Studies on Heterocyclic Chemistry. Part XVIII.[1] Thermally Induced Isomerisation of 3-*p*-Alkoxyphenyl-5-methoxyisoxazoles in Aryl Aldehydes and Dehydration of 5-Amino-3,4-diarylisoxazoles in Hexamethylphosphoric Triamide

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3-*p*-Alkoxyphenyl-5-methoxyisoxazoles (1), when heated in an aryl aldehyde under reflux, yield 4'-alkoxybenzanilides (5) through isomerisation of the initially produced methyl 3-*p*-alkoxyphenyl-2*H*-azirine-2-carboxylate (2) to a ketenimine (3). In addition, isomerisation to 2-*p*-ethoxyphenyl-5-methoxyoxazole (4; $Ar^1 = p\text{-}EtOC_6H_4$) was observed for the isoxazole (1; $Ar^1 = p\text{-}EtOC_6H_4$). 5-Amino-3,4-diarylisoxazoles (7), when heated in hexamethylphosphoric triamide under reflux, undergo dehydration *via* 2,3-diaryl-2*H*-azirine-2-carboxamides (8), producing 2-arylindole-3-carbonitriles (11) as the major product.

5-ALKOXY-3-ARYLISOXAZOLES undergo thermally-induced valence-bond isomerisation to alkyl 3-aryl-2*H*-azirine-2-carboxylates.[2] Among the isoxazoles studied, 5-methoxy-3-*p*-methoxyphenylisoxazole (1; $Ar^1 = p\text{-}MeOC_6H_4$) often reacts so vigorously at 200° that methyl 3-*p*-methoxyphenyl-2*H*-azirine-2-carboxylate (2; $Ar^1 = p\text{-}MeOC_6H_4$) cannot be isolated. In order to determine the fate of this isoxazole and the corresponding azirine at high temperature, the thermal reactions of this and related isoxazoles (1; $Ar^1 = p\text{-}EtOC_6H_4$ and $o\text{-}MeOC_6H_4$) in arylaldehydes were studied; if ring-opening of the azirine (2) to the corresponding ketenimine (3) occurs at high temperature, the latter might form an adduct with a carbonyl compound by means of the thermal $[_\pi 2_s + _\pi 2_a]$ cycloaddition.[3] The present study is also concerned with the chemistry of the short-lived 2,3-diaryl-2-cyano-2*H*-azirines.[4] These azirines, if produced at high temperature, are expected to change to a more thermally stable valence bond isomer and some insight regarding their thermal behaviour could be gained.

Heating 5-methoxy-3-*p*-methoxyphenylisoxazole (1; $Ar^1 = p\text{-}MeOC_6H_4$) in benzaldehyde under reflux yielded 4'-methoxybenzanilide (5; $Ar^1 = p\text{-}MeOC_6H_4$, $Ar^2 =$ Ph). Similar reactions of this isoxazole with *p*-tolualdehyde, *p*-anisaldehyde, and *o*-chlorobenzaldehyde, either neat or in decalin solution, produced 4-methyl-4'-methoxy-, 4,4'-dimethoxy-, and 2-chloro-4'-methoxy-benzanilides, respectively. The reaction mixtures were carefully chromatographed, but no products other than these were identified.

However, heating 3-*p*-ethoxyphenyl-5-methoxyisoxazole (1; $Ar^1 = p\text{-}EtOC_6H_4$) in benzaldehyde–decalin gave two products, 4'-ethoxybenzanilide (5; $Ar^1 =$

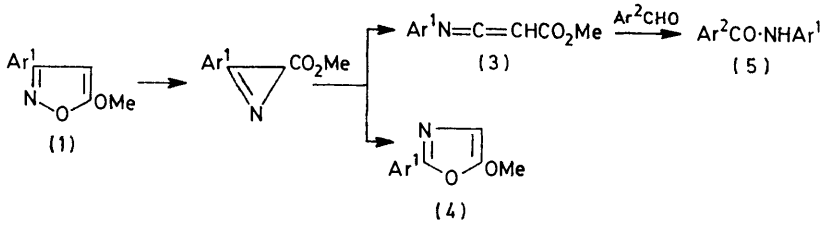
[1] Part XVII, T. Nishiwaki and T. Takahashi, *Synthesis*, 1973, 363.

[2] T. Nishiwaki, T. Kitamura, and A. Nakano, *Tetrahedron*, 1970, **26**, 453.

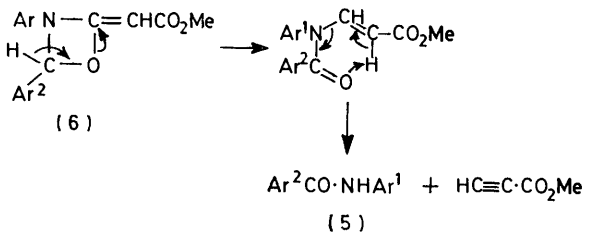
[3] G. R. Krow, *Angew. Chem. Internat. Edn.*, 1971, **10**, 435.

[4] T. Nishiwaki and F. Fujiyama, *J.C.S. Perkin I*, 1973, 817.

p-$EtOC_6H_4$, Ar^2 = Ph) and 2-p-ethoxyphenyl-5-methoxyoxazole (4; Ar^1 = p-$EtOC_6H_4$), the latter identified (m.p., i.r., and t.l.c.) by comparison with an authentic specimen prepared from p-ethoxyhippuric acid. This is the first instance in which an isoxazole derivative undergoes thermally induced isomerisation to an oxazole derivative, but this is not unexpected; the azirine having an α-carbonyl function at C-2 undergoes ring expansion to an oxazole [5] and the isoxazole (1; Ar^1 = p-$EtOC_6H_4$) must have first isomerised to methyl 3-p-ethoxyphenyl-2H-azirine-2-carboxylate (2; Ar^1 = p-$EtOC_6H_4$) under the conditions employed.

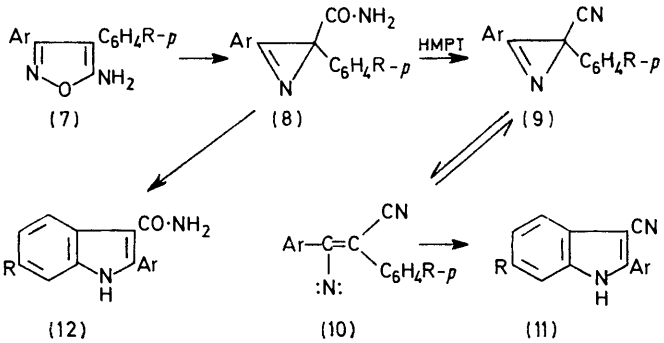


The oxazole (4) is not an intermediate for the anilide (5); the compound (4; Ar^1 = p-$EtOC_6H_4$) was largely unchanged after heating in the presence or absence of benzaldehyde. Formation of the anilide (5) from the isoxazole (1) requires migration of a p-alkoxyphenyl group from carbon to nitrogen and strongly suggests the intermediacy of the ketenimine (3); formation of p-alkoxyaniline and oxidation of the aldehyde under the reaction conditions are unlikely. Thermal instability of the azirine (2; Ar^1 = p-$MeOC_6H_4$)[2] may be due to its rapid isomerisation to the corresponding ketenimine (3; Ar^1 = p-$MeOC_6H_4$) and further reactions of the latter. However, the formation of the anilide (5) from the ketenimine (3) cannot be accounted for on the basis of the $[_\pi 2_s + _\pi 2_a]$ cycloaddition of the ketenimine (3) and the arylaldehyde to give a 2-imino-oxetan and then further reactions of this. One of the likely intermediates is the 1,3-oxazetidine derivative (6). Its ring-opening as shown could produce the benzanilide (5). However, formation of methyl propiolate was not confirmed; possibly it may have eluded detection.



The thermal isomerisation of the isoxazole derivatives to ketenimine (3) appears feasible only when the 3-aryl group bears a p-alkoxy-substituent; the isoxazoles (1; Ar^1 = o-$MeOC_6H_4$ or Ph), when heated in benzaldehyde–decalin, did not yield the corresponding benzanilides. Further, this reaction could not be induced photochemically. Irradiation of the isoxazole (1; Ar^1 = p-$MeOC_6H_4$) in benzaldehyde–ether (1 : 5) with 2537 Å light did not produce the benzanilide (5; Ar^1 = p-$MeOC_6H_4$, Ar^2 = Ph), although 3,4,5-triphenylisoxazole is known to isomerise to benzoylphenylketen N-phenylimine under irradiation.[6]

Heating the 5-amino-3,4-diphenylisoxazoles (7; Ar = Ph, R = H or Cl) in hexamethylphosphoric triamide (HMPT) under reflux afforded two products formed with concomitant evolution of dimethylamine; the first were the 2-phenylindole-3-carbonitriles (11; Ar = Ph, R = H or Cl) which were identified by spectrometry and by reference to the reported [7] physical data. The indoles (11) must have arisen *via* dehydration of the initially produced 2,3-diaryl-2H-azirine-2-carboxamide (8) to 2,3-diaryl-2-cyano-2H-azirine (9) and ring-opening of (9) to the corresponding vinylnitrene (10). It is known that azirines bearing a 2-aryl group undergo ring expansion to indoles when heated at high temperature [8] and HMPT dehydrates primary amides to nitriles.[9] The other products obtained in a smaller quantity were also nitriles [$C_{22}H_{12}R_2N_2$ (R = H or Cl)] as inferred by i.r. spectrometry, but unfortunately they could not be identified; the molecular formulae indicate that they are fragmentation products of the azirine (9).



The indole (11) and the nitrile $C_{22}H_{12}R_2N_2$ were also produced in comparable yields when the corresponding 2,3-diaryl-2H-azirine-2-carboxamides (8; Ar = Ph, R = H or Cl) were heated in HMPT under reflux. To support the precedence of the dehydration of the azirine-2-carboxamide (8) over the ring-opening of the azirine (9)

[5] G. L'abbé and A. Hassner, *Angew. Chem. Internat. Edn.*, 1971, **10**, 98.
[6] D. W. Kurtz and H. Schechter, *Chem. Comm.*, 1966, 689.
[7] J. D. Loudon and G. Tennant, *J. Chem. Soc.*, 1960, 3466.
[8] K. Isomura, S. Kobayashi, and H. Taniguchi, *Tetrahedron Letters*, 1968, 3499; H. Hementsberger, D. Knittel, and H. Weidmann, *Monatsh.*, 1970, **101**, 161; T. L. Gilchrist, G. E. Gymer, and C. W. Rees, *J.C.S. Perkin I*, 1973, 555; J. H. Bowie and B. Nussey, *ibid.*, p. 1693.
[9] R. S. Monson and D. N. Priest, *Canad. J. Chem.*, 1971, **49**, 2897.

to the corresponding vinylnitrene and cyclisation of this to the 2-arylindole-3-carboxamide (12), the azirine (8; Ar = Ph, R = H) and the isoxazole (7; Ar = Ph, R = Cl) were each heated in diphenyl ether under reflux. The only products isolated were the 2-arylindole-3-carboxamides (12; Ar = Ph, R = H or Cl). The amide (12), when heated in HMPT under reflux, gave the indole-3-carbonitriles (11) in moderate yield but not the nitrile $C_{22}H_{12}R_2N_2$.

EXPERIMENTAL

Petroleum refers to the fraction of b.p. 70—110° unless otherwise stated. Commercial arylaldehydes were washed with aqueous sodium hydrogen carbonate solution and distilled under reduced pressure immediately before use. N.m.r. spectra were recorded at 60 MHz.

Reaction of 3-p-*Alkoxyphenyl-5-methoxyisoxazole with Aryl-aldehydes.*—The isoxazole (1; Ar^1 = *p*-$MeOC_6H_4$) (0·99 g) was heated in benzaldehyde (20 ml) under reflux for 4 h in nitrogen (method A). The reaction of the isoxazole with *p*-tolualdehyde was carried out similarly, whereas the reaction with *p*-anisaldehyde or *o*-chlorobenzaldehyde was performed by heating the isoxazole (1; Ar^1 = *p*-$MeOC_6H_4$) (1·00 g) and the aldehyde (4—5 ml) in decalin (5 ml) for 1·5 h under nitrogen (method B). The excess of solvent and aldehyde was removed under reduced pressure and the residue dissolved in ether. The ethereal solution was washed with 5% aqueous sodium hydrogen carbonate solution, the solvent evaporated, and the residue chromatographed on alumina with ether and then ether–ethyl acetate (10 : 1). The 4′-methoxybenzanilides (5; Ar^1 = *p*-$MeOC_6H_4$) were isolated from the first eluates and their physical data and analyses are shown in the Table. The last eluate gave the starting material in the case of the reaction with *o*-chlorobenzaldehyde. The benzanilides (5) had $\nu_{max.}$ (NH) and $\nu_{max.}$ (C=O) in the expected region of their i.r. spectra.

The isoxazole (1; Ar^1 = *o*-$MeOC_6H_4$) was treated with benzaldehyde by method B. The starting material (23% recovery) and a small amount of a compound, m.p. 108—117°, were isolated from the reaction mixture. Although the product could not be purified, the presence of 2′-methoxybenzanilide (5; Ar^1 = *o*-$MeOC_6H_4$, Ar^2 = Ph) was ruled out by the m.p. (lit.,[11] 66—69°) and t.l.c.

The isoxazole (1; Ar^1 = *p*-$EtOC_6H_4$) (1·00 g) was treated with benzaldehyde by method B. The solvent and the aldehyde were removed under reduced pressure and alumina chromatography of the residue with ether gave a solid, which crystallised from petroleum as needles (0·07 g, 8% yield), m.p. 74—76° (Found: C, 65·8; H, 5·95; N, 6·3. $C_{12}H_{13}NO_3$ requires C, 65·7; H, 6·0; N, 6·4%), $\lambda_{max.}$ (EtOH) 289 nm (log ε 4·55). This compound was identified as 2-p-*ethoxyphenyl-5-methoxyoxazole* (4; Ar^1 = *p*-$EtOC_6H_4$) by mixed m.p. (74—75°), i.r., and t.l.c. comparison with an authentic specimen (see below). Elution with ether–ethyl acetate (3 : 1) gave 4′-*ethoxybenzanilide* (5; Ar^1 = *p*-$EtOC_6H_4$, Ar^2 = Ph) (see the Table).

2-p-*Ethoxyphenyl-5-methoxyoxazole* (4; Ar^1 = *p*-$EtOC_6H_4$).—Dry hydrogen chloride was passed into a mixture of p-*ethoxyhippuric acid* [prepared by a standard procedure,[12] m.p. 143—145° (from water) (Found: C, 59·3; H, 5·8. $C_{11}H_{13}NO_4$ requires C, 59·2; H, 5·9%); 10·0 g] and dry methanol (200 ml) and the solvent was removed under reduced pressure. *Methyl* p-*ethoxyhippurate* (7·0 g, 66%) crystallised from ethyl acetate–petroleum as rods, m.p. 82—84° (Found: C, 60·5; H, 6·1. $C_{12}H_{15}NO_4$ requires C, 60·75; H, 6·4%). A mixture of this ester (7·0 g) and phosphorus pentaoxide (35·0 g) was heated on a boiling water-bath for 4 h and worked up as described.[13] Evaporation of the ethereal solution and alumina chromatography of the residue with petroleum (b.p. 30—70°)–ether (3 : 1) gave 2-p-*ethoxyphenyl-5-methoxyoxazole* (0·80 g, 13%), which crystallised from petroleum as needles, m.p. 73—75°.

Physical data and analyses of benzanilides (5) ($Ar^2CO{\cdot}NHAr^1$)

			Cryst.	Yield	Found (%)				Required (%)		
Ar^1	Ar^2	M.p. (°C)	solvent *	(%)	C	H	N	Formula	C	H	N
p-$MeOC_6H_4$	Ph	153—155 [a,b]	C	22							
p-$MeOC_6H_4$	*p*-MeC_6H_4	161—163 [b]	C	10	74·2	6·0	5·8	$C_{15}H_{15}NO_2$	74·7	6·3	5·8
p-$MeOC_6H_4$	*p*-$MeOC_6H_4$	200—201 [b]	E	6	70·3	5·9	5·4	$C_{15}H_{15}NO_3$	70·0	5·9	5·4
p-$MeOC_6H_4$	*o*-ClC_6H_4	133—133·5 [b]	E	6	64·15	4·5	5·3	$C_{14}H_{12}ClNO_2$	64·25	4·6	5·35
p-$EtOC_6H_4$	Ph	169—170 [b]	E	4	74·4	6·2		$C_{15}H_{15}NO_2$	74·7	6·3	

* C = Carbon tetrachloride, E = ethyl acetate–petroleum.

[a] Lit.,[10] 156°. [b] M.p. not depressed on admixture with an authentic specimen.

3-p-*Ethoxyphenyl-5-methoxyisoxazole* (1; Ar^1 = *p*-$EtOC_6H_4$).—p-*Ethoxybenzoylacetonitrile* prepared by the method described [14] [m.p. 120° (from petroleum) (Found: C, 69·7; H, 6·0. $C_{11}H_{11}NO_2$ requires C, 69·8; H, 5·9%)] was condensed with hydroxylamine hydrochloride as reported [15] to give 5-*amino*-3-p-*ethoxyphenylisoxazole*, m.p. 125—126° (from benzene) (Found: C, 64·8; H, 5·9. $C_{11}H_{12}N_2O_2$ requires C, 64·7; H, 5·9%), $\nu_{max.}$ ($CHCl_3$) 3470 and 3380 cm^{-1} (NH_2), $\lambda_{max.}$ (EtOH) 255 nm (log ε 4·33). This was hydrolysed with 6N-sulphuric acid in methanol to give 3-p-*ethoxyphenylisoxazol-5*(4H)-*one*, m.p. 133—134·5° (from benzene–petroleum) (Found: C, 64·6; H, 5·6; N, 6·8. $C_{11}H_{11}NO_3$ requires C, 64·4; H, 5·4; N, 6·8%), $\nu_{max.}$ ($CHCl_3$) 1800 cm^{-1} (C=O), $\lambda_{max.}$ (EtOH) 279 nm (log ε 4·33). Treatment of this compound with ethereal diazomethane gave 3-p-*ethoxyphenyl-5-methoxyisoxazole* (87%), which crystallised from methanol as plates, m.p. 84—86° (Found: C, 65·7; H, 6·2; N, 6·6. $C_{12}H_{13}NO_3$ requires C, 65·7; H, 6·0; N, 6·4%), $\lambda_{max.}$ (EtOH) 255 nm (log ε 4·30).

5-*Methoxy*-3-o-*methoxyphenylisoxazole* (1; Ar^1 = *o*-$MeOC_6H_4$).—o-*Methoxybenzoylacetonitrile* prepared by the method described [14] [m.p. 86—88° (from benzene–petroleum) (Found: C, 68·5; H, 5·2. $C_{10}H_9NO_2$ requires C, 68·6; H, 5·2%)] was condensed with hydroxylamine hydrochloride by the method of Obrégia [16] and the crude material

[10] R. Grammaticakis, *Bull. Soc. chim. France*, 1948, 979.
[11] P. A. S. Smith, *J. Amer. Chem. Soc.*, 1954, **76**, 431.
[12] W. Ingersoll and S. H. Babcock, *Org. Synth.*, Coll. Vol. II, 1943, p. 328.
[13] P. Karrer, E. Miyamichi, H. C. Storm, and R. Widmer, *Helv. Chim. Acta*, 1925, **8**, 205.
[14] T. Nishiwaki and T. Saito, *J. Chem. Soc.* (*C*), 1971, 3021.
[15] T. Nishiwaki and T. Saito, *J. Chem. Soc.* (*C*), 1971, 2648.
[16] A. Obrégia, *Annalen*, 1891, **266**, 324.

was extracted with chloroform. *5-Amino-3-o-methoxyphenylisoxazole* was isolated from the extracts, m.p. 95—97° (from carbon tetrachloride) (Found: C, 62·9; H, 5·1; N, 14·5. $C_{10}H_{10}N_2O_2$ requires C, 63·15; H, 5·3; N, 14·7%), $\nu_{max.}$ ($CHCl_3$) 3470 and 3380 cm^{-1} (NH_2), $\lambda_{max.}$ (EtOH) 237 and 286 nm (log ε 4·22 and 3·91), and was hydrolysed as described above to give *3-o-methoxyphenylisoxazol-5(4H)-one*, as needles (from ethanol), m.p. 103—105° (Found: C, 62·9; H, 4·6; N, 7·3. $C_{10}H_9NO_3$ requires C, 62·8; H, 4·75; N, 7·3%), $\nu_{max.}$ ($CHCl_3$) 1800 and 1725 cm^{-1} (C=O), $\lambda_{max.}$ (EtOH) 249 and 300 nm (log ε 4·12 and 3·99). The i.r. spectrum indicates that this compound contains an appreciable quantity of the -5(2*H*)-one tautomer. This isoxazoline (6·50 g) was treated with ethereal diazomethane, and the product was distilled at 150—160° at 2 mmHg. The distillate solidified on cooling, and two recrystallisations from petroleum (b.p. 30—70°) gave *5-methoxy-3-o-methoxyphenylisoxazole* as prisms, (1·47 g, 21%), m.p. 55—56° (Found: C, 64·4; H, 5·3; N, 6·7. $C_{11}H_{11}NO_3$ requires C, 64·4; H, 5·4; N, 6·8%), $\lambda_{max.}$ (EtOH) 240 and 293 nm (log ε 4·19 and 3·72). The i.r. spectrum showed no absorption at 1725 cm^{-1}. The filtrates were combined and concentrated, giving crystals (0·46 g), m.p. 43—48°, which had a strong i.r. absorption at 1725 cm^{-1} and were discarded.

Reaction of 5-Amino-3,4-diphenylisoxazole (7; Ar = Ph, R = H) *with HMPT*.—A solution of the isoxazole (2·00 g) in HMPT (30 ml) was heated under reflux for 1 h and the solvent was removed under reduced pressure. Alumina chromatography of the residue with petroleum (b.p. 30—70°)–chloroform (5 : 1) gave a solid (0·07 g) which crystallised from petroleum as light green needles, m.p. 205—206° (Found: C, 86·35; H, 4·6; N, 9·1%; M^+, 306. Calc. for $C_{22}H_{14}N_2$: C, 86·25; H, 4·6; N, 9·15%; *M*, 306), $\nu_{max.}$ (Nujol) 2210 cm^{-1} (C≡N), $\lambda_{max.}$ (EtOH) 252, 265, and 342 nm (log ε 4·38, 4·38, and 3·84), τ [$(CD_3)_2SO$] 1·7—2·5 (m). Elution with ether gave 2-phenylindole-3-carbonitrile (11; Ar = Ph, R = H) (0·185 g, 8%), which crystallised from benzene as light yellow rods, m.p. 237—239° [lit.,[7] 243° (decomp.)] (Found: C, 82·55; H, 4·8; N, 12·2%; M^+, 218. Calc. for $C_{15}H_{10}N_2$: C, 82·5; H, 4·6; N, 12·8%; *M*, 218), $\nu_{max.}$ (Nujol) 3220 (NH) and 2230 cm^{-1} (C≡N), $\lambda_{max.}$ (EtOH) 239 and 306 nm (log ε 4·50 and 4·43), τ [$(CD_3)_2SO$] 1·8—2·75 (m).

Reaction of 2,3-Diphenyl-2H-azirine-2-carboxamide (8; Ar = Ph, R = H) *with HMPT*.—A solution of the azirine (1·60 g) and HMPT (25 ml) was heated under reflux for 1 h and treated as described above, giving the nitrile $C_{22}H_{14}N_2$ (0·06 g) and 2-phenylindole-3-carbonitrile (0·18 g, 8%).

2-Phenylindole-3-carboxamide (12; Ar = Ph, R = H).—A solution of 2,3-diphenyl-2*H*-azirine-2-carboxamide (8; Ar = Ph, R = H) (1·00 g) in diphenyl ether (50 ml) was heated under reflux for 1 h and the solvent was removed under reduced pressure. Trituration of the residue with ether gave *2-phenylindole-3-carboxamide* (0·47 g, 47%), which crystallised from chloroform as rods, m.p. 180—181° (Found: C, 66·4; H, 4·5; N, 10·0; Cl, 13·1. $C_{15}H_{12}N_2O$,-0·33$CHCl_3$ requires C, 66·7; H, 4·5; N, 10·15; Cl, 12·8%), $\nu_{max.}$ (Nujol) 3480 and 3280 (NH_2), 3150 (NH), and 1640 cm^{-1} (C=O), $\lambda_{max.}$ (EtOH) 241 and 300 nm (log ε 4·42 and 4·22), τ [$(CD_3)_2SO$] 1·8—3·0 (m). This compound (0·37 g) and HMPT (10 ml) were heated under reflux for 1 h and the solvent was removed under reduced pressure. Alumina chromatography of the residue with ether gave 2-phenylindole-3-carbonitrile (0·18 g, 53%), m.p. 236—238° (from benzene).

Reaction of 5-Amino-4-p-chlorophenyl-3-phenylisoxazole (7; Ar = Ph, R = Cl) *with HMPT*.—A solution of the isoxazole (3·00 g) and HMPT (40 ml) was heated under reflux for 1 h and the solvent was removed under reduced pressure. Alumina chromatography of the residue with petroleum (b.p. 30—70°) and then with petroleum–chloroform (5 : 1) gave a solid (0·023 g) which crystallised from cyclohexane as light yellow needles, m.p. 232—234° (Found: C, 70·7; H, 3·2; N, 7·7; Cl, 18·4%; M^+, 376/375/374. Calc. for $C_{22}H_{12}Cl_2N_2$: C, 70·4; H, 3·2; N, 7·4; Cl, 18·9%; *M*, 376/375/374), $\nu_{max.}$ (Nujol) 2200 cm^{-1} (C≡N), $\lambda_{max.}$ (EtOH) 262 and 353 nm (log ε 4·62 and 4·00). Elution with ether gave *6-chloro-2-phenylindole-3-carbonitrile* (11; Ar = Ph, R = Cl) (0·043 g, 14%), which crystallised from benzene–petroleum as tan-coloured plates, m.p. 283—285° (Found: C, 71·3; H, 3·6; N, 11·0%; M^+, 254/252. $C_{15}H_9ClN_2$ requires C, 71·3; H, 3·6; N, 11·1%; *M*, 254/252), $\nu_{max.}$ (Nujol) 3240 (NH), 2220 (C≡N), 850 (isolated benzene 1H), and 800 cm^{-1} (adjacent benzene 2H), $\lambda_{max.}$ (EtOH) 240 and 315 nm (log ε 4·50 and 4·41), τ [$(CD_3)_2SO$] 2·2—2·9 (m). Mixed m.p. with the dehydration product of 6-chloro-2-phenylindole-3-carboxamide (12; Ar = Ph, R = Cl) was not depressed.

Reaction of 2-p-Chlorophenyl-3-phenyl-2H-azirine-2-carboxamide (8; Ar = Ph, R = Cl) *with HMPT*.—A solution of the azirine (0·90 g) in HMPT (20 ml) was heated under reflux for 1 h and treated as before. The nitrile $C_{22}H_{12}Cl_2N_2$ (0·01 g) and 6-chloro-2-phenylindole-3-carbonitrile (0·11 g, 13%) were obtained.

6-Chloro-2-phenylindole-3-carboxamide (12; Ar = Ph, R = Cl).—A solution of 5-amino-4-*p*-chlorophenyl-3-phenylisoxazole (7; Ar = Ph, R = Cl) (1·00 g) and diphenyl ether (50 ml) was heated under reflux for 2 h. The solvent was removed under reduced pressure and trituration of the residue with ether gave *6-chloro-2-phenylindole-3-carboxamide* (0·12 g, 12%). Crystallisation from chloroform–petroleum gave cream needles, m.p. 237—239° (decomp.) (Found: C, 66·15; H, 4·1; N, 10·35. $C_{15}H_{11}ClN_2O$ requires C, 66·55; H, 4·1; N, 10·35%), $\nu_{max.}$ (Nujol) 3450 and 3300 (NH_2), 3150 (NH), and 1620 cm^{-1} (C=O), $\lambda_{max.}$ (EtOH) 242 and 307 nm (log ε 4·46 and 4·18), τ [$(CD_3)_2SO$] 2·2—3·0 (m). This compound (0·20 g) and HMPT (10 ml) were heated under reflux for 1 h, the solvent was removed under reduced pressure, and the residue was chromatographed on alumina with ether–ethyl acetate (3 : 1). 6-Chloro-2-phenylindole-3-carbonitrile (0·06 g, 30%) was obtained.

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