Vinyl Azides in Heterocyclic Synthesis. Part 3.[1] Isolation of Azirine Trimers (1,3,8-Triazatricyclo[4.3.0.0^{3,5}]non-7-enes) and Intramolecular Interception of Nitrile Ylides by Neighbouring π-Bonds or Nucleophiles[2]

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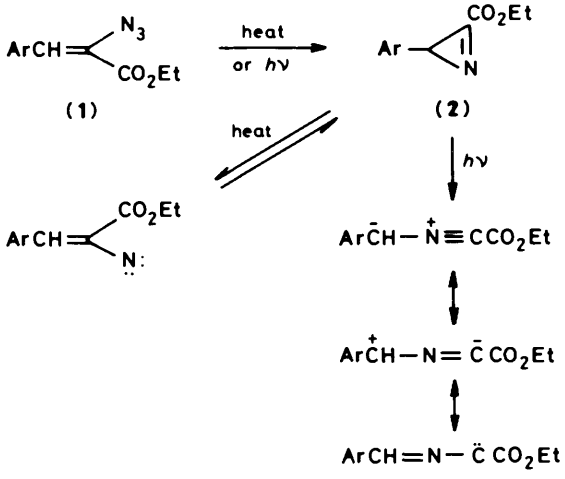
Photolysis of azidocinnamates (**1a**—**e**) at 300 nm in light petroleum gives exclusively the triazatricyclononenes (**7a**—**e**) in a highly stereospecific trimerisation of the corresponding azirine (**2**). A mechanism is proposed involving the sequence: azide (**1**) ⟶ azirine (**2**) ⟶ nitrile ylide (**8**) ⟶ dimer (**9**) ⟶ azomethine ylide (**10**) ⟶ trimer (**7**) (Scheme 2). This mechanism not only rationalises the formation of the trimers (**7**), rather than dimers or oligomers, but also their stereochemistry. Further evidence for it is provided by photolyses of the azidocinnamates (**1f**—**h**) which give the 'dimer' (**13**), the cyclopropaisoquinoline (**16**), and the imidazopyridine (**20**), respectively; these three products result from intramolecular interception of the azomethine ylide or nitrile ylide intermediates.

In previous papers[1,3] we have described the thermal decomposition of a variety of azidocinnamates bearing *ortho*-alkyl and alkenyl substituents. In each case, some, or all, of the products arise by loss of nitrogen from the azide (**1**) with formation of azirines (**2**), followed by reversible thermal[4] C–N bond cleavage to give the corresponding vinylnitrenes (Scheme 1). On the other hand, azirines are known[5–10] to undergo irreversible C–C bond cleavage on photolysis to give nitrile ylides, which can react as 1,3-dipoles or as iminocarbenes in both inter- and intra-molecular reactions, and thus the azirines (**2**) derived from azidocinnamates might be expected to behave similarly (Scheme 1).



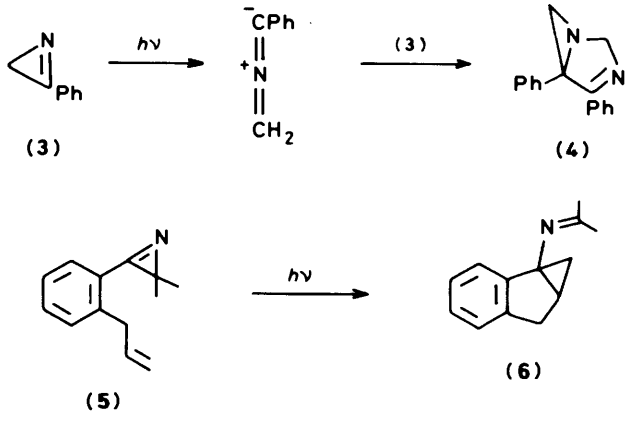
Scheme 1.

The photochemical reactions of azirines have been summarised in several papers and reviews,[5–10] and typical reactions include dimerisation to give 1,3-diazabicyclo[3.1.0]hex-3-enes [*e.g.* (**3**) to (**4**)],[8] and intramolecular cycloadditions [*e.g.* (**5**) to (**6**)].[10]

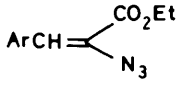
To complement our work on the thermal decomposition of azidocinnamates (**1**) we have investigated their photolysis, and we now report our results in detail.

Results and Discussion

The starting azidocinnamates (**1a**) and (**1b**) were known[11] compounds, azides (**1c**), (**1d**), (**1e**), (**1f**), and (**1g**) were prepared



as described previously,[1,3] and azide (**1h**) was prepared by condensation of pyridine-2-carbaldehyde with ethyl azidoacetate under the usual conditions.



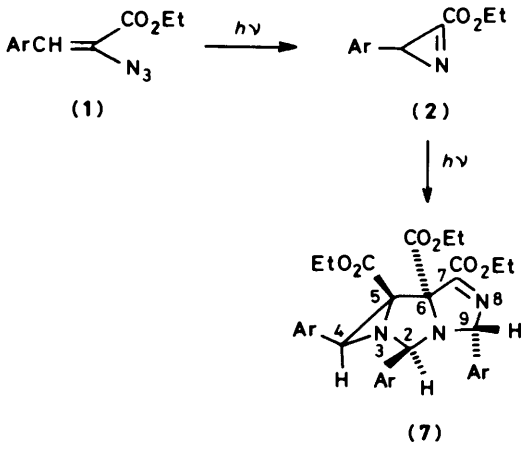
(**1**)

a; Ar = 2-MeC_6H_4
b; Ar = Ph
c; Ar = 2-$PhCH_2C_6H_4$
d; Ar = 2-$Me_2CHC_6H_4$
e; Ar = Fluoren-1-yl
f; Ar = 2-$H_2C{=}CHCH_2C_6H_4$
g; Ar = 2-$PhCH{=}CHC_6H_4$ (*trans*)
h; Ar = 2-pyridyl

Photolysis of the azidocinnamate (**1a**) in light petroleum at 300 nm gave one major product, a trimer of the azirine (**2a**). The novel 1,3,8-triazatricyclo[4.3.0.0^{3,5}]non-7-ene structure (**7a**), and the relative stereochemistry, was unambiguously determined by an *X*-ray crystallographic analysis, the details of which have already been published.[2] In a separate experiment, the azirine (**2a**) was isolated by irradiation of azide (**1a**) at lower light intensity, and shown to be converted into the trimer (**7a**) on further irradiation. Photolysis of the other azidocinnamates containing *ortho*-alkyl groups (**1b**—**e**) gave analogous triazatricyclononenes on photolysis and the results are

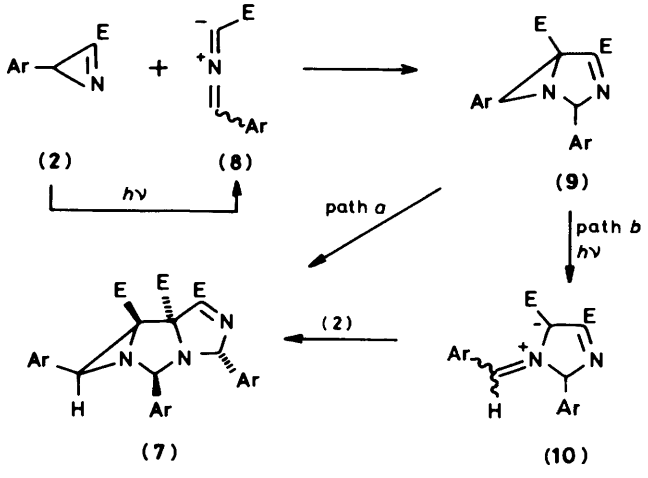
Table. Photochemical conversion of azidocinnamates (1) into the triazatricyclononenes (7)

(1)/(2)/(7)	Ar	% Yield of (7)
a	2-MeC_6H_4	50
b	Ph	66
c	2-$PhCH_2C_6H_4$	40
d	2-$Me_2CHC_6H_4$	57
e	Fluoren-1-yl	61



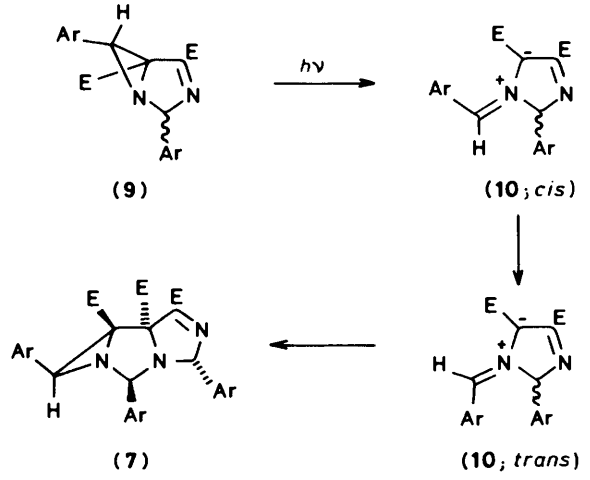
summarized in the Table. In each case only one (racemic) stereoisomer of the trimer was isolated, suggesting that the reaction is highly stereospecific.

The trimers (7) probably arise by initial formation of a dimer (9), followed by either addition of another nitrile ylide (8) (path *a*), or by ring opening of the dimer to give ylide (10) and subsequent addition of another azirine (2) (path *b*) (Scheme 2).



Scheme 2. E = CO_2Et, Ar groups as in (**1a**—**e**)

However, in order to explain the observed stereospecificity of the reaction, path *a* requires that the initial addition of the nitrile ylide (8) to the azirine (2) be stereospecific, followed by a stereospecific addition of nitrile ylide (8) to the *more* hindered face of the dimer (9). This is highly unlikely, and thus path *b* seems more reasonable. In path *b* (Scheme 2), the formation of dimer (9) need not be stereospecific since photochemical ring opening to the azomethine ylide (10) destroys the stereochemistry at two centres. Therefore we favour a mechanism for trimer formation which involves initial dimerisation to give (9) as a mixture of diastereoisomers formed by addition of the nitrile ylide to the least hindered face of the azirine, followed by photochemical disrotatory ring opening of the three-membered ring to give the *cis*-azomethine ylide (10; *cis*), which rapidly isomerises to the more thermodynamically stable *trans*-ylide (10; *trans*). Similar *cis* to *trans* isomerisations have been observed for other azomethine ylides under photochemical conditions.[12] Addition of the more stable *trans*-ylide (10; *trans*) to the azirine (2) so that the aryl groups cause minimum steric hindrance gives the observed trimer stereochemistry (Scheme 3). It should be noted that the relative configuration of *five* asymmetric centres in the trimer (7) is determined solely by the geometry of the ylide (10; *trans*) which contains only one stereocentre.

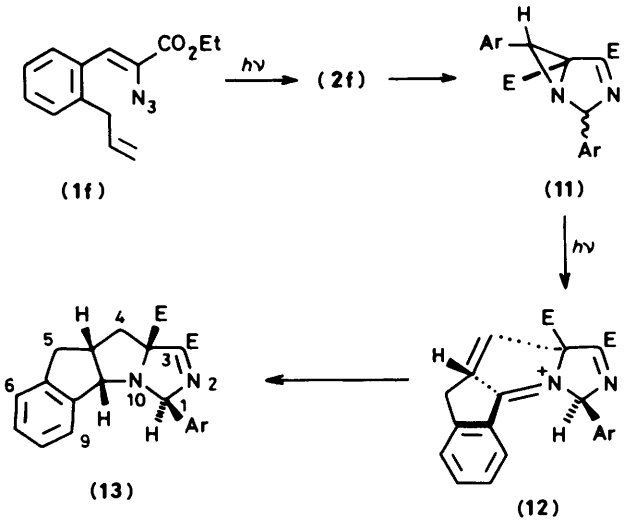


Scheme 3. E = CO_2Et, Ar groups as in (**1a**—**e**)

The above mechanism (Scheme 2, path *b*, and Scheme 3) also explains why trimers should be formed to the exclusion of dimers and oligomers. Ring opening of the aziridine (9) gives an azomethine ylide (10) in which the negative charge is stabilised by both the ester and the C=N moiety, and therefore occurs readily whilst the azirine (2), a good dipolarophile, is still present. Any further ring opening of the trimer (7) would give a less stable azomethine ylide, and hence is less likely.

Further evidence for this mechanism was obtained in the photolysis of the azide (**1f**) containing an *ortho*-allyl substituent which gave a 'dimeric' product (44%) in which only one allyl group was retained. The structure and stereochemistry were assigned from ^1H n.m.r. decoupling and n.O.e. measurements as that shown in structure (13), and it results from initial non-stereospecific dimerisation, as before, to the aziridine (11) by addition of the nitrile ylide to the least hindered face of the azirine, followed by photochemical ring opening to give, eventually, the more stable *trans*-azomethine ylide (12), which is intercepted intramolecularly by the adjacent allyl group (Scheme 4).

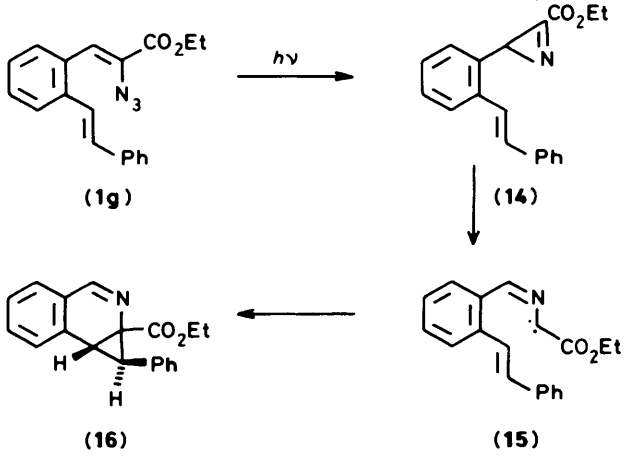
The nitrile ylide intermediates derived by photochemical ring opening of azirines can also be intercepted in their iminocarbene form by neighbouring π-bonds or nucleophiles. Thus irradiation of the azide (**1g**) gave the cyclopropaisoquinoline (16) in 68% yield, the *trans*-stereochemistry being assigned by comparison with other systems.[13] The addition was stereospecific and no isomerisation to the *cis*-isomer was observed. The simplest mechanism for the formation of (16) involves photochemical ring opening of the azirine (14) to give



Scheme 4. E = CO_2Et, Ar = 2-H_2C=$CHCH_2C_6H_4$

the iminocarbene (**15**) which undergoes stereospecific addition to the neighbouring double bond (Scheme 5).

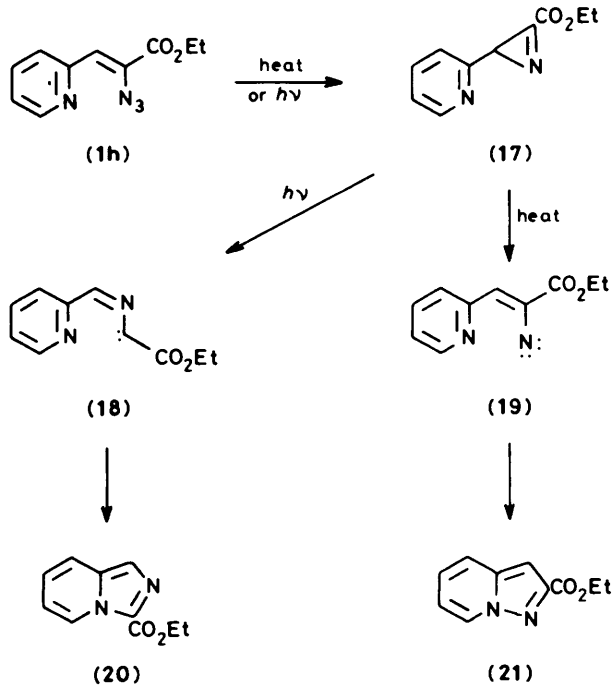
Similar photochemical 1,1-cycloadditions of iminocarbenes derived from azirines have been observed to be non-stereospecific, and postulated to occur by a stepwise mechanism.[8]



Scheme 5.

Alternatively it has been proposed that the apparent non-stereospecificity was due to epimerisation of the products rather than a stepwise reaction.[7]

Since 2-imidoylazirines are known to give imidazoles on photolysis,[7,14] we expected that a 2-pyridyl azirine would give an imidazopyridine. This expectation was realised in the photolysis of azide (**1h**) which gave the imidazopyridine (**20**) (55%), together with a smaller amount (15%) of the 'thermal' product, the pyrazolopyridine (**21**), formed by heating of the solution during the irradiation. That this was a genuine thermal product was shown by the fact that it was formed in very high yield (95%) by refluxing the azide (**1h**) in toluene. This particular example illustrates the diverging thermal and photochemical reactions of the azirine (**17**), the imidazopyridine (**20**) being formed *via* the iminocarbene (**18**), and the pyrazolopyridine (**21**) by cyclisation of the vinylnitrene (**19**) (Scheme 6).



Scheme 6.

Experimental

Photochemical reactions were carried out in quartz tubes in a Rayonet reactor using lamps of 300 nm wavelength; normally 4 lamps were used, but for low intensity irradiation only 1 was used. The solutions were degassed with dry nitrogen, and nitrogen was bubbled through the solvent during the irradiation. For other general points see ref. 3.

Ethyl 2-Azido-3-(2-pyridyl)propenoate (**1h**).—This was prepared in the usual way[3] by condensation of pyridine-2-carbaldehyde with ethyl azidoacetate in 32% yield as pale yellow prisms, m.p. 36—38 °C (from ether) (Found: C, 54.75; H, 4.7; N, 25.4. $C_{10}H_{10}N_4O_2$ requires C, 55.0; H, 4.6; N, 25.4%); $\nu_{max.}$ (Nujol) 2 120, 1 710, and 1 617 cm^{-1}; δ (90 MHz; $CDCl_3$) 1.36 (3 H, t), 4.38 (2 H, q), and 7.00—8.70 (5 H, m); *m/z* 218 (M^+), 190, 162, 144, 118 (base), 90, and 78.

Photolysis of the Azide (**1a**).—(*a*) A solution of the azide (**1a**) (312 mg) in light petroleum (200 ml) was irradiated for 1 h. Evaporation of the solvent and chromatography gave *triethyl 2,4,9-tri-(o-tolyl)-1,3,8-triazatricyclo*[4.3.0.$0^{3,5}$]*non-7-ene-5,6,7-tricarboxylate* (**7a**) (138 mg, 50%), m.p. 135—136 °C (Found: C, 70.75; H, 6.45; N, 6.9. $C_{36}H_{39}N_3O_6$ requires C, 70.9; H, 6.45; N, 6.9%); $\nu_{max.}$ (Nujol) 1 755, 1 733, and 1 652 cm^{-1}; δ (250 MHz; $CDCl_3$) 0.77 (3 H, t), 1.34 (3 H, t), 1.38 (3 H, t), 1.77 (3 H, s), 1.79 (3 H, s), 2.58 (3 H, s), 3.85 (2 H, qq), 4.18 (1 H, s), 4.23—4.50 (4 H, m), 5.20 (1 H, s), 6.39 (1 H, s), 6.80—6.90 (2 H, m), 7.00—7.38 (7 H, m), 7.44—7.50 (2 H, m), and 8.44 (1 H, d); *m/z* 609 (M^+), 536, 417, 315, 311, 239, 222 (base), and 168.

(*b*) A solution of the azide (**1a**) was irradiated at low light intensity for 3.5 h. Evaporation of the solvent left an oil assigned as the azirine (**2a**). $\nu_{max.}$ (CCl_4) 1 760 and 1 725 cm^{-1}; δ (90 MHz; $CDCl_3$) 1.35 (3 H, t), 2.49 (3 H, s), 3.52 (1 H, s), 4.45 (2 H, q), and 6.70—7.30 (4 H, m); *m/z* 203 (M^+, base). Further irradiation of the azirine (**2a**) at normal light intensity for 1 h gave the trimer (**7a**) (*ca.* 60%).

Photolysis of the Azide (**1b**).—A solution of the azide (**1b**) (411 mg) in light petroleum (250 ml) was irradiated for 1 h. Evaporation of the solvent and chromatography gave *triethyl* 2,4,9-*triphenyl*-1,3,8-*triazatricyclo*[4.3.0.0^{3,5}]*non*-7-*ene*-5,6,7-*tricarboxylate* (**7b**) (236 mg, 66%), m.p. 105—106 °C (Found: C, 69.7; H, 5.9; N, 7.4. $C_{33}H_{33}N_3O_6$ requires C, 69.8; H, 5.9; N, 7.4%); $\nu_{max.}$ (Nujol) 1 745br and 1 640 cm^{-1}; δ (250 MHz; $CDCl_3$) 0.84 (3 H, t), 0.90 (3 H, t), 1.36 (3 H, t), 3.79—4.17 (4 H, m), 4.28 (1 H, s), 4.22—4.46 (2 H, m), 5.47 (1 H, s), 6.01 (1 H, s), and 7.15—7.55 (15 H, m); *m/z* 567 (M^+), 521, 494, 301, and 299 (base).

Photolysis of the Azide (**1c**).—A solution of the azide (**1c**) (185 mg) in light petroleum (150 ml) was irradiated for 1 h. Evaporation of the solvent and chromatography gave *triethyl* 2,4,9-*tri*-(2-*benzylphenyl*)-1,3,8-*triazatricyclo*[4.3.0.0^{3,5}]*non*-7-*ene*-5,6,7-*tricarboxylate* (**7c**) (66 mg, 40%), m.p. 135—136.5 °C (Found: C, 77.65; H, 6.2; N, 5.0. $C_{54}H_{51}N_3O_6$ requires C, 77.4; H, 6.1; N, 5.0%); $\nu_{max.}$ (Nujol) 1 758, 1 740, 1 719, and 1 646 cm^{-1}; δ (250 MHz; $CDCl_3$) 0.80 (3 H, t), 1.32 (3 H, t), 1.35 (3 H, t), 3.15 (1 H, d, *J* 15 Hz), 3.18 (1 H, d, *J* 15 Hz), 3.66 (1 H, d, *J* 15 Hz, coupled to δ 3.18), 3.69 (1 H, d, *J* 15 Hz, coupled to δ 3.15), 3.87 (2 H, m) 4.06 (1 H, s), 4.22—4.52 (6 H, m), 5.10 (1 H, s), 6.59 (1 H, s), and 6.60—8.52 (27 H, m); *m/z* 837 (M^+).

Photolysis of the Azide (**1d**).—A solution of the azide (**1d**) (393 mg) in light petroleum (200 ml) was irradiated for 1 h. Evaporation of the solvent and chromatography gave *triethyl* 2,4,9-*tri*-(2-*isopropylphenyl*)-1,3,8-*triazatricyclo*[4.3.0.0^{3,5}]-*non*-7-*ene*-5,6,7-*tricarboxylate* (**7d**) (200 mg, 57%), m.p. 128—130 °C (Found: C, 72.95; H, 7.5; N, 6.05. $C_{42}H_{51}N_3O_6$ requires C, 72.7; H, 7.4; N, 6.1%); $\nu_{max.}$ (Nujol) 1 750 and 1 740 cm^{-1}; δ (250 MHz; $CDCl_3$) 0.37 (3 H, d, *J* 6 Hz), 0.66—0.83 (6 H, m), 1.00 (3 H, d, *J* 6 Hz), 1.10 (3 H, d, *J* 6 Hz), 1.25—1.40 (12 H, m), 1.60 (1 H, septet), 1.88 (1 H, septet), 2.65—2.97 (3 H, m), 3.20—3.45 (5 H, m), 5.42 (1 H, s), 6.51 (1 H, s), and 6.95—8.36 (12 H, m); *m/z* 693 (M^+), 647, 620, 503, and 472 (base).

Photolysis of the Azide (**1e**).—A solution of the azide (**1e**) (93 mg) in light petroleum (100 ml) was irradiated for 10 min. Evaporation of the solvent and chromatography gave *triethyl* 2,4,9-*trifluoren*-1-*yl*-1,3,8-*triazatricyclo*[4.3.0.0^{3,5}]*non*-7-*ene*-5,6,7-*tricarboxylate* (**7e**) (52 mg, 61%), m.p. 159—160 °C, $\nu_{max.}$ (Nujol) 1 742 and 1 725 cm^{-1}; δ (250 MHz; $CDCl_3$) 0.66 (3 H, t), 1.33 (3 H, t), 1.35 (3 H, t), 2.95 (1 H, d, *J* 23 Hz), 3.22 (1 H, d, *J* 23 Hz), 3.63 (1 H, d, *J* 23 Hz), 3.72 (1 H, d, *J* 23 Hz), 3.70—4.00 (2 H, m), 4.19 (2 H, s), 4.25—4.50 (5 H, m), 5.51 (1 H, s,) 6.35 (1 H, s), and 7.06—8.13 (21 H, m); *m/z* 831 (M^+).

Photolysis of the Azide (**1f**).—A solution of the azide (**1f**) (100 mg) in light petroleum (100 ml) was irradiated for 1 h. Evaporation of the solvent and chromatography gave *diethyl* 1-(2-*allylphenyl*)-1,3a,4,4a,5,9b-*hexahydroindeno*[2′,1′:4,5]-*pyrrolo*[1,2-c]*imidazole*-3,3a-*dicarboxylate* (**13**) (39 mg, 44%) as a colourless oil, $\nu_{max.}$ (CCl_4) 1 742, 1 725, and 1 638 cm^{-1}; δ (250 MHz; $CDCl_3$), 1.28 (3 H, t), 1.32 (3 H, t), 1.98 (1 H, dd, *J* 5, 13 Hz), 2.71 (1 H, dd, *J* 6, 17 Hz), 3.15 (4 H, m), 3.56 (1 H, m), 4.26 (2 H, m), 4.31 (2 H, q), 4.88 (2 H, m), 5.00 (1 H, d, *J* 7 Hz), 5.68 (1 H, m), 6.13 (1 H, s), and 6.77—7.75 (8 H, m); n.O.e. experiments allowed the following assignments: δ 1.98 (5-H or 4-H, α-proton), 2.71 (4-H or 5-H α-proton), 3.15 (5-H and 4-H, β-protons), 3.56 (5a-H), 5.00 (9b-H), and 6.13 (1-H); *m/z* 458 (M^+), 385 (base), 339, 311, and 269.

Photolysis of the Azide (**1g**).—A solution of the azide (**1g**) (410 mg) in light petroleum (200 ml) was irradiated for 1 h. Evaporation of the solvent and chromatography gave *ethyl* 1-*phenyl*-1,2-*dihydro*-8bH-*cyclopropa*[1,2-c]*isoquinoline*-2-*carboxylate* (**16**) (254 mg, 68%), m.p. 92—93 °C (Found: C, 78.4; H, 5.9; N, 4.8. $C_{19}H_{17}NO_2$ requires C, 78.3; H, 5.9; N, 4.8%); $\nu_{max.}$ (Nujol) 1 743, 1 617, and 1 140 cm^{-1}; δ (90 MHz; $CDCl_3$) 1.04 (3 H, t), 1.90 (1 H, d, *J* 7 Hz), 3.82 (1 H, d, *J* 7 Hz), 4.06 (2 H, qq), 7.20—7.66 (9 H, m), and 8.24 (1 H, s); *m/z* 219 (M^+), 262, 245, and 218 (base).

Photolysis of the Azide (**1h**).—A solution of the azide (**1h**) (158 mg) in light petroleum (150 ml) was irradiated for 1 h. Evaporation of the solvent and chromatography gave (i) *ethyl pyrazolo*[1,5-a]*pyridine*-2-*carboxylate* (**21**), (21 mg, 15%), data given below, and (ii) *ethyl imidazo*[1,5-a]*pyridine*-3-*carboxylate* (**20**) (74 mg, 55%), m.p. 80 °C (Found: C, 63.1; H, 5.3; N, 14.7. $C_{10}H_{10}N_2O_2$ requires C, 63.15; H, 5.3; N, 14.7%); $\nu_{max.}$ (Nujol) 1 687 and 1 633 cm^{-1}; δ (90 MHz; $CDCl_3$) 1.49 (3 H, t), 4.57 (2 H, q), 6.86—7.23 (2 H, m), 7.60—7.77 (2 H, m), and 9.36 (1 H, m); *m/z* 190 (M^+, base), 145, 131, and 118.

Thermolysis of the Azide (**1h**).—A solution of the azide (**1h**) (101 mg) in toluene (25 ml) was heated under reflux for 16 h to give *ethyl pyrazolo*[1,5-a]*pyridine*-2-*carboxylate* (**21**) (83 mg, 95%), m.p. 47—48 °C (Found: C, 63.0; H, 5.3; N, 14.6. $C_{10}H_{10}N_2O_2$ requires C, 63.15; H, 5.3; N, 14.7%); $\nu_{max.}$ (Nujol) 1 744 and 1 635 cm^{-1}; δ (90 MHz; $CDCl_3$) 1.46 (3 H, t), 4.54 (2 H, q), 6.85—7.05 (1 H, m), 7.15 (1 H, s), 7.26 (1 H, m), 7.67 (1 H, m), and 8.59 (1 H, m); *m/z* 190 (M^+), 162, 145, 118 (base), 90, and 78.

Acknowledgements

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