnesium sulphate was added to the bright yellow organic layer whereupon the colour disappeared immediately. T.l.c. analysis of the colourless solution showed it to contain only one component. Evaporation of the solvent gave *methyl 8,9-dihydro-4-methoxy-7H-benzo*[de]*quinoline-2-carboxylate* (**9**) (80 mg, 93%) as colourless plates, m.p. 122—123 °C (Found: C, 70.1; H, 5.9; N, 5.4. $C_{15}H_{15}NO_3$ requires C, 70.0; H, 5.8; N, 5.45%); $\nu_{max.}$(Nujol) 1 715 and 1 615 cm^{-1}; δ (60 MHz; $CDCl_3$) 1.95—2.30 (2 H, m), 2.8—3.4 (4 H, m), 3.95 (3 H, s), 4.00 (3 H, s), 7.05 (2 H, AB, *J* 8.5 Hz), and 8.7 (1 H, s); *m/z* 257 (M^+), 199 (base), 182, 154, and 127.

(vii) TEP (82 mg, 0.49 mmol) was added to a suspension of the azidocinnamate (**3**) (100 mg, 0.33 mmol) in xylene (10 ml), and the mixture was stirred at room temperature for 18 h, and then at 60 °C for 8 h. The solution was washed with water, dried, and evaporated to give methyl 3-(9-oxofluoren-1-yl)-2-iminotriethoxyphosphoranylpropenoate (**11a**) (147 mg, *ca.* 100%) as an orange gum, δ (60 MHz; $CDCl_3$) 1.3 (9 H, dt, *J* 8, 1 Hz), 3.8 (3 H, s), 4.1 (6 H, m), 6.9—7.7 (6 H, m), 8.0 (1 H, d, *J* 9 Hz), and 8.9 (1 H, dd, *J* 6, 3 Hz). After exposure to air for several days, the iminophosphorane (**11a**) was hydrolysed to the corresponding *phosphoramidate*, m.p. 166—168 °C (Found: C, 60.8; H, 5.4; N, 3.3. $C_{21}H_{22}NO_6P$ requires C, 60.7; H, 5.3; N, 3.4%); $\nu_{max.}$(Nujol) 3 090, 1 720, 1 700, 1 630, 1 610, 1 435, 1 300, 1 280, 1 240, 1 190, 1 130, 1 035, 970, and 750 cm^{-1}; δ (250 MHz; $CDCl_3$) 1.28 (6 H, dt, *J* 7.6, 0.3 Hz), 3.91 (3 H, s), 3.98 (4 H, dq, *J* 7.6, 3.8 Hz), 4.98 (1 H, br, D_2O exch.), 7.31 (1 H, dt, *J* 7.0, 0.3 Hz), 7.45—7.56 (4 H, m), 7.64 (1 H, br d, *J* 7.0 Hz), 7.76 (1 H, m), and 7.89 (1 H, d, *J* 1.7 Hz); *m/z* 415 (M^+) and 220 (base).

(viii) A mixture of azidocinnamate (**3**) (500 mg, 1.64 mmol), triphenylphosphine (473 mg, 1.81 mmol), and xylene (50 ml) was stirred at room temperature for 16 h. The solvent was evaporated and the residue chromatographed to give *methyl 3-(9-oxofluoren-1-yl)-2-triphenylphosphoranylideneaminopropenoate* (**11b**) (871 mg, 99%) as a bright orange solid, m.p. 209—211 °C (Found: C, 77.7; H, 4.8; N, 2.5. $C_{35}H_{26}NO_3P$ requires C, 77.9; H, 4.8; N, 2.6%); $\nu_{max.}$(Nujol) 1 700 cm^{-1}; δ (90 MHz; $CDCl_3$) 3.55 (3 H, s), 7.14—7.89 (21 H, m), 8.03 (1 H, d, *J* 8 Hz), and 9.10 (1 H, dd, *J* 6, 3 Hz); *m/z* 539 (M^+).

(ix) A solution of the azidocinnamate (**3**) (1.00 g, 3.28 mmol) and 1,2,5-triphenylphosphole (1.53 g, 4.90 mmol) in toluene (50 ml) was heated under reflux for 1.5 h. On cooling to room temperature, the product precipitated and was collected by filtration and dried to give *methyl 3-(9-oxofluoren-1-yl)-2-(1,2,5-triphenylphosphol-1-ylideneamino)propenoate* (**12**) (1.37 g, 71%) as a dark red microcrystalline solid, m.p. 249—251 °C (Found: C, 79.3; H, 4.7; N, 2.3. $C_{39}H_{28}NO_3P$ requires C, 79.5; H, 4.75; N, 2.4%); $\nu_{max.}$(Nujol) 1 700, 1 690, 1 610, and 1 580 cm^{-1}; δ (90 MHz; $CDCl_3$) 3.69 (3 H, s), 7.05—8.20 (23 H, m), 8.15 (1 H, d, *J* 8 Hz), and 9.20 (1 H, dd, *J* 7, 3 Hz); *m/z* 589 (M^+).

(x) The iminophosphorane (**11a**) (200 mg) was placed in a sublimation apparatus which was then lowered into a Wood's metal bath at 300 °C. After 1 min the heating bath was removed, and the cold finger washed with dichloromethane. The washings were evaporated and the residue chromatographed to give *methyl 1-azafluoranthene-2-carboxylate* (**10**) (12 mg, 10%) as a pale yellow solid, m.p. 115—117 °C (Found: M^+, 261.0797. $C_{17}H_{11}NO_2$ requires *M*, 261.0789); $\nu_{max.}$(Nujol) 1 710 and 1 625 cm^{-1}; δ (90 MHz; $CDCl_3$) 4.15 (3 H, s), 7.30—7.95 (6 H, m), 8.21 (1 H, m), and 8.50 (1 H, s); *m/z* 261 (M^+), 203 (base), 175, 101, and 87.

(xi) The iminophosphorane (**11b**) (50 mg) was pyrolysed under the conditions described above to give the azafluoranthene (**10**) (4.7 mg, 19%).

(xii) The phosphole (**12**) (100 mg) was pyrolysed at 300 °C for 2 min as described above to give the azafluoranthene (**10**) (15 mg, 34%).

Thermolysis of Azidocinnamates.—(i) A solution of the azidocinnamate (**1a**) (253 mg) in toluene (40 ml) was heated under reflux for 2.5 h. The solvent was evaporated and the residue chromatographed to give ethyl 4-benzoylindole-2-carboxylate (**13a**) (24 mg, 10%), δ (90 MHz; $CDCl_3$) 1.35 (3 H, t), 4.40 (2 H, q), 7.00—8.20 (10 H, m), and 9.60 (1 H, br).

(ii) A solution of the azidocinnamate (**1b**) (330 mg) in toluene (50 ml) was heated under reflux for 22 h. The solvent was evaporated and the residue chromatographed to give (i) *ethyl 3-oxo-1a,7b-dihydro-3H-azirino*[2,3-c]*-2-benzopyran-1a-carboxylate* (**15**) (262 mg, 89%), m.p. 100—101 °C (Found: C, 61.8; H, 4.75; N, 6.0. $C_{12}H_{11}NO_4$ requires C, 61.8; H, 4.75; N, 6.0%); $\nu_{max.}$(Nujol) 3 300, 1 733, and 1 717 cm^{-1}; δ (90 MHz; $CDCl_3$) 1.36 (3 H, t), 3.07 (1 H, br d, *J* 10 Hz, D_2O exch.), 3.78 (1 H, d, *J* 10 Hz), 4.44 (2 H, q), 7.40—7.83 (3 H, m), and 8.15 (1 H, m); δ_C ($CDCl_3$) 14.0 (q), 37.2 (d), 63.5 (t), 69.9 (s), 122.1 (s), 128.8 (d), 129.1 (d), 131.2 (d), 134.1 (d), 138.4 (s), 160.8 (s), and 166.7 (s); *m/z* 233 (M^+) 159 and 132 (base), and (ii) a second product (*ca.* 6%) tentatively assigned as 2-ethoxycarbonylindole-4-carboxylic acid (**13b**).

A solution of nitrosyl chloride in carbon tetrachloride (0.417M; 0.44 ml, 0.185 mmol) was added dropwise to a solution of the aziridine (**15**) (43 mg, 0.185 mmol) and triethylamine (19 mg, 0.185 mmol) in THF (5 ml) at −60 °C. The mixture was allowed to reach room temperature after which it was stirred for a further 14 h, diluted with ether, filtered, and the filtrate evaporated, and the residue chromatographed to give *ethyl 1-oxo-1H-2-benzopyran-3-carboxylate* (**17a**) (30 mg, 75%), m.p. 124—125 °C (Found: M^+, 218.0576. $C_{12}H_{10}O_4$ requires *M*,

218.0579); $\nu_{max.}$(CCl_4) 1 754 and 1 727 cm^{-1}; δ (250 MHz; $CDCl_3$) 1.42 (3 H, t), 4.45 (2 H, q), 7.50 (1 H, s), 7.55—7.72 (2 H, m), 7.81 (1 H, m), and 8.37 (1 H, m); *m/z* 218 (M^+) 145 and 89 (base).

A sample of the above ester (**17a**) was dissolved in methanol and a catalytic amount of sodium methoxide added. The mixture was refluxed for 1 h, diluted with ether, washed with water, and evaporated to give the corresponding methyl ester (**17b**), m.p. 172—175 °C (lit.,[26] 173—174 °C). Hydrolysis of the ethyl ester (**17a**) gave the corresponding carboxylic acid (**17c**), m.p. 250—252 °C (lit.,[27] 245—246 °C).

(iii) A solution of the azidocinnamate (**1c**) (231 mg) in toluene (30 ml) was heated under reflux for 4 h. The solvent was evaporated, and the residue purified by chromatography to give diethyl indole-2,4-dicarboxylate (**13c**) (165 mg, 79%), m.p. 142—143 °C (lit.,[28] 143.4—144.2 °C); $\nu_{max.}$(Nujol) 3 300, 1 702, and 1 685 cm^{-1}.

(iv) A solution of the azidocinnamate (**1d**) (15 mg) in xylene (10 ml) was heated under reflux for 1 h. The solvent was evaporated and the residue chromatographed to give (i) *methyl 4-formylindole-2-carboxylate* (**13d**) (3.7 mg, 28%), m.p. 187—189 °C (Found: M^+, 203.0591. $C_{11}H_9NO_3$ requires *M*, 203.0582); $\nu_{max.}$(Nujol) 3 180, 1 705, and 1 670 cm^{-1}; δ (90 MHz; $CDCl_3$) 3.99 (3 H, s), 7.38—7.80 (3 H, m), 8.00 (1 H, d, *J* 2.6 Hz), 9.26 (1 H, br), and 10.26 (1 H, s); *m/z* 203 (M^+) and 171 (base), and (ii) the isoquinolone ester (**18**) (4.2 mg, 32%).

(v) A solution of the azidocinnamate (**1e**) (100 mg) in xylene (100 ml) was heated under reflux for 1.5 h. The solvent was evaporated and the residue chromatographed to give *methyl 4-acetylindole-2-carboxylate* (**13e**) (19 mg, 22%), m.p. 178.5—179.5 °C (Found: C, 66.6; H, 5.1; N, 6.4. $C_{12}H_{11}NO_3$ requires C, 66.4; H, 5.1; N, 6.45%); $\nu_{max.}$(Nujol) 3 240, 1 720, and 1 655 cm^{-1}; δ (250 MHz; $CDCl_3$) 2.72 (3 H, s), 3.98 (3 H, s), 7.40 (1 H, m), 7.65 (1 H, d, *J* 8.5 Hz), 7.78 (1 H, d, *J* 8.5 Hz), 8.00 (1 H, d, *J* 2 Hz), and 9.40 (1 H, br); *m/z* 217 (M^+), 202, 185, 170 (base), 142, and 114.

(vi) A solution of the azidocinnamate (**3**) (200 mg) in xylene (175 ml) was heated under reflux for 4 h. After the mixture had cooled to room temperature, the product was filtered off and dried to give *methyl 10-oxoindeno*[2,1-b]*indole-2-carboxylate* (**14**) (138 mg, 76%), m.p. 280—282 °C (Found: C, 73.55; H, 3.9; N, 5.1. $C_{17}H_{11}NO_3$ requires C, 73.65; H, 4.0; N, 5.05%); $\nu_{max.}$(Nujol) 3 320, 1 705, 1 700, and 1 610 cm^{-1}; δ [250 MHz; $(CD_3)_2SO$] 3.90 (3 H, s), 7.18—7.30 (2 H, m), 7.43—7.52 (2 H, m), 7.60—7.64 (2 H, m), 7.65 (1 H, s), and 11.30 (1 H, br); *m/z* 277 (M^+).

(vii) A solution of the azidocinnamate (**6a**) (100 mg) in xylene (100 ml) was heated under reflux for 1.5 h. The solvent was evaporated and the residue chromatographed to give (i) *methyl 4-(1,3-dioxolan-2-yl)indole-2-carboxylate* (**19a**) (47.6 mg, 53%), m.p. 145—146 °C (Found: C, 62.9; H, 5.3; N, 5.6. $C_{13}H_{13}NO_4$ requires C, 63.2; H, 5.3; N, 5.7%); $\nu_{max.}$(Nujol) 3 330 and 1 695 cm^{-1}; δ (250 MHz; $CDCl_3$) 3.94 (3 H, s), 4.15 (4 H, m), 6.15 (1 H, s), 7.23—7.43 (4 H, m), and 9.35 (1 H, br); *m/z* 247 (M^+, base), and (ii) *methyl 1-(2-hydroxyethoxy)isoquinoline-3-carboxylate* (**20**) (39.7 mg, 44%), m.p. 101—102 °C (Found: C, 63.0 H, 5.3; N, 5.7. $C_{13}H_{13}NO_4$ requires C, 63.2; H, 5.3; N, 5.7%); $\nu_{max.}$(Nujol) 3 500, 1 715, and 1 590 cm^{-1}; δ (250 MHz; $CDCl_3$) 4.00 (3 H, s), 4.06 (2 H, br s), 4.77 (2 H, m), 5.57 (1 H, br), 7.64—7.90 (3 H, m), 8.17 (1 H, s), and 8.30 (1 H, m); *m/z* 247 (M^+) and 203 (base).

(viii) A solution of the azidocinnamate (**6b**) (100 mg) in xylene (100 ml) was heated under reflux for 1.5 h. The solvent was evaporated to give *methyl 4-(2-methyl-1,3-dioxolan-2-yl)indole-2-carboxylate* (**19b**) (90 mg, 100%), m.p. 179—180 °C (Found: C, 64.5; H, 5.8; N, 5.3. $C_{14}H_{15}NO_4$ requires C, 64.4; H, 5.75; N, 5.4%); $\nu_{max.}$(Nujol) 3 310 and 1 690 cm^{-1}; δ [60 MHz; $(CD_3)_2SO$] 1.7 (3 H, s), 3.9 (3 H, s), 3.7—4.1 (4 H, m), 7.2 (1 H, d, *J* 2 Hz), 7.3—7.6 (3 H, m), and 10.9 (1 H, br); *m/z* 261 (M^+) 246 (base), 214, 202, 170, 142, 114, and 87.

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