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SOME DIELS–ALDER REACTIONS WITH 4-VINYL ISOQUINOLINE DERIVATIVES

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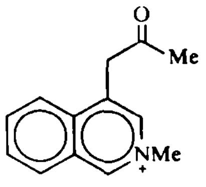
Abstract—The first preparation of 4-vinylisoquinoline derivatives is described. 1,4-Cycloadducts have been obtained by their interaction with the dienophiles maleic anhydride, acrylic acid, *p*-benzoquinone, propriolic acid and benzyne. The structures of the adducts have been assigned on the basis of chemical, but mainly spectroscopic evidence.

VERY few simple vinyl derivatives of isoquinolines have been prepared and studied. 1-Vinyl-3,4-dihydroisoquinoline has been obtained[1] from β-phenylethyl bromide and acrylonitrile, utilising an isoquinoline ring synthesis first reported by Lora–Tamayo *et al*[2] and 1-vinylisoquinoline itself has been prepared[3] by condensing 1-methylisoquinoline with formaldehyde and dimethylamine, followed by distillation over KOH. The formation of 1-styrylisoquinolines by condensation of 1-methylisoquinoline with aromatic aldehydes has been known[4] for some time, and 3-styrylisoquinolines can now[5] be prepared in a similar manner. 4-Styrylisoquinoline derivatives were first described by Abramovitch and Tertzakian[6] who utilised isoquinoline-4-acetic acid as starting material; more recently these compounds have been obtained[7] by applying the Wittig reaction to isoquinoline-4-aldehyde, and also by[8] condensing arylglyoxals with 1,2-dihydroisoquinolines, followed by reduction and dehydration. The last mentioned route is probably the most efficient one, although we[9] have also improved upon the original[6] method. Our interest in 4-substituted isoquinolines prompted us to synthesise 4-vinylisoquinoline derivatives in the belief that they might be useful intermediates in the synthesis of phenanthridines, benzo[*c*]phenanthridines and more complex heterocyclic compounds.

Our first approach was to condense 1,2-dihydroisoquinolines, generated either by reduction of isoquinolinium methosalts with LAH or by acid-catalysed cyclisation of benzylaminoacetals such as 3, with suitable aldehydes. However, 2-methyl-1,2-dihydroisoquinoline failed to react with acrylaldehyde or propargylaldehyde, and the product 1 obtained[10] with pyruvic aldehyde could not be reduced and dehydrated to 2.



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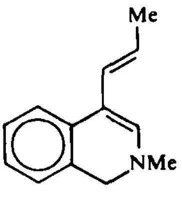

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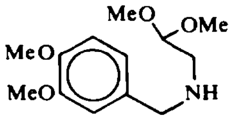

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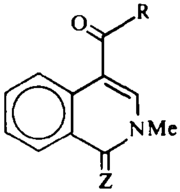
The Vilsmeir reaction,[11] which had been successfully used[12] to prepare indole-3-aldehyde, has now been applied to 2-methyl-1,2-dihydroisoquinoline, and yields of 33% of 4(R = H, Z = H_2) can be obtained. With 2-methyl-6,7-dimethoxy-1,2-dihydroisoquinoline, the yield of the C_4-formyl derivative approaches 50%. As expected for a vinylogous amide, 4(R = H, Z = H_2) does not possess any carbonyl properties, but the derived isocarbostyril 4(R = H, Z = O), obtained from it by oxidation with MnO_2, condenses with 2,4-dinitrophenylhydrazine etc. With methyl magnesium bromide, 4 (R = H, Z = O) yields the expected alcohol 5, which is easily oxidised with MnO_2 to 2-methyl-4-acetylisocarbostyril 4 (R = Me, Z = O). When



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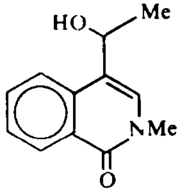

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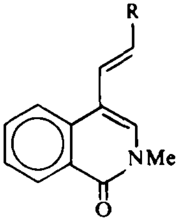

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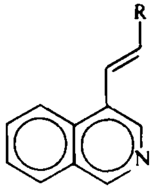

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4 (R = H, Z = O) was treated with methylene triphenylphosphorane only trace amounts of 6 (R = H) could be detected in the complex reaction mixture, but with carbomethoxymethylenetriphenylphosphorane, the diene ester 6 (R = CO_2Me) was formed. The same product was obtained more easily and in better yield by condensing 4 (R = H, Z = O) with malonic acid, followed by esterification. The structure 6 (R = CO_2Me) follows from the compound's mass spectrum and NMR spectrum All attempts to decarboxylate 6 (R = CO_2H) failed.

Isoquinoline-4-aldehyde, which is now[13] readily available, reacts with methylene triphenylphosphorane to give 4-vinylisoquinoline (45%), but although a unique NMR spectrum (Fig 1) was obtained on a freshly prepared sample, both it and the derived methiodide decomposed before elemental analysis could be carried out. The ester 7 (R = CO_2Et) is readily available from isoquinoline-4-aldehyde via the Wittig reaction.

There are very few reports in the literature concerning the use of isoquinoline derivatives as dienes in the Diels–Alder reaction.[14] Maleic anhydride reacts with isoquinoline itself,[15] and moderate yields of the expected adducts have been obtained with 1-styryl-6,7-dimethoxy-3,4-dihydroisoquinoline[16] and with 1-(1'-cyclohexenyl)-6,7-dimethoxy-3,4-dihydroisoquinoline.[17]

When equimolecular amounts of 6 (R = CO_2Me) and maleic anhydride were heated under reflux in acetonitrile solution for 6 hr, a solid mp 245–246° separated slowly in

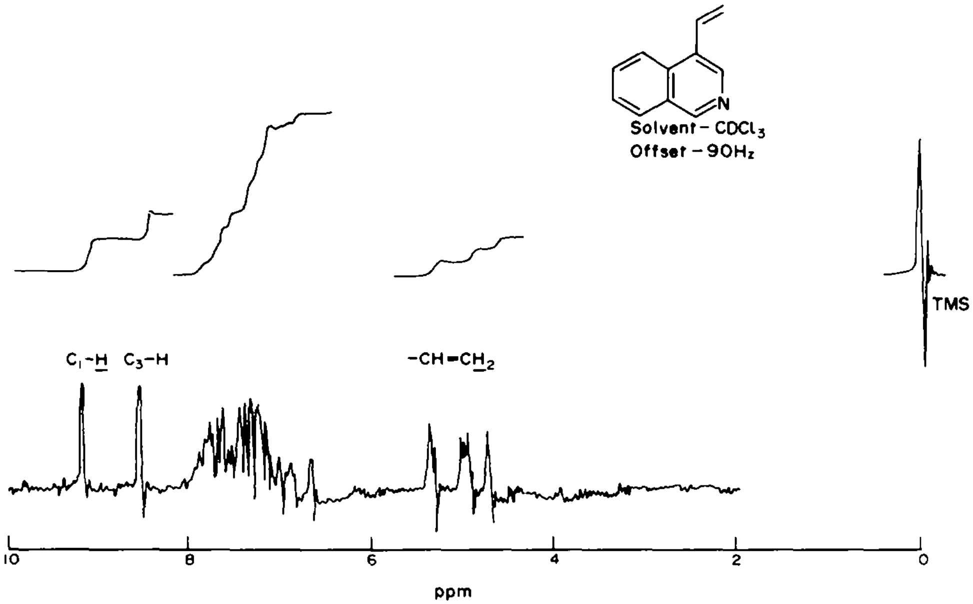
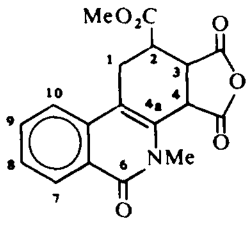


FIG. 1

89% yield. This analysed correctly for the expected product (**8** or **9**; M.W. by mass spectrometry 341·088; $C_{18}H_{15}NO_6$ requires: 341·089). The UV spectrum of the adduct is similar to that of a styrene, but different from that expected for an isocarbostyril.



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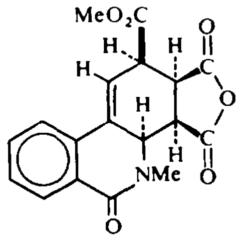

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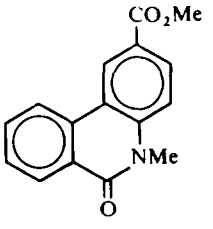

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The NMR spectrum at 60 MHz (in CF_3CO_2H soln) exhibited the required ratio of 2:1 for aliphatic:aromatic protons, thus supporting structure **9** rather than **8**. A complex one proton multiplet at 8·1 δ is assigned to the hydrogen at C_7; the only other recognisable absorptions were three proton singlets at 4·03 δ (OCH_3) and at 3·6 δ (NMe). In the IR spectrum, peaks at 1865 and 1770 cm^{-1} are associated with the absorptions due to a saturated anhydride, and a peak at 1750 cm^{-1} is assigned to the ester CO group. An amide CO band occurs at 1650 cm^{-1}. Conclusive evidence for the structure **9** (though not the stereochemistry indicated) is provided by an interpretation of the mass spectrum of the adduct, where the base peak (*m/e* 243) corresponds to the retro Diels–Alder reaction.[18] In fact the spectrum below *m/e* 243 is very similar to the spectrum of the diene ester **6** (R = CO_2Me) itself. The major fragmentations are interpreted as indicated in Chart I.

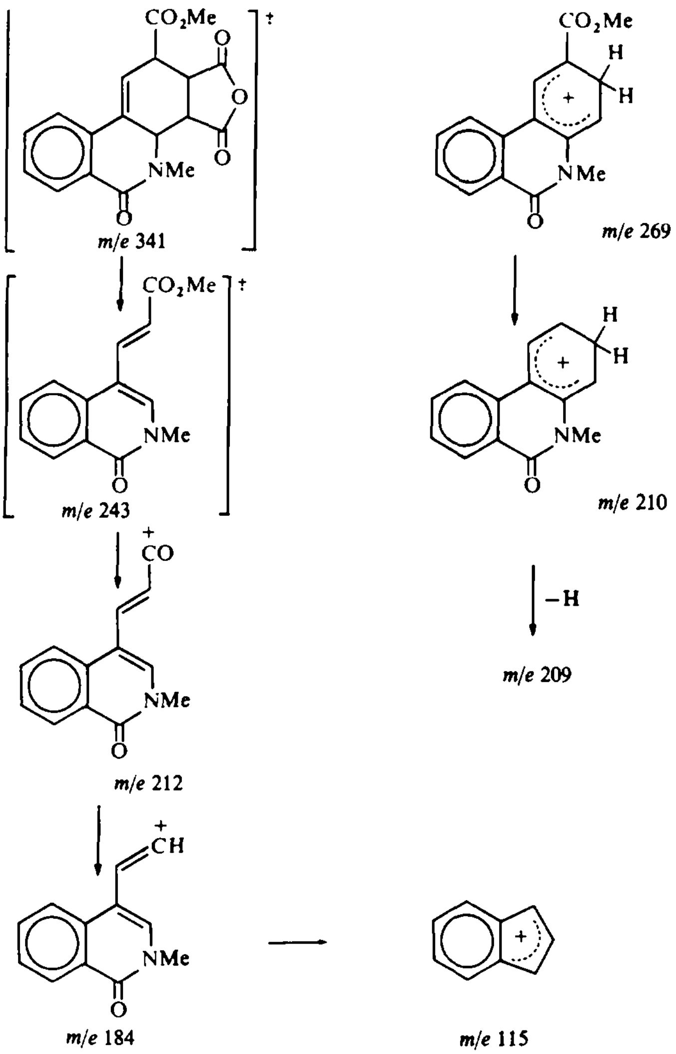


Chart I

From the known *trans*-geometry of the double bond αβ to the ester function in 6(R = CO_2Me), and since the Diels–Alder reaction is a stereospecific *cis* addition leading to the endo adduct, the geometry implied in **9** is preferred for our product. This conclusion is strongly supported by a study of the NMR spectrum at 100 MHz (Fig 2). From the assignments made, and from the decoupling experiments, the following coupling constants have been estimated: $J_{1,2} = 4$–5 Hz; $J_{1,4a} = 3$ Hz; $J_{1,3} = 0$ Hz and $J_{3,4} = 9$ Hz. The value of $J_{1,2}$ suggests[19] that C_2-H is axial, and a value of $J_{1,4a}$ of about 3 Hz indicates an angle between C_{4a}-H and the perpendicular of about 25°, in agreement with that estimated from the Drieding model of **9**. The value for $J_{3,4}$ is in keeping with the dihedral angle of 20° observed on this model.

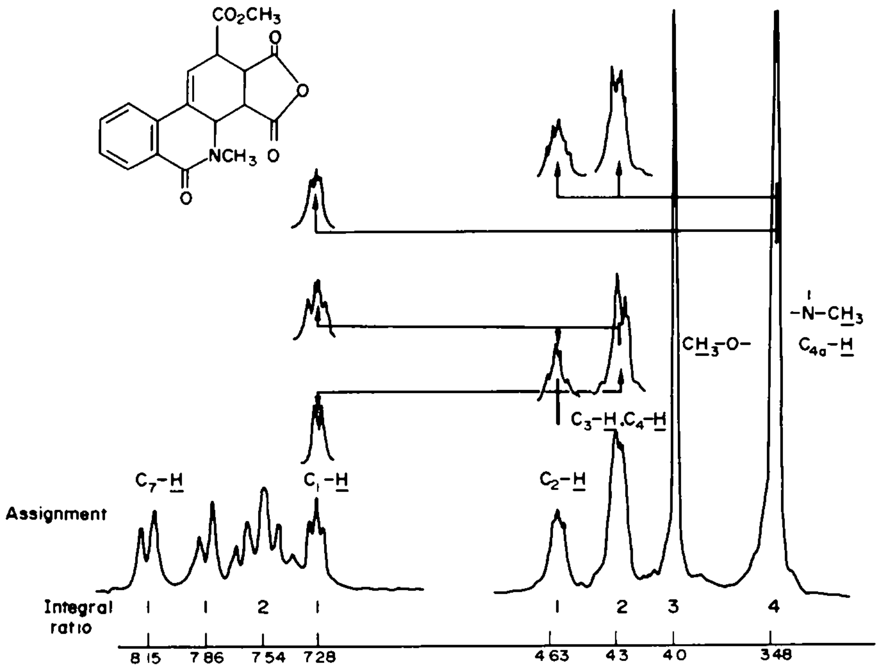
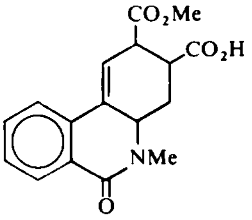


FIG. 2

Since the C_{4a}-H signal is masked by the $>NCH_3$ absorption, it is not possible to deduce the value of $J_{4,4a}$. However, simultaneous irradiation of C_1-H and C_{4a}-H leaves C_2-H as a poorly resolved quartet, and since this signal has a width of only 18–19 Hz, $J_{2,3}$ cannot be more than about 8–10 Hz, which corresponds to a dihedral angle between C_2-H and C_3-H of about 40°. The exo-adduct would have $J_{2,3}$ greater than 10 Hz, with a dihedral angle of about 180°.

The insolubility of the adduct **9** in the more common solvents frustrated most of the attempts to establish the structure by chemical methods. It has been reported[20] that alkaline potassium ferricyanide causes oxidative decarboxylation of dicarboxylic acids very similar in structure to our adduct, and when a solution of **9** in K_2CO_3aq was allowed to remain in contact with an excess of potassium ferricyanide for several days at room temperature, a 5% yield of the known[21] phenanthridone **10** was recovered.

With the successful addition of maleic anhydride to the diene ester **6** (R = CO_2Me), the reactions with other dienophiles were studied. With acrylic acid, an adduct was isolated in 85% yield, and of the two possible structures **11** and **12**, the expected isomer **11** is preferred from a study of the mass spectral fragmentation pattern (Chart II). As before, the base peak at *m/e* 243 is due to the retro Diels–Alder reaction leading to **6** (R = CO_2Me). However, a peak is observed at *m/e* 283 (M − 32) which is best interpreted as anhydride formation—a simple process for **11** but not for **12**. The ensuing fragmentations are then best explained on this basis. When the diene acid **6** (R = CO_2H) was condensed with acrylic acid, the resulting adduct was easily



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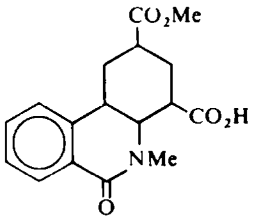

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transformed into an anhydride by reaction with acetic anhydride. Analogous adducts to **11** were formed when **6** (R = CO_2Me) was reacted with ethyl acrylate, acrolein and crotonic acid, although the purification problems were more severe. Curiously, acrylonitrile failed to react with **6** (R = CO_2Me).

When the diene ester **6** (R = CO_2Me) was reacted with an excess of *p*-benzoquinone, in boiling glacial acetic acid, a 60% yield of an adduct was isolated. The mass spectrum

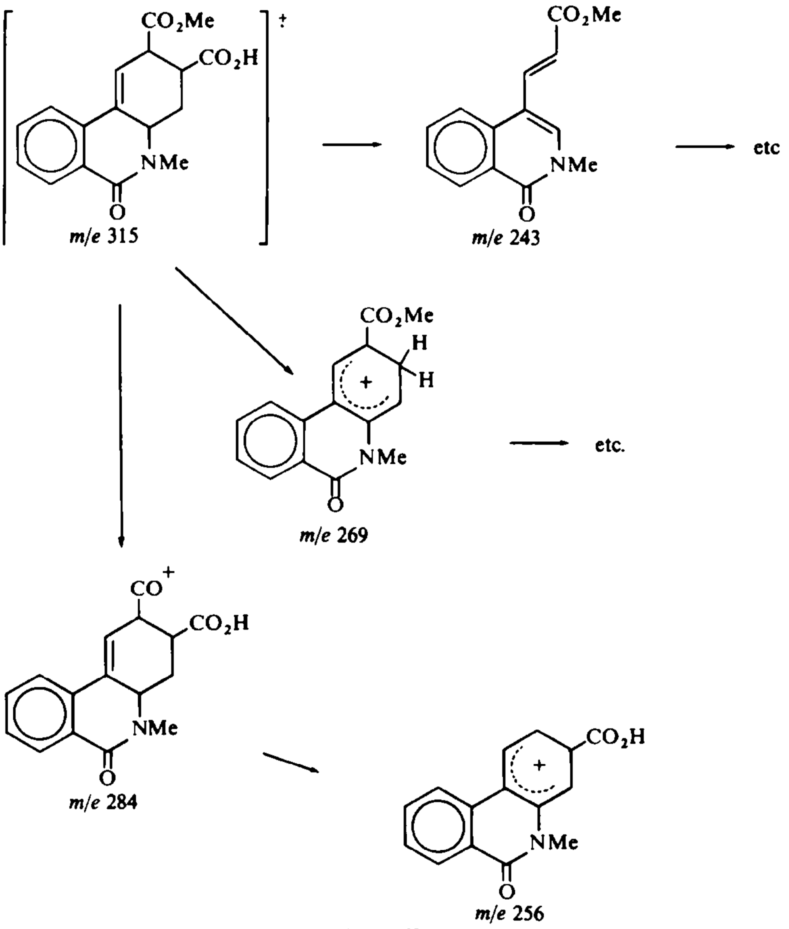
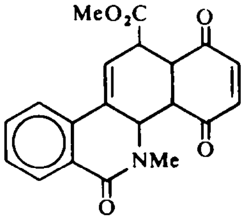
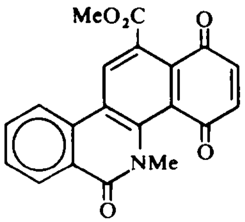


CHART II





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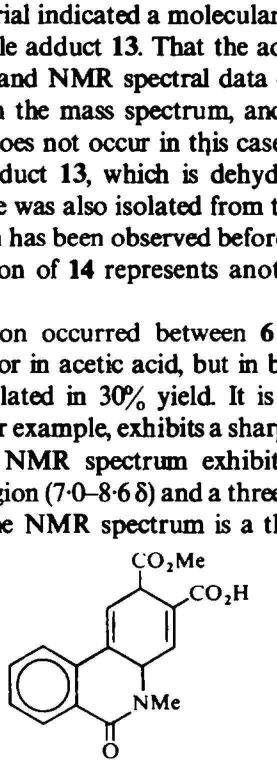
of this material indicated a molecular weight of 347, four units less than that required for the simple adduct 13. That the adduct is 14 was concluded from an examination of the mass and NMR spectral data of the compound. The molecular ion is also the base peak in the mass spectrum, and significantly a retro Diels–Alder type of fragmentation does not occur in this case. The product 14 almost certainly arises via the expected adduct 13, which is dehydrogenated by excess of *p*-benzoquinone (some quinhydrone was also isolated from the reaction mixture). This type of dehydrogenation reaction has been observed before[14] in diene reactions involving *p*-benzoquinone. The formation of 14 represents another[9a] synthesis of the benzo[*c*]phenanthridine ring system.

No reaction occurred between 6 (R = CO_2Me) and propriolic acid in boiling acetonitrile or in acetic acid, but in boiling xylene a product, $C_{17}H_{15}NO_5$ is formed and was isolated in 30% yield. It is not, however, the expected adduct 15; the IR spectrum, for example, exhibits a sharp band at 3100 cm^{-1}, suggestive of a —CONH— group. The NMR spectrum exhibits absorptions due to SEVEN protons in the aromatic region (7·0–8·6 δ) and a three proton singlet at 3·9 δ (CO_2Me). The significant feature of the NMR spectrum is a three proton doublet (J = 7 Hz) at 2·6 δ, which



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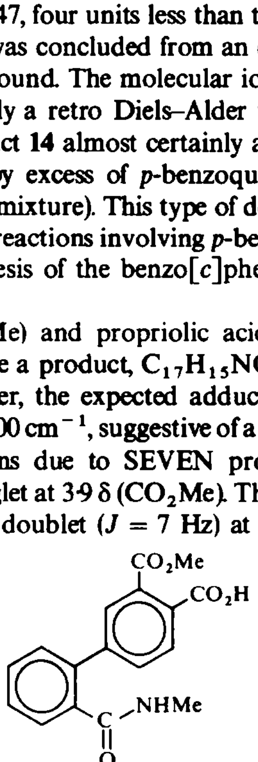

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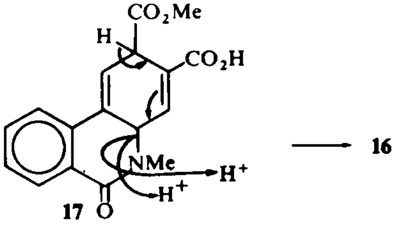
collapses to a singlet on deuteration. The structure 16 is proposed for this compound, and this is supported by the mass spectral data, where again no retro Diels–Alder fragmentation is observed. The formation of 16 is best rationalised by assuming that 15 is first formed, and that aromatisation occurs as indicated in 17. Similar aromatisations have been observed[22] from Diels–Alder adducts involving enamines or dienamines.



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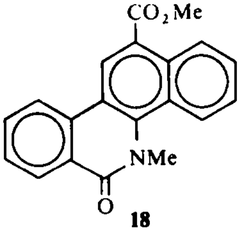
An interest in aryne chemistry in this laboratory[23] prompted us to examine the reaction between diazotised anthranilic acid and the diene ester **6** (R = CO_2Me). After column chromatography over alumina, two crystalline solids were isolated in yields of 1·2% and 0·1%. These compounds were shown, by the usual spectroscopic methods, to be the benzo[*c*]phenanthridine **18** and the secondary amide **19**,



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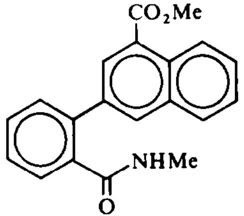
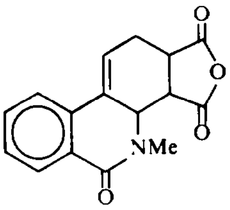


19

respectively, so that this reaction with benzyne shows the characteristics of both the *p*-benzoquinone and the propriolic acid pathways.

Our attempts to dehydrate **5** to **6** (R = H) failed, but when **5** was heated under reflux with maleic anhydride in acetonitrile solution, a 55% yield of the adduct **20**



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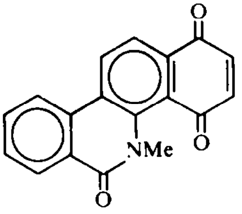

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was obtained. This technique has been used before[24] in Diels–Alder reactions. Repetition of the reaction with *p*-benzoquinone in place of maleic anhydride resulted in the isolation of **21** in 67% yield. Its structure follows from mass and NMR spectral data.

EXPERIMENTAL

M.ps are uncorrected. UV spectra were determined on EtOH solns and IR spectra as nujol mulls. NMR spectra were measured with a Varian A60 spectrometer and chemical shifts are expressed as ppm downfield from TMS as internal standard.

2-Methyl-4-formyl-1,2-dihydroisoquinoline (**4**, R = H, Z = H_2)

2-Methyl-1,2-dihydroisoquinoline (from 20·0 g isoquinoline methiodide) in ether (200 ml) was added at 0° to the complex formed from $POCl_3$ (9·0 ml) and DMF. The resulting slurry was warmed at 50° for 2 hr, with removal of the ether. After cooling, crushed ice (150 g) and water (160 ml) were cautiously added, followed by a soln of NaOH (80 g) in water (160 ml). The yellow oil which slowly solidified, was crystallised from water containing a small amount EtOH to give off-white plates of **4** (R = H, Z = 2H), (14·3 g; 39%) m.p. 130–131°; λ_{max} nm (ε): 274(41,000), 335(35,3000); ν_{max} cm^{-1}: 1610, 1600; NMR ($CDCl_3$): 8·4 s [1] (—C$\underline{H}$O); 8·1 m [1] ($C_8\underline{H}$); 6·6 m [4] (3 adj. aromatic $\underline{H}$ + $C_3\underline{H}$); 4·25 s [2] (ArC$\underline{H}_2$N—); 2·8 s [3] (>NC$\underline{H}_3$. [Found: C, 75·95; H, 6·4; N, 8·1, $C_{11}H_{11}NO$ requires: C, 76·4; H, 6·4, N, 8·1%].

2-*Methyl-4-formyl*-6,7-*dimethoxy*-1,2-*dihydroisoquinoline*

This was obtained in 47% yield from 2-methyl-6,7-dimethoxyisoquinolinium iodide by the above method. The required product had m.p. 134–135° (water); NMR ($CDCl_3$): 9·0 s [1] ($-C\underline{H}O$); 8·39 s [1] ($C_3\underline{H}$); 6·73 s [1] and 6·45 s [1] $C_5\underline{H}$ and $C_8\underline{H}$); 4·51 s [2] ($-C\underline{H}_2$); 3·94 s [3] and 3·72 s [3] (2 × $-OC\underline{H}_3$); 2·94 s [3] ($-\overset{|}{N}C\underline{H}_3$). [Found: C, 66·7; H, 6·3; N, 6·2. $C_{13}H_{15}NO_3$ requires: C, 66·9; H, 6·5; N, 6·0%).

2-*Methylisocarbostyril-4-aldehyde* (4, R = H, Z = O)

A mixture of **4** (R = H, Z = O; 1·0 g), active MnO_2 (5·0 g) and acetone (100 ml) was stirred at room temp for 2 days. Removal of the MnO_2 and acetone, left a pale yellow solid, which was crystallised from water to give 2-methylisocarbostyril-4-aldehyde (0·95 g; 90%) m.p. 151–152°; λ_{max} nm (ε): 221(37,3000); 252(sh), 297 (9,950); ν_{max} cm^{-1}: 2730 (doublet); 1660, 1625, 1610; NMR (CF_3CO_2H): 9·8 s [1] ($-C\underline{H}O$); 9·0 m [1] ($-C_5\underline{H}$); 8·4 m [1] ($C_8\underline{H}$); 8·13 s [1] ($C_3\underline{H}$); 7·8 m [2] ($C_6\underline{H}$ + $C_7\underline{H}$); 3·87 s [3] ($-\overset{|}{N}C\underline{H}_3$). [Found: C. 70·9; H, 4·7; N, 7·4 $C_{11}H_9NO_2$ requires: C, 70·6; H, 4·8; N, 7·5%].

2-*Methyl*-4(α-*hydroxyethyl*)*isocarbostyril* (5)

MeMgI (from 0·5 g Mg and 1·5 ml MeI) in ether (100 ml) was added to a soln of **4** (R = H, Z = O; 1·0 g) in THF (50 ml). After stirring at room temp for 2 hr, the complex was decomposed with NH_4Cl soln. Water was added and the mixture was extracted with benzene. The organic layer was washed, dried ($MgSO_4$) and evaporated to leave a grey solid which was crystallised from petrol (80–100°): acetone (9:1). The product **5** (0·63 g; 60%) had m.p. 150–151°; λ_{max} nm (ε) 211(40,500); 292(10,250); 335(5,275); ν_{max} cm^{-1}: 3270, 1655, 1635, 1605; NMR ($CDCl_3$): 8·3 m [1] ($C_8\underline{H}$); 7·7 m [3] (aromatic protons); 6·9 s [1] ($C_3\underline{H}$); 4·0 s [1] ($O\underline{H}$, removed by D_2O soln); 3·1 s [3] ($-\overset{|}{N}C\underline{H}_3$); 5·15 q [1] ($-\overset{|}{\underline{C}\underline{H}}-CH_3$; J = 6·7Hz); 1·55 d [3] ($\overset{|}{\underline{C}}\underline{H}_3CH-$–; J = 6·7 Hz). [Found: C, 70·2; H, 6·4; N, 6·8 $C_{12}H_{13}NO_2$ requires: C, 70·9; H, 6·45; N, 6·9%].

Simultaneous dehydration and addition reactions of 5

(a) *With maleic anhydride.* A mixture of 2-Methyl-4-(α-hydroxyethyl)-isocarbostyril (0·5 g) and maleic anhydride (0·5 g) was heated under reflux in acetonitrile soln (20 ml) for 17 hr. On cooling and standing, a colourless crystalline solid separated. This was collected and recrystallised from acetonitrile to give **20**; 55% yield m.p. 282–284; λ_{max} (ε) nm 224(42,150): 246(40,100); ν_{max} cm^{-1}: 1840, 1780 ($-CO-O-OC-$), 1650 ($-CON<$), 1610 ($>C=C<$); NMR (CF_3CO_2H). 7·5 m [1] ($C_7\underline{H}$), 7·0 m [3] (aromatic protons), 6·3 m [1] ($C_1-\underline{H}$); 4·1 – 1·0 m [5] (aliphatic protons) 2·9 s [3] ($N-\underline{CH}_3$). [Found: C, 67·5; H, 4·8: N, 4·9 $C_{16}H_{13}NO_4$ requires: C, 67·8; H, 4·6: N, 5·0%]; mass (*m/e* 283 (10%), 185 (100%), 115 (12%).

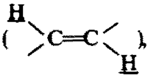
(b) *With* p-*benzoquinone.* A mixture of **5** (0·5 g) and *p*-benzoquinone (0·5 g) was heated in boiling glacial AcOH (20 ml) for 6 hr. On cooling the soln was filtered and evaporated to leave a dark oil. On trituration with ether this crystallised and the dark brown product was then purified by chromatography on silica, eluting with chloroform. Recrystallisation from a large volume of 60–80° petrol gave off-white prisms of **21**, mp > 320°, yield 0·47 g (67%); ν_{max} cm^{-1}, ~1660 ($>CO$), NMR ($CDCl_3$): 9·0–7·2 m [6] (aromatic protons), 7·0 s [2] ($\overset{\underline{H}}{>}C{=}C\overset{H}{<}$), 3·5 s [3] ($>N-C\underline{H}_3$). [Found: C, 74·5; H, 3·6; N, 4·6 $C_{18}H_{11}NO_3$ requires: C, 74·7; H, 3·8; N, 4·8%]; mass (*m/e*) 289 (100%), 272 (25%), 260 (80%), 232 (20%).

β-[4-(2-*Methylisocarbostyryl*)]*acrylic acid* (6, R = CO_2H)

A soln of 2-methylisocarbostyril-4-aldehyde (1·0 g), malonic acid (1·0 g) and piperidine (2 ml) in pyridine (20 ml) was heated under reflux for 3 hr. After cooling, the soln was carefully acidified (2N H_2SO_4) and the resulting ppt collected and washed (0·95 g; 80%). The product **6** (R = CO_2H) was purified by precipitation from Na_2CO_3aq, m.p. 260° (dec); λ_{max} nm (ε): 221 (36,200), 330 (19.725); $\nu_{max}$$cm^{-1}$: 3200–2500 (broad), 1690, 1660, 1610, 975; NMR (CD_3SOCD_3): 8·7–7·3 m [6] (4 aromatic protons + $C_3\underline{H}$ + 1 olefinic proton); 6.36 d [2] J = 16 Hz ($-C\underline{H}{=}C-$), 3·53 s [3] ($-\overset{|}{N}C\underline{H}_3$). [Found: C, 68·2; H, 5·0; N, 6·2. $C_{13}H_{11}NO_3$ requires C, 68·2; H, 4·8; N, 6·1%].

β-Methyl-[4-(2-methylisocarbostyril)]acrylate (6, R = CO_2Me)

The acid 6 (R = CO_2H) was reacted with MeOH and HCl to give 6 (R = CO_2Me) in 95% yield as a crystalline solid, m.p. 75–76° (MeOH-water); NMR ($CDCl_3$) 9·3–7·9 m [5] (C_3—H and aromatic protons, isoquinoline nucleus), 8·0 d [1] J = 16 Hz and 6·3 d [1] J = 16 Hz (



$\overset{H}{\ }\!>C{=}C<\!\underset{H}{\ }$), 3·6 s [3] (—CO_2Me) and 3·35 s [3] ($-\overset{|}{N}CH_3$). [Found: C, 69·0; H, 5·3; N, 5·7 $C_{14}H_{13}NO_3$ requires: C, 69·1: H, 5·4; N, 5·8%]; mass (*m/e*) 243 (100%), 212 (55%), 184 (45%).

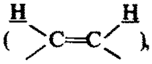
The ethyl ester was similarly prepared, colourless needles m.p. 89–90° (EtOH-water).

Diels–Alder reactions with the diene ester (6, R. = .CO_2Me)

(a) *With maleic anhydride.* The ester (0·5 g) and maleic anhydride (0·5 g) were heated under reflux in acetonitrile soln (20 ml) for 6 hr. On cooling the white solid (9) which separated was removed and recrystallised from acetonitrile, yield 0·58 g (89%), m.p. 245–246°; λ_{max} 250, 335 nm. [Found: C, 63·8; H, 4·4; N, 4·6 $C_{18}H_{15}NO_6$ requires: C, 63·3; H, 4·4; N, 4·1%].

(b) *With acrylic acid.* A repetition of the above reaction using acrylic acid (5 ml) instead of maleic anhydride yielded an oil, after removal of the solvent. Trituration of this oil with ether afforded a colourless solid (11), which was recrystalised from dil AcOH, yield 0·49 g (85%), m.p. 222–224°; ν_{max} cm^{-1}, 3100–2500 (—OH), 1740 (>C=O), 1635 (>C=O). NMR (CD_3SOCD_3): 8·2–7·0 m [4] (aromatic protons), 6·5 m [1] (olefinic proton), 4·65–2·0 m [6] (aliphatic protons), 3·66 s [3] (—OCH_3), 3·0 s [3] ($-\overset{|}{N}CH_3$). [Found: C, 64·9; H, 5·3; N, 4·4 $C_{17}H_{17}NO_5$ requires C, 64·8; H, 5·4; N, 4·4%.]

(c) *With* p-*benzoquinone.* The ester (0·2 g) was heated with *p*-benzoquinone (0·5 g) under reflux in glacial AcOH (50 ml). for 4 hr. After removal of the solvent, the residue was heated at 150°/3 mm to remove impurities. Chromatographic purification on silica, eluting with CH_2Cl_2/EtOH (98 : 2), yielded colourless prisms (14), m.p. 262–263° (0·18 g, 75%) NMR ($CDCl_3$) 9·0–7·5 m [5] (aromatic protons); 7·3 s [2] (



$\overset{H}{\ }\!>C{=}C<\!\overset{H}{\ }$), 3·7 s [3] (—CO_2CH_3), 3·0 s [3] ($-\overset{|}{N}CH_3$), mass (*m/e*) 347 [M$^+$] (100%), 330 (10%), 318 (10%), 289 (19%), 260 (18%). [Found: C, 69·8; H. 3·9; N, 4 3. $C_{20}H_{13}NO_5$ requires: C, 69·2; H, 3·8; N, 4·0%].

(d) *With propriolic acid.* The ester (0·5 g) was heated with propriolic acid (1 g) in xylene (50 ml) at reflux for 18 hr. On cooling a colourless ppt formed. This was removed and recrystallised from xylene to yield prisms (16), m.p. 229–231°, yield 0·32 g, 60%; ν_{max}cm^{-1}, 3400–2500 (—OH), 3100 ($-\overset{|}{N}H$), 1735 (—CO_2Me), 1700 (—CO_2H), 1620 (Ar CONHMe); mass (*m/e* 313 [M$^+$] (60%), 283 (50%), 265 (54%), 251 (100%), 238 (20%), 224 (22%), 207 (25%). M$^+$ = 313·0950 $C_{17}H_{15}NO_5$ requires: 313·095. [Found: C, 64·7; H, 4·8; N, 4·2 $C_{17}H_{15}NO_5$ requires: C, 65·2; H, 4·8; N, 4·5%).

(c) *With benzyne.* Solns of amyl nitrite (10ml) in acetonitrile (100 ml) and anthranilic acid (1·8 g) in acetonitrile (100 ml) were added concurrently to the diene ester (3 g) in acetonitrile (100 ml) at reflux during a 4 hr period. After a further 1 hr, the solvent was removed to give a dark oily product, which was dissolved in ether (50 ml). Acidic impurities were removed by washing with 2N NaOH and the ether was then evaporated to yield an oil (2·1 g). This material was chromatographed upon basic grade alumina (200 g).

Eluting Solvent	benzene (1,950 ml)	fraction A (0·01 g)
Eluting Solvent	25% $CHCl_3$ in benzene (1,520 ml)	fraction B (0·03 g)
Eluting Solvent	45% $CHCl_3$ in benzene (900 ml)	fraction C (1·10 g)
Eluting Solvent	75% $CHCl_3$ in benzene (1,800 ml)	fraction D (0·15 g)
Eluting Solvent	chloroform (1,370 ml)	fraction E (0·02 g)

Fractions A, B, D and E were shown by TLC to be complex mixtures, whereas fraction C contained two main components: this fraction on trituration with acetone afforded colourless prisms of 18, which were recrystallised from acetone (0·5 g), m.p. 184–185°; λ_{max} (ε) nm 225 (21,400), 252 (28,400), 281 (49,900), 320 (12,400), 338 (12,400), 353 (10,100); ν_{max}cm^{-1} 1720 (—CO_2CH_3), 1670 (Ar CON<); NMR ($CDCl_3$): 8·6 s [1] 9(C_1—H), 9·0–8·1 m [8] (aromatic protons), 3·1 s [3] (—CO_2CH_3), 2·8 s [3] ($-\overset{|}{N}CH_3$); mass (*m/e*) 317 [M$^+$] (100%), 316 [M-1$^+$] (70%), 288 [M-31$^+$] (16%), 212 [M-105$^+$] (20%, metastable 209·5). [Found: C, 75·2; H, 4·7; N, 4·4 $C_{20}H_{15}NO_3$ requires: C, 75·7; H, 4·8; N, 4·4%].

Isolation of **19**. Evaporation of the acetone mother-liquor from which **18** separated gave a residue (0·4 g), which was repeatedly chromatographed upon alumina, eluting with chloroform:benzene (1:1). Eventually a small amount (10 mg) of crystalline material was isolated; recrystallisation from chloroform/benzene gave colourless prisms, m.p. 127–129°; λ_{max} nm, 250, 296, 320; ν_{max} cm^{-1}, 3400 (—NHCO Ar), 1710 (—CO_2Me), 1650 (—NHCO Ar). NMR ($CDCl_3$): 8·6–7·1 m [10] (aromatic protons), 5·3 broad doublet [1] (—N**H**CO—, removed by prolonged deuteration); 3·5 s [3] (—CO_2C**H**$_3$), 2·6 d [3] (—NHCOC**H**$_3$) $J = 7$ Hz, collapses to singlet on prolonged deuteration); mass (*m/e*) 319 [M^+] (75%), 251 (100%), 230 (35%), $M^+ = 319·1210$, $C_{20}H_{17}NO_3$ requires: 319·1208.

Potassium ferricyanide degradation of **9**

The maleic anhydride adduct, from experiment (a) above, (0·15 g) was dissolved in a soln of K_2CO_3 (1 g) in water (50 ml) (complete soln requires approximately 30 min) and treated with potassium ferricyanide (2 g) in water (10 ml). After 5 hr at room temp the soln was acidified and stored at 0° for several days. The fine ppt which had then formed was collected and recrystallised from benzene to give 2-methoxy carbonylphenanthridone as needles (10 mg) m.p. 221–222° (lit.[21], 223–224°; ν_{max} cm^{-1}, 1715 (—CO_2Me), 1645 ($\text{ArCO}\overset{|}{\text{N}}$—); NMR ($CDCl_3$) 8·9 d [1] ($C_7$—**H**). 8·6–7·2 m [6] (aromatic protons), 3·9 s [3] (—OC**H**$_3$), 3·78 s [3] (—$\overset{|}{\text{N}}$—C**H**$_3$). [Found: C, 71·6; H, 4·6; N, 5·0 calc. for $C_{16}H_{13}NO_3$; C, 71·9; H, 4·9; N, 5·2%].

4-Vinylisoquinoline (**7**, R = H)

Methyltriphenylphosphonium bromide (2·5 g) suspended in ether (100 ml) was treated with BuLi (1 g) in ether (50 ml), the mixture being protected by an atmosphere of N_2. After stirring for 15 min isoquinoline-4-aldehyde (1g) in ether (50 ml) was introduced, and the suspension stirred at room temp for 20 hr. Solids were then removed and the filtrate was worked up for basic material to yield (0·46 g) (45%) of almost pure **7** (R = H) as a pale red oil; ν_{max} ~900 cm^{-1} ($>C{=}CH_2$).

β-Ethyl-[4-isoquinolyl]acrylate (**7**, R = CO_2Et)

A mixture of isoquinoline-4-aldehyde (0·1 mol) and carboethoxymethylenetriphenylphosphorane (0·1 mol) was heated under reflux with benzene for 4 hr. After cooling, the mixture was extracted with 2N HCl and the combined extracts were basified (Na_2CO_3) and extracted with ether. The ethereal soln was washed with water, saturated $NaHSO_3$aq, water and dried. Evaporation left **7**, (R = CO_2Et) as a red oil, which was characterised as the methiodide m.p. 159–160°, yield 75%; ν_{max} cm^{-1}, 1710 (—CO_2Et), 1640 ($>C{=}\underset{|}{\overset{+}{N}}$—Me), 1610 ($>C{=}C<$); NMR ($CF_3CO_2H$) 9·7 s [1] ($C_1$—**H**), 9·0–8·0 m [6] (aromatic protons, C_3—**H** and one olefinic proton), 6·9 d [1] $J = 16$ Hz (olefinic proton), 4·7 s [3] (—$\underset{|}{\overset{|}{N}}{}^{+}$—C**H**$_3$), 4·5 q [2] $J = 7$ Hz (CO_2C**H**$_2$—CH_3), 1·5 t [3] $J = 7$ Hz (CO_2—CH_2—C**H**$_3$). [Found: C, 48·5; H, 4·5: N, 4·0; I, 34·0 $C_{15}H_{16}NO_2I$ requires: C, 48·7; H, 4·4; N, 3·8; I, 34·3%].

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