Intramolecular Reactions of Pyridinium-2-carbonyl Azides: Conversion of Amines into Aldehydes

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Upon photolysis *N*-benzyl-2-azidocarbonylpyridinium salts give benzaldehydes, partially *via* the γ-lactams (5). *N*-(2-Phenylethyl) analogues give mixtures of phenylacetaldehydes and benzaldehydes *via* γ- (12) and δ-lactams (13).

Following our demonstration of the synthetic utility of intermolecular displacement reactions on pyridinium,[1] we are now studying intramolecular reactions. In cognate work we have demonstrated the possibilities for intramolecular nucleophilic attack on 1-aryl [2] and 1-heteroaryl [3] groups. We now report the investigation of the susceptibility of 1-alkyl substituents toward intramolecular attack by an α-carbonyl nitrene.

Preparation of 1-Substituted 2-Azidocarbonylpyridinium Salts.—2-Ethoxycarbonyl-4,6-diphenyl- and -4-*p*-tolyl-6-phenyl-pyridinium tetrafluoroborates were converted in the usual way into a series of pyridinium compounds (1) (Table 1). The alkyl and aralkyl derivatives (1) readily formed the corresponding hydrazides (Table 2) on being heated under reflux in EtOH with 1.5 equiv. of N_2H_4 for 2 h: longer reaction times or an excess of N_2H_4 decreased the yields. The phenyl derivative (1i) failed to give (2i): probably some ANRORC † had occurred.[4]

The hydrazides (2) with HONO formed in high yield the corresponding azides (3) (Table 3). These [with the exception of the stable compound (3e)] slowly and spontaneously lost N_2 with the formation, by proton abstraction, of the amides (4); this was demonstrated by the appearance in the i.r. spectrum of ν (NH_2) at 3 340 and 3 440 cm^{-1} and ν (C=O) at 1 650 cm^{-1}. Consequently, nitrogen analyses for the azides (3) were low.

The esters (1), hydrazides (2), and azides (3) were all characterized on the basis of their spectra; ν (C=O) occurred at 1 740 cm^{-1} in (1), at 1 670 cm^{-1} in (2), and at 1 700 cm^{-1} in (3). The azides (3) showed ν (N_3) at 2 145—2 150 cm^{-1} with a weak band at 2 180—2 210 cm^{-1}.‡

The 4-tolyl-6-phenyl derivatives (3j) and (3k) were prepared in order to assist in elucidating the ^1H n.m.r. spectra in mixtures of photolysis products: the methyl signal was used to determine the number of aromatic protons.

Attempts to form azides *via* acid chlorides failed: when ethyl 1-benzyl-4,6-diphenylpyridine-2-carboxylate (1a) was treated with thionyl chloride the benzyl group was lost, as shown by the isolation of 2-phenylcarbamido-4,6-diphenylpyridine (4a) on addition of aniline.

Photolyses of 1-Benzyl-2-azidocarbonylpyridinium Salts (3a—c).—Irradiation in CH_2Cl_2 solution gave aldehydes, isolated and characterized as their dinitrophenylhydrazone (DNP) derivatives (Table 4). The 1-*p*-chlorobenzyl carbonyl azides (3h) gave, in addition, 2-carbamoyl-4,6-diphenylpyridines (10), 2-cyano-4,6-diphenylpyridine (8), and 2,4-diphenylpyridine (11) together with the tetrafluoroborate of compound (10). The mechanism of Scheme 1 is proposed to account for the formation of these products: compound (3) from singlet nitrene which inserts to give the bicyclic compound (5) which can break down by path (a) *via* (7) to give (10). In addition, a minor proportion of the reaction follows path (b) *via* (6) and (9) to give (11), and some nitrile (8) is formed, possibly by *o*-alkylation of the azide or an intermediate.

2-Carbamoyl-4,6-diphenylpyridine (10) was isolated from the mixture of ether-soluble products and characterized on the basis of its i.r. [ν (NH) at 3 500 cm^{-1} and ν (C=O) at 1 680 cm^{-1}] and ^1H n.m.r. spectra (broad NH at δ 5.9, 1H doublet for 3-H at δ 8.32, 5-H doublet with the aromatic protons at δ 7.95). Minor amounts of what were believed to be the pyridines (8) and (11) were revealed by gas chromatography–mass spectroscopy (g.c.–m.s.). The gas chromatogram showed five bands: [5] (1) molecular ion peak at *m/e* 140 assigned to chlorobenzaldehyde; (2) *m/e* 231 as required for 2,4-diphenylpyridine (11); (3) *m/e* 256 corresponding to 2-cyano-4,6-diphenylpyridine (8); (4) *m/e* 274 for 2-carbamoyl-4,6-diphenylpyridine (10); (5) *m/e* 320 unknown.

Irradiation of the azides (3) gave, in addition to the ether-soluble products (benzaldehydes and a mixture of pyridines just described), a mixture of ether-insoluble products. Since the i.r. and ^1H n.m.r. spectra of the residues were almost identical in all cases, a detailed study was carried out only for the *p*-chlorobenzyl derivative (3b). In other cases identification

Table 1. Preparation of 1-substituted 2-ethoxycarbonyl-4,6-diarylpyridinium tetrafluoroborates (1)

Compd. no.	Reaction time (h)	Yield (%)	M.p. (°C)	Crystal form [a]	Literature [b] Yield (%)	Literature [b] M.p. (°C)
(1a)	1	94	172—174	Needles	93	172—174
(1b)	1.5	84	150—152	Needles	80	150—152
(1c)	1.5	73	127—129	Needles	72	127—129
(1d)	1.5	74	125—127	Prisms	83	130—132
(1e)	2	88	148—149	Needles	85	147—150
(1f)	2	81	188—190	Plates	81	188—190
(1g)	12 [c]	75	126—127	Prisms	46	126—128
(1h)	4	62	153—155	Plates	63	153—155
(1i)	3	85	185—186	Needles	95 [f]	186—187
(1j)	2	88	144—145	Needles	*d*	
(1k)	1.5	68	115—117	Needles	*e*	

[a] All recrystallized from EtOH. [b] From ref. 6. [c] AcOH used as a catalyst. [d] Found: C, 68.3; H, 5.9; N, 3.1. $C_{29}H_{28}BF_4NO_2$ requires C, 68.5; H, 5.5; N, 2.8%. [e] Found: C, 65.1; H, 5.9; N, 3.1. $C_{25}H_{29}BF_4NO_2$ requires C, 65.1; H, 6.0; N, 3.0%. [f] Except (1i), A. Cozens, personal communication.

† ANRORC = addition nucleophilic, ring opening, ring closure.

‡ The ^1H n.m.r. and i.r. spectroscopic results are available as a Supplementary publication [SUP No. 23408 (5 pp.)]. For details of the Supplementary publications Scheme, see Notice to Authors No. 7, *J. Chem. Soc., Perkin Trans. 1*, 1981, Index issue.

Table 2. Preparation of 1-substituted 2-hydrazidocarbonyl-4,6-diarylpyridinium tetrafluoroborates (2)

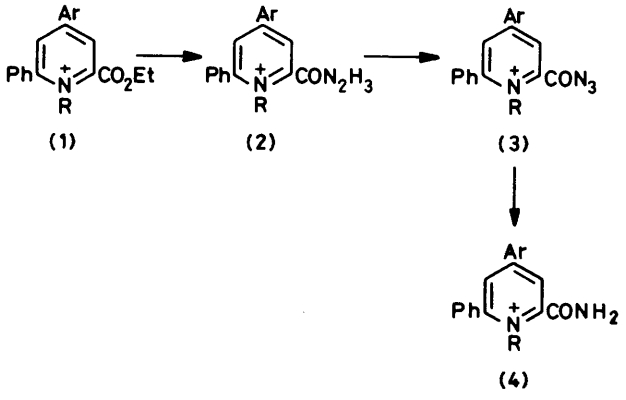
Compound no.	Reaction time (h)	Yield (%)	M.p. (°C)	Crystal form [a]	Formula	Found (%) C	H	N	Required (%) C	H	N
(2a)	2	74	171—172	Needles	$C_{25}H_{22}BF_4N_3O$	64.1	4.7	8.6	64.2	4.7	9.0
(2b)	2.5	73	125—126	Needles	$C_{25}H_{21}BClF_4N_3O$ [c]	59.7	4.1	8.1	59.8	4.2	8.3
(3c)	2.5	68	115—117	Needles	$C_{26}H_{24}BF_4N_3O$	64.7	4.9	8.8	64.8	5.0	8.7
(2d)	1.5	65	*b*								
(2e)	1.5	66	*b*								
(2f)	2	83	156—157	Needles	$C_{26}H_{24}BF_4N_3O$	65.0	4.8	8.8	64.8	5.0	8.7
(2g)	2	78	145—146	Needles	$C_{26}H_{23}BClF_4N_3O$ [d]						
(2h)	2	72	*b*								
(2j)	2	65	147—148	Needles	$C_{27}H_{26}BF_4N_3O$	65.2	5.2	8.5	65.4	5.3	8.5
(2k)	1.5	73	*b*								

[a] Recrystallized with absolute ethanol–ether. [b] Hygroscopic, failed to crystallize. [c] Cl; found 6.9, required 7.0%. [d] Cl; found 6.7, required 6.8%.

Table 3. Preparation of 1-substituted 2-azidocarbonyl-4,6-diarylpyridinium tetrafluoroborates (3)

Compound no.	Reaction time (h)	Yield (%)	M.p. (°C)	Formula	Found (%) C	H	N	Required (%) C	H	N
(3a)	2	93	100	$C_{25}H_{19}BF_4N_4O$	62.4	3.9	11.0	62.7	4.0	11.7
(3b)	2	93	123—125	$C_{25}H_{18}BClF_4N_4O$ [b]	58.6	3.6	10.2	58.5	3.5	10.9
(3c)	2	90	110—112	$C_{26}H_{21}BF_4N_4O$	63.6	4.5	10.7	63.4	4.29	11.0
(3d)	1.5	93.5	75—76	$C_{22}H_{21}BF_4N_4O$	59.8	5.1	11.1	59.4	4.7	12.6
(3e)	2	94	123—125	$C_{26}H_{21}BF_4N_4O$	63.5	4.3	11.1	63.4	4.0	11.0
(3f)	2	92	105—107	$C_{26}H_{20}BClF_4N_4O$ [c]	59.3	3.9	10.2	59.2	3.8	10.6
(3g)	1.5	88	*a*							
(3h)	2	90	*a*							
(3j)	2	90	133—137	$C_{27}H_{23}BF_4N_4O$	63.7	4.4	10.5	64.0	4.5	11.0
(3k)	1.5	92	108—110	$C_{23}H_{22}BF_4N_4O$	60.5	5.1	11.6	60.4	4.8	12.2

[a] Decompose readily, m.p. not recorded and could not be analysed. [b] Cl, Found 6.6; required 6.9%. [c] Cl, Found 6.4; required 6.7%.



R	Ar	R	Ar
a; CH_2Ph	Ph	g; Pr^i	Ph
b; $CH_2C_6H_4Cl$-*p*	Ph	h; cy-Hex	Ph
c; $CH_2C_6H_4Me$-*p*	Ph	i; Ph	Ph
d; Bu^n	Ph	j; $CH_2C_6H_4Me$-*p*	*p*-Tolyl
e; CH_2CH_2Ph	Ph	k; Bu^n	*p*-Tolyl
f; $CH_2CH_2C_6H_4Cl$-*p*	Ph		

of the products was carried out by comparison with the products from the *p*-chlorobenzyl derivative.[5] When the latter residue was treated with 5M-NaOH in MeOH, a mixture of *p*-chlorobenzaldehyde and the pyridines (8), (10), and (11) was obtained (identified by g.c-m.s) suggesting the presence of the lactam (5).

Irradiation of 1-(2-*Phenylethyl*) *Azides.*—1-(2-Phenylethyl)-2-azidocarbonyl-4,6-diphenylpyridinium tetrafluoroborate (3e) on irradiation for 12 h gave a mixture of benzaldehyde and phenylacetaldehyde in a *ca.* 2 : 1 ratio (^{1}H n.m.r.) in an overall yield of *ca.* 65%. As further products, 2-carbamoyl-4,6-diphenylpyridine (10), 2-cyano-4,6-diphenylpyridine (8), and 2,4-diphenylpyridine (11) were identified by comparison of products obtained from the *p*-chlorobenzyl derivative (3b). The probable presence of 2-carbamoyl-1-methyl-4,6-diphenylpyridinium (16) and 1-methyl-2,4-diphenylpyridinium tetrafluoroborate (17) was inferred from the spectroscopic data. Here, both the β-hydrogen and α-hydrogen atoms (attached to the carbon adjacent to positively charged nitrogen) are active. Thus, insertion into the β-C–H bond leading to the formation of a δ-lactam (13) competes with α-C–H insertion to give compound (12) (Scheme 2). The δ-lactam (13) undergoes C–C bond cleavage to form the benzaldehyde (15) and the 1-methylpyridinium salts (16) and (17).

Irradiation of the 1-[2-(4-chlorophenylethyl)] derivative (3f) gave 4-chlorobenzaldehyde (60%); no 4-chlorophenylacetaldehyde was detected. The 4-chloro-substituent further activates the β-hydrogen atoms considerably, hence β-C–H insertion occurs.

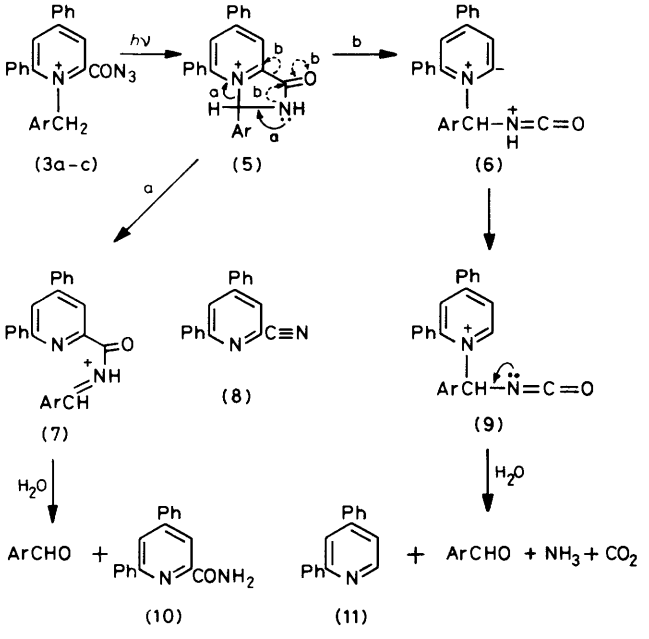
The mixtures of ether-soluble and ether-insoluble products from the 1-(2-phenylethyl) derivatives (3e) and (3f) were similar (by comparison of i.r. and ^{1}H n.m.r. spectra) in content to those obtained for the benzyl derivatives (discussed earlier).[5]

Irradiation of 1-*Alkyl Derivatives.*—The 1-butyl-2-azidocarbonyl-4,6-diphenylpyridinium salt (3d) on irradiation for 12 h gave a *ca.* 60% yield of butanal (identified as DNP derivative). The remaining products were similar to those obtained from the benzyl derivatives (3a—c).[5] Irradiation of

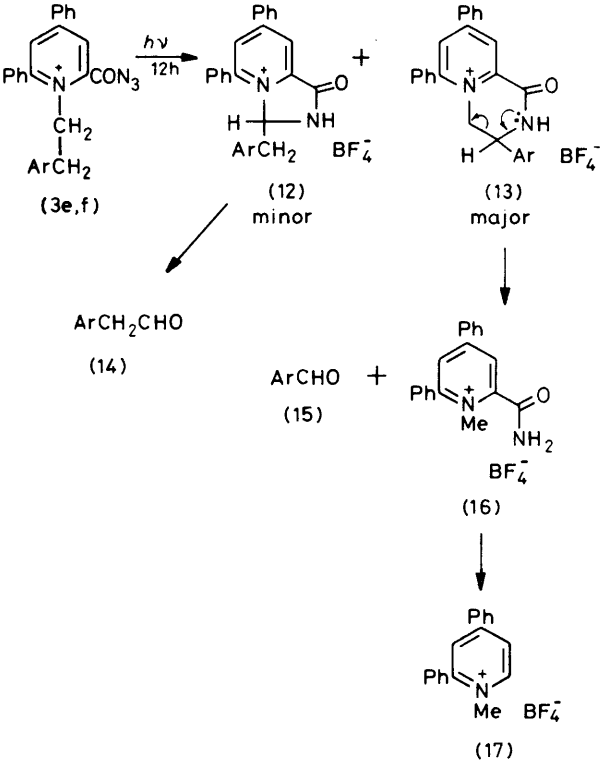
Table 4. Photolysis of 1-substituted 2-azidocarbonyl-4,6-diphenylpyridinium tetrafluoroborates (3)

1-Substituent R	Primary product	of Dinitrophenyl hydrazone Yield [d] (%)	M.p. (°C)	Lit. m.p.[a] (°C)
CH_2Ph	Benzaldehyde	72	235—236	237
$CH_2C_6H_4Cl$-*p*	*p*-Chlorobenzaldehyde	76	264	266
$CH_2C_6H_4Me$-*p*	*p*-Tolualdehyde	70	232—233	232.5—234.5
Bu	Butyraldehyde	60	121	123
CH_2CH_2Ph	Benzaldehyde and Phenylacetaldehyde (2 : 1) [b]	65	*ca.* 220 [c]	
$CH_2CH_2C_6H_4Cl$-*p*	*p*-Chlorobenzaldehyde	62	262	

[a] Dictionary of Organic Compounds (4th edn)., 1965, pp. 322, 599, 3075, 500. [b] Approximate ratio determined by ^1H n.m.r. (aldehydic proton). [c] Mixture. [d] Yields quoted are of aldehydes obtained from the ether soluble fraction (and do not include aldehydes obtained from ether insoluble fraction).



Scheme 1



Scheme 2

the cyclohexyl derivative (3h) gave no detectable cyclohexanone.

Experimental

M.p.s were measured on a Reichert hot-stage microscope and are uncorrected. Elemental analyses were carried out at University of East Anglia using a Carlo Erba Model 1106 elemental analyser. I.r. spectra were recorded on a Perkin-Elmer 297 spectrophotometer. ^1H N.m.r. spectra were recorded on a Perkin-Elmer R 12 (60 MHz), Varian HA-100 (100 MHz), and Jeol FX-100 Fourier transform (100 MHz) n.m.r. spectometers, using $SiMe_4$ as internal standard.

2-Ethoxycarbonyl-4,6-diphenylpyrylium Tetrafluoroboate.[6]—This compound (30%) had m.p. 155—157 °C (lit.,[6] m.p. 155—157 °C).

2-Ethoxycarbonyl-4-(p-tolyl)-6-phenylpyrylium Tetrafluoroborate.—4-Methylchalcone [7] (8 g, 36 mmol), ethyl pyruvate (3.0 g, 26 mmol), and boron trifluoride–diethyl ether (45%, 12 ml) were heated at 100 °C for 15 min. Addition of diethyl ether precipitated the tetrafluoroborate (4 g, 38%), which crystallized from absolute ethanol as bright yellow needles, m.p. 155—157 °C (Found: C, 61.9; H, 4.6. $C_{21}H_{19}BF_4O_3$ requires C, 62.0; H, 4.7%), $\nu_{max.}$ ($CHBr_3$) 1 750, 1 630, 1 600, and 1 050 cm^{-1}; δ (60 MHz, $CDCl_3$) 1.52 (3 H, t), 2.52 (3 H, s), 4.65 (2 H, q), and 7.45—8.95 (9 H, m).

General Method for the Preparation of 1-Substituted 2-Ethoxycarbonyl-4,6-diarylpyridinium Tetrafluoroborates.—To a suspension of the pyrylium ester (3 mmol) in CH_2Cl_2 (15 ml) was added the appropriate amine (4.5 mmol) dropwise. After *ca.* 60 min ether was added. The precipitated pyridinium salts were recrystallized from ethanol (Table 1).

General Method for the Preparation of 1-Substituted 2-Hydrazidocarbonyl-4,6-diarylpyridinium Tetrafluoroborates (2).

—To the 1-substituted 2-ethoxycarbonyl-4,6-diarylpyridinium tetrafluoroborate (4.2 mmol) in ethanol (10 ml) at 70 °C was added dropwise hydrazine hydrate (6—8 mmol). The mixture was refluxed for 1.5 h after which the solvent was removed and the residue triturated with ether (2 × 15 ml) and then taken up in a small quantity of ethanol (*ca.* 2 ml). Diethyl ether precipitated the 2-hydrazido-salts which were recrystallized from ethanol (Table 2).

General Method for the Preparation of 1-*Substituted* 2-*Azidocarbonyl*-4,6-*diarylpyridinium Tetrafluoroborates* (3).—To the substituted 2-hydrazidocarbonyl-4,6-diarylpyridinium tetrafluoroborate (2.5 mmol) in acetonitrile (10 ml) was added sodium nitrite (4—5 mmol). The mixture was cooled to 0 °C and 1.5 ml of 4M-HCl (200 mg, *ca.* 4.5 mmol) was added dropwise; it was then stirred for 1—2 h at 0 °C. Solvent was removed at 20 °C/20 mmHg, the residue was extracted with CH_2Cl_2, and the extracts washed with water (2 × 15 ml) and dried ($MgSO_4$). Removal of the solvent and addition of diethyl ether (10 ml) gave the azido tetrafluoroborates (Table 3). (In irradiation experiments, the CH_2Cl_2 solution of the azidocarbonyl compounds was used directly.)

2-*Phenylcarbamido*-4,6-*diphenylpyridine*.—To 1-benzyl-4,6-diphenylpyridine-2-carboxylate (1 g, 3 mmol) in CH_2Cl_2 (10 ml) was added thionyl chloride (700 mg, *ca.* 6 mmol). The mixture was refluxed for 15 min after which it was cooled and aniline (730 mg, 3 mmol) added; the mixture was then stirred for 2 h. Removal of the solvent at 30 °C/20 mmHg gave 2-phenylcarbamido-4,6-diphenylpyridine which crystallized from EtOH (590 mg, 60%), m.p. 96—98 °C (Found: C, 83.1; H, 5.1; N, 7.9. $C_{24}H_{18}N_2O$ requires C, 83.3; H, 5.1; N, 8.0%), $\nu_{max.}$ ($CHBr_3$) 3 340, 1 660, and 1 600 cm^{-1}; δ ($CDCl_3$) 8.32 (1 H, d) 7.36—7.52 (8 H, m), 7.60—7.76 (5 H, m), and 7.88—8.10 (4 H, m).

General Method for the Photolysis of 1-*Substituted* 2-*Azidocarbonyl*-4,6-*diphenylpyridinium Tetrafluoroborates*.—A solution of the azidocarbonylpyridinium salt (3) (2 mmol) in dichloromethane (80 ml) was irradiated (12 h or 1 h) in an immersion vessel photolysis apparatus using a 125-W medium-pressure mercury lamp. The solvent was removed and the residue extracted with diethyl ether (2 × 15 ml).

Diethyl Ether-soluble Fraction.—Diethyl ether was removed at 20 °C/15 mmHg and the residue obtained was taken up in ethanol (3—4 ml). A known proportion of the ethanolic solution was treated with an acidic solution of 2,4-dinitrophenylhydrazine in MeOH to give the corresponding aldehyde derivatives (see Table 4).

From the remaining ethanolic solution 2-*carbamoyl*-4,6-*diphenylpyridine* (10) crystallized, m.p. 210—212 °C (Found: C, 78.6; H, 5.3; N, 10.3. $C_{18}H_{14}N_2O$ requires C, 78.8; H, 5.1; N, 10.3%), $\nu_{max.}$ ($CHBr_3$) 3 500, 1 680, 1 600, 1 540, 1 490, and 750 cm^{-1}; δ ($CDCl_3$) 5.9 (2 H, br s), 7.34—7.52 (5 H, m), 7.60—7.76 (3 H, m), 7.88—8.10 (3 H, m), and 8.32 (1 H, d). The mother-liquor after the pyridine (10) had been filtered off was evaporated and the residue subjected to g.c-m.s. (2 m 3% OV-1/Chromosorb W HP column, 270 °C, helium as the carrier gas; 15 ml/min) and identified as 2-carbamoyl-4,6-diphenylpyridine (10) (55—60%), 2-cyano-4,6-diphenylpyridine (8) (8%), and 2,4-diphenylpyridine (11) (25%).

Diethyl Ether-insoluble Residue.—To a methanolic solution of the residue (200 mg) was added 0.5M-NaOH (0.5 ml) and the mixture stirred at 25 °C. Solvent was removed (25 °C/15 mmHg) and the residue taken up in diethyl ether (30 ml); the solution was then washed with water and dried ($MgSO_4$). On removal of the solvent, the residue was taken up in ethanol and subjected to g.c.-m.s. (2 m 3% OV-1/Chromosorb W HP column, 270 °C; helium as the carrier gas; 15 ml/min), and identified as a mixture of 2-carbamoyl-4,6-diphenylpyridine (10) (64%), 2-cyano-4,6-diphenylpyridine (8) (5%), 2,4-diphenylpyridine (11) (18%) and the corresponding aldehyde (10—12%).

Acknowledgements

We thank the British Council for a maintenance grant and Dr. D. N. Rogers and Dr. R. C. Patel for discussions.

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Received 18*th January* 1982; *Paper* 2/085