Base-Catalyzed Rearrangement of N-(Aryloxy)pyridinium Salts. Effect of a 3-Substituent in the Pyridine Ring upon Orientation. Synthesis of Novel Tricyclic Rings

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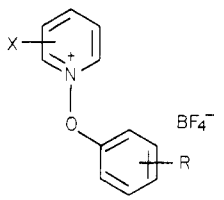
The orientation in the base-catalyzed rearrangement of 3-substituted N-(aryloxy)pyridinium tetrafluoroborates (5) to 2- or 6-(2-hydroxyaryl)pyridines has been studied. A 3-methyl group directs exclusively to the 6-position while inductively electron-withdrawing substituents (Cl, Br, I, OMe, CO_2Me, COMe) direct mainly, if not exclusively, to C-2. The phenols derived from 3-CO_2Me derivatives cyclize spontaneously to the substituted pyrido[3,2-*d*]coumarins (8) in useful yields, and that from the 3-COMe compound gives 10-hydroxy-10-methyl-6-nitropyrido[2,3-*d*]benzopyran (9). The 3-halo-2-(2-hydroxyaryl)pyridines cyclize to benzofuro[3,2-*b*]pyridines (10, 15) on heating with potassium hydroxide and copper powder. Authentic benzofuro[3,2-*b*]pyridine (12) is obtained by the Pschorr ring closure of the diazonium salt of 3-(*o*-aminophenoxy)pyridine (14). The substituent effects are explained mainly on the basis of the inductive effect of the substituent: steric effects play a slight role. A minor side reaction is thought to involve the intermediacy of free radicals.

N-(Aryloxy)pyridinium salts (1), first reported in 1971,[1]



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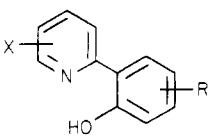

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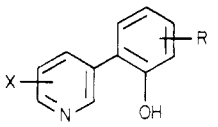

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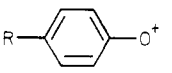

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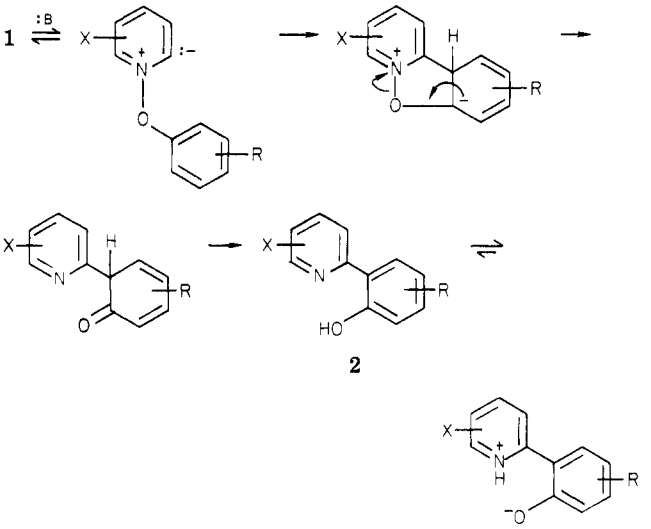
are proving to be valuable synthons, undergoing base-catalyzed rearrangement to 2-(*o*-hydroxyaryl)pyridines (2),[1,2] azide-catalyzed rearrangement to 3-(*o*-hydroxyaryl)pyridines (3),[3] and thermal heterolysis to yield aryloxenium ions (4).[1,4] We now report a study of the effect of 3-substituents in the pyridine ring upon the orientation of the base-catalyzed rearrangement of 1 and the use of some of the products formed in the synthesis of tricyclic heterocyclic compounds.

It has been shown[5,6] that pyridine 1-oxides and pyridinium salts undergo base-catalyzed proton abstraction under mild conditions, and this occurs most easily at the α positions. On that basis, it has been proposed[1,2] that the base-catalyzed rearrangement of 1 involves the initial abstraction of a proton followed by intramolecular nucleophilic attack by the arylcarbanion formed on the adjacent aromatic nucleus (Scheme I). We now report the effect of a 3-substituent in the pyridine ring upon the orientation of the rearrangement and the use of some of the products so formed in convenient syntheses of novel tricyclic systems.

The starting materials 1 were obtained from the corresponding N-oxide and an aryldiazonium tetrafluoroborate.[1,2] The rearrangements were usually carried out in dry acetonitrile, using potassium phenolate as the base. With a 3-substituted pyridine (5) two possible rearrangement products can result: 2-(*o*-hydroxyaryl)-3-substituted pyridine (6) and 2-(*o*-hydroxyaryl)-5-substituted pyridine (7). Table I summarizes the results obtained in these rearrangements.

Scheme I



The only isomer isolated from the rearrangement of 5 (X = Me) was the 2,5-disubstituted compound 7. Some *p*-nitrophenol was also formed in this and a number of other rearrangements, and this will be discussed later.

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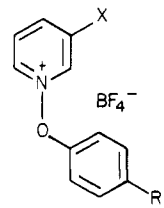

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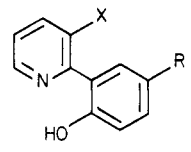

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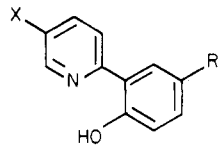

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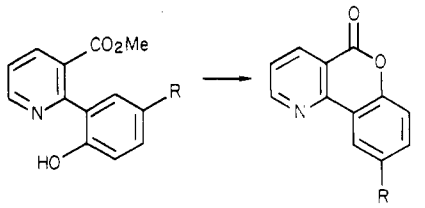
Assignment of the structure of 7 (R = NO_2, X = Me) was based on its NMR spectrum and, in particular, the 1 H doublet at δ 8.43 ($J_{4,6}$ = 1.2 Hz) attributed to the α proton in the pyridine ring (H-6). Base-catalyzed H–D exchange of 3-picoline methiodide in NaOD–D_2O at 26 °C was found to take place very slightly faster at C-2 than at C_6: $k_{H\text{-}2}{}^{26}/k_{H\text{-}6}{}^{26}$ = 1.2.[5] Reaction of 3-picoline 1-oxide with *n*-butyllithium in THF–ether at −65 °C followed by addition of cyclohexanone gave 6-(1-hydroxycyclohexyl)-3-picoline 1-oxide (25.1%) and the 2,6-dialkylated product (4.6%).[7] Preferential attack at C-6 was attributed to steric hindrance by the methyl group to the approach of the base to C-2–H in the plane of the ring. It seems likely, however, that the regiospecificity observed now owes a little to steric hindrance by the methyl group to the in-plane approach of phenoxide ion to C-2–H, but mostly to the electron-releasing effect of the 3-Me group, which is expected to influence C-2 more than C-6.[8] This is seen more clearly from the apparent lack of important steric effects exerted by a 3-Br, a 3-I, or a 3-CO_2Me group (vide infra).

A 3-halogen atom exerts exactly the opposite effect, leading to rearrangement mainly to the 2,3- rather than the 2,5-isomer (Table I). Again, orientations were assigned on the basis of NMR data. Base-catalyzed H–D exchange for 3-bromopyridine 1-oxide led[5] to the following pseudo-first-order rate constants: $k_{H\text{-}2}{}^{5}$ = 1.7 × 10^{-4} s^{-1}; $k_{H\text{-}6}{}^{50}$ = 3.9 × 10^{-5} s^{-1}; $k_{H\text{-}4}{}^{50}$ = 4.6 × 10^{-6} s^{-1}. A similar study[9] with 3-chloropyridine 1-oxide gave the following relative rates of exchange: 1-:6-:4- = 1840:12.2:0.37. Consequently, the regioselectivity (regiospecificity for X = Cl, I) is in accord with the above H–D data and with the electron-withdrawing character of the 3-halo substituent. It should be noted that since the carbanion is developing in the plane of the pyridine ring (eventually sp^2), inductive and field effects of substituents should be much more important than mesomeric effects, as has been found in the case of aryne formation.[10] This also accounts for the fact that a 3-methoxy group directs the rearrangement to C-2, albeit in relatively low yield (28%).

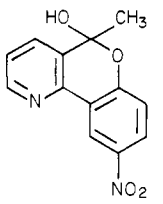
One would therefore expect an electron-withdrawing 3-methoxycarbonyl group to lead to rearrangement taking place at C-2,[5] and this is what is observed except that the expected 3-carbomethoxy-2-(2-hydroxy-5-R-phenyl)-pyridine (6, X = CO_2Me, R = NO_2 or CN) is not obtained. Instead, a 6-R-pyrido[3,2-*d*]coumarin (8, R = NO_2, CN) is formed in acceptable yields, obviously by lactonization of the phenolic ester. The structure of **8a** (R = NO_2) was confirmed by the presence of a lactone carbonyl band (1755 cm^{-1}) and by its NMR spectrum (see Experimental Section). The size of the attacking base did not play a role



8a, R = NO_2
b, R = CN

in this case as indicated by the fact that when 2,2,6,6-tetramethylpiperidine was used instead of phenoxide ion the yield of **8a** actually *increased* slightly (to 54.5%). This two-step process (from the corresponding pyridine 1-oxide) provides convenient access to the interesting tricyclic γ-lactones **8** (for a review of syntheses of pyrido[3,2-*d*]-coumarins, see ref 11). These compounds, not bearing any other substituents in the pyridine ring, do not appear to have been available before.

Attempts to O-arylate 3-benzoylpyridine 1-oxide failed. On the other hand, we were able to prepare 1-(*p*-nitrophenoxy)-3-acetylpyridinium tetrafluoroborate (**5**, R = NO_2, X = $COCH_3$) which, on rearrangement, gave a low yield (10.8%) of 10-hydroxy-10-methyl-6-nitropyrido[3,2-*d*]benzopyran (**9**), undoubtedly derived from the hemi-



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ketalization of **6** (X = $COCH_3$, R = NO_2). It exhibited ν_{OH} (unbonded) at 3520 cm^{-1} and ν_{OH} (bonded) at 3400–3020 cm^{-1} (br) but no band in the C=O stretching region.

The 3-halo-2-(*o*-hydroxyaryl)pyridines could be readily cyclized with potassium hydroxide and copper powder at elevated temperatures. For example, heating the potassium salt of **6** (R = NO_2, X = Br) with copper powder at 200 °C for 12 h gave a 70% yield of 7-nitrobenzofuro-[3,2-*b*]pyridine (**10**). The structure of the latter was confirmed by its NMR and mass spectra. It was reduced to the primary amine (**11**) with $SnCl_2$–HCl, and the latter diazotized and deaminated with hypophosphorus acid to give the parent benzofuro[3,2-*b*]pyridine (**12**). The latter was identical with an authentic sample prepared [together with benzofuro[2,3-*c*]pyridine (**13**)] by the Pschorr cyclization of the diazonium salt of 3-(2-aminophenoxy)pyridine (**14**, Scheme II). Compounds **12** and **13** could be distinguished from one another quite readily not only by the alternate route to **12** (but not **13**) but also by the characteristic quartet for the pyridine α proton in the NMR spectrum of **12**, δ 8.64 ($J_{4,6}$ = 1.4 Hz, $J_{5,6}$ = 4.9 Hz), and the absence of a singlet for the other pyridine α proton.

In a similar manner, the potassium salt of **6** (R = CN, X = Br) cyclized to give 7-cyanobenzofuro[3,2-*b*]pyridine (**15**, 60%). An attempt was made to use the technique developed by Roques et al.[12] to establish the position of substituents in heteroaromatic systems, using the Nuclear Overhauser Effect. The methiodide (**16**) of **15** was prepared, but irradiation of the *N*-methyl peak did not lead to any perceptible changes in the intensities of the aro-

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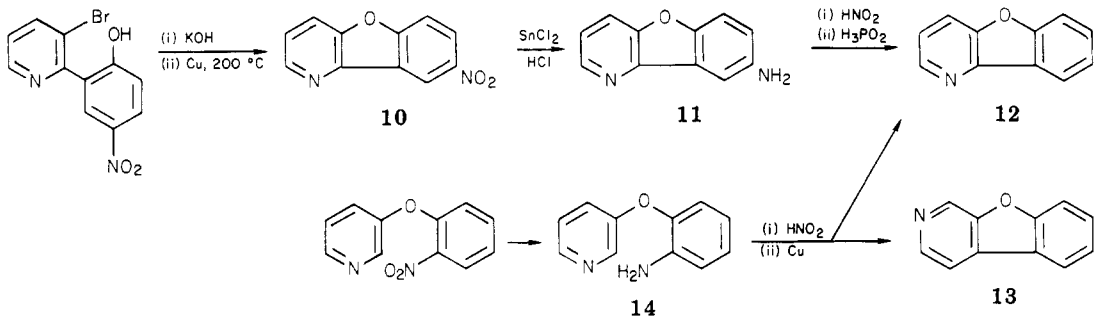
Table I. Base-Catalyzed Rearrangement of 5 to 6 and/or 7

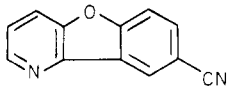
5		yield, %		
X	R	6	7	other products formed
Me	NO_2		52	*p*-nitrophenol (11%)
Cl	NO_2	60		*p*-nitrophenol (3.2%)
Br	NO_2	60	<1%	
Br	CN	68		
Br	3,5-$(NO_2)_2$	49		
I	NO_2	24		2-(2-hydroxy-5-nitrophenyl)pyridine (**6**, X = H, R = NO_2; 1%)
OMe	NO_2	28		*p*-nitrophenol (24.7%)
CO_2Me	NO_2 [a]			6-nitropyrido[3,2-*d*]coumarin (**8a**; 50.5%)
CO_2Me	CN			6-cyanopyrido[3,2-*d*]coumarin (**8b**; 49.2%)
COMe	NO_2			10-hydroxy-10-methyl-6-nitropyrido[2,3-*d*]benzopyran (**9**; 10.8%)

[a] Use of 2,2,6,6-tetramethylpiperidine as the base gave a 54.5% yield of **8a**.

Scheme II



matic C–H signals. The NMR spectra of **15** and **16** confirm unambiguously the structure proposed, however.



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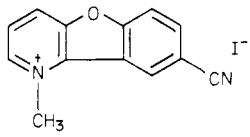

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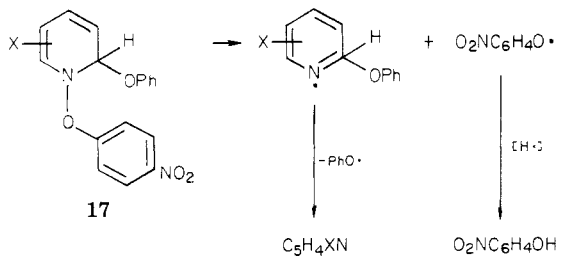
The potassium salts of 3-chloro- and 3-iodo-2-(2-hydroxy-5-nitrophenyl)pyridine also cyclized to **10** under similar conditions. This sequence thus provides a convenient three-step route to the benzofuro[3,2-*b*]pyridine system.

Some comments regarding the minor products formed in some of these reactions are warrented. In three of the examples studied (X = Me, Cl, OMe) small amounts of *p*-nitrophenol are formed as well (with X = OMe the yields of the two products are almost the same). This suggests that a homolytic process may be competing with the hydrogen-abstraction reaction, as was observed in the azide ion catalyzed reactions of **1**.[3] A possible pathway could involve the *addition* of phenoxide to **1** to give a dihydro derivative (**17**), which could then undergo homolysis. The



pyridine was not isolated, but no serious attempt was made to do so. The isolation of some 2-(2-hydroxy-5-nitrophenyl)pyridine (**6**, X = H, R = NO_2; identical with an authentic sample, confirmed by the preparation of the *O*-acetate) from the reaction with the 3-iodo derivative (**5**, X = I, R = NO_2) also suggests the intervention of a minor homolytic pathway, but none can be proposed at this time.

Experimental Section

Melting points are uncorrected. IR spectra were determined on a Perkin-Elmer 357 or a Beckman Acculab 3 instrument and NMR spectra on a Varian Associates HA-100 or 360 spectrometer with Me_4Si as internal standard. Mass spectra were determined on a Hitachi Perkin-Elmer RMU-6M instrument.

1-(Aryloxy)-3-substituted Pyridinium Tetrafluoroborates. General Procedure. The appropriate 3-substituted pyridine 1-oxide (0.01–0.03 mol) in dry acetonitrile was added to a stirred solution of the aryldiazonium tetrafluoroborate (0.01–0.03 mol) in acetonitrile (25–80 mL) at room temperature, stirred at room temperature for 4–12 h, and in some cases, then heated under reflux for 4–8 h. The solvent was evaporated to dryness and the pyridinium tetrafluoroborate recrystallized. In this manner the following were prepared:

3-Methyl-1-(*p*-nitrophenoxy)pyridinium tetrafluoroborate (70%): mp 126–127 °C (from MeOH).

Anal. Calcd for $C_{12}H_{11}N_2O_3BF_4$: C, 45.31; H, 3.49. Found: C, 45.41; H, 3.55.

3-Bromo-1-(*p*-nitrophenoxy)pyridinium tetrafluoroborate (60%): mp 155–156 °C (from MeOH); ^1H NMR (Me_2SO-d_6) δ 9.74 (s, 1 H, H_2), 9.24 (d, 1 H, $J_{5,6}$ = 7 Hz, H-6), 8.62 (d, 1 H, $J_{4,5}$ = 8 Hz, H-4), 7.83 (t, 1 H, $J_{4,5}$ = 8 Hz $\simeq$ $J_{5,6}$ = 7 Hz, H-5), 7.85 (d, 2 H, $J_{\alpha\beta}$ = 9 Hz, H_α), 7.00 (d, 2 H, $J_{\alpha\beta}$ = 9 Hz, H_β).

Anal. Calcd for $C_{11}H_8BrN_2O_3BF_4$: C, 34.50; H, 2.09. Found: C, 34.47; H, 2.14.

3-Bromo-1-(*p*-cyanophenoxy)pyridinium tetrafluoroborate (88%): mp 179–181 °C (MeOH); IR (KBr) 2250 cm^{-1} (C≡N).

Anal. Calcd for $C_{12}H_8Br\ N_2OBF_4$: C, 39.67; H, 2.20. Found: C, 39.48; H, 2.29.

3-Bromo-1-(3,5-dinitrophenoxy)pyridinium tetrafluoroborate (57%, mp 156–158 °C) was prepared in freshly distilled sulfolane and heated at 100 °C for 30 min. Addition of ether followed by methanol–ethyl acetate (1:20 v/v) and trituration give a yellow solid (68%), which was purified by dissolving it in acetonitrile, treating with activated carbon, filtering, and adding dry ether until the turbidity persisted. The salt crystallized from this solution at 0 °C; IR (KBr) 1545, 1351 (NO_2), 1100 cm^{-1} (BF_4^-).

Anal. Calcd for $C_{11}H_7BrN_3O_5BF_4$: C, 30.84; H, 1.67; N, 9.81. Found: C, 30.99; H, 1.67; N, 9.76.

3-Chloro-1-(*p*-nitrophenoxy)pyridinium tetrafluoroborate (41.4%): mp 132–133 °C (from acetonitrile–ether (1:3 v/v)).

Anal. Calcd for $C_{11}H_8ClN_2O_3BF_4$: C, 38.99; H, 2.36; N, 8.27. Found: C, 38.66; H, 2.37; N, 8.14.

3-Iodo-1-(*p*-nitrophenoxy)pyridinium tetrafluoroborate (29%): mp 159–165 °C (sublimation); IR (KBr) 1520, 1350 (NO_2), 1130–1030 cm^{-1} (BF_4^-).

Anal. Calcd for $C_{11}H_8IN_2O_3BF_4$: C, 30.70; H, 1.86; N, 6.51. Found: C, 30.97; H, 2.02; N, 6.49.

3-Methoxy-1-(*p*-nitrophenoxy)pyridinium tetrafluoroborate (54.4%): mp 148–149 °C (from acetonitrile–ether (1:3)).

Anal. Calcd for $C_{12}H_{11}N_2O_4BF_4$: C, 43.11; H, 3.29; N, 8.38. Found: C, 43.44; H, 3.34; N, 8.29.

3-Carbomethoxy-1-(*p*-nitrophenoxy)pyridinium tetrafluoroborate (41.5%; from acetonitrile–ether (2:1)): mp 126–127 °C; mass spectrum, *m/e* 322 ($M^{+\cdot}$ – 2HF), 274 ($M^{+\cdot}$ – HBF_4), 138 ($NO_2C_6H_4O^{+\cdot}$).

Anal. Calcd for $C_{13}H_{11}N_2O_5BF_4$: C, 43.09; H, 3.04. Found: C, 43.20; H, 3.10.

3-Carbomethoxy-1-(*p*-cyanophenoxy)pyridinium tetrafluoroborate (57%): mp 150–151 °C (MeOH); IR (KBr) 2210 (C≡N), 1730 cm^{-1} (C=O).

Anal. Calcd for $C_{14}H_{11}N_2O_3BF_4$: C, 49.12; H, 3.22. Found: C, 49.22; H, 3.25.

3-Acetyl-1-(*p*-nitrophenoxy)pyridinium tetrafluoroborate (62.1%): mp 149–150 °C; (from acetonitrile–ether (1:1)); IR (KBr) 1700 (C=O), 1510, 1335 (NO_2), 1140–1000 cm^{-1} (BF_4^-).

Anal. Calcd for $C_{13}H_{11}N_2O_4BF_4$: C, 45.08; H, 3.18. Found: C, 44.88; H, 3.27.

2-(2-Hydroxy-5-nitrophenyl)-5-methylpyridine (7, X = Me, R = NO_2). A solution of 3-methyl-1-(*p*-nitrophenoxy)pyridinium tetrafluoroborate (1.27 g) and potassium phenoxide (0.63 g) in acetonitrile (20 mL) was heated under reflux for 12 h. The solvent was evaporated to dryness, and the residue was treated with 2 N hydrochloric acid (20 mL). Extraction with chloroform (3 × 30 mL) and evaporation of the dried ($MgSO_4$) $CHCl_3$ extracts left a residue (0.65 g) that was chromatographed on a column of silica gel (2.4 × 18 cm). Elution with benzene (300 mL) gave 2-(2-hydroxy-5-nitrophenyl)-5-methylpyridine (0.49 g, 52%): mp 183 °C (EtOH); IR (KBr) 2600 ($^+$NH=), 1490, 1340 cm^{-1} (NO_2); ^{1}H NMR ($CDCl_3$) δ 8.82 (d, 1 H, J_{BC} = 3 Hz, H_C (*o* to NO_2)), 8.43 (d, 1 H, $J_{4,6}$ = 1.2 Hz, H-6), 8.25 (dd, 1 H, J_{AB} = 9 Hz, J_{BC} = 3 Hz, H_B (*o'* to NO_2)), 7.90 (m, 2 H, H_3, H_4), 7.08 (d, 1 H, J_{AB} = 9 Hz, H_A (*m* to NO_2)), 2.45 (s, 3 H, CH_3); mass spectrum, *m/e* 230 ($M^{+\cdot}$, 100), 200 ($M^{+\cdot}$ – NO).

Anal. Calcd for $C_{12}H_{10}N_2O_3$: C, 62.61; H, 4.38. Found: C, 62.52; H, 4.48.

Elution with benzene–chloroform (4:1, v/v) gave *p*-nitrophenol (0.07 g, 11%): mp 114 °C; identical (IR) with an authentic sample.

3-Chloro-2-(2-hydroxy-5-nitrophenyl)pyridine (6, X = Cl, R = NO_2). 3-Chloro-1-(*p*-nitrophenoxy)pyridinium tetrafluoroborate (1.69 g) and potassium phenoxide (1 g) in dry acetonitrile (20 mL) were boiled under reflux for 4 h. The solvent was evaporated and the residue brought to pH 3 with dilute HCl. It was extracted with chloroform (4 × 50 mL), and the extracts were dried ($MgSO_4$) and evaporated. The residue was recrystallized from ethanol to give 3-chloro-2-(2-hydroxy-5-nitrophenyl)pyridine (0.75 g, 60%): mp 161 °C; ^{1}H NMR ($CDCl_3$) δ 9.26 (d, 1 H, $J_{B,C}$ = 3 Hz, H_C), 8.5 (dd, 1 H, $J_{5,6}$ = 5 Hz, $J_{4,6}$ = 1 Hz, H-6), 8.17 (dd, 1 H, $J_{A,B}$ = 9 Hz, $J_{B,C}$ = 3 Hz, H_B), 7.96 (dd, 1 H, $J_{4,5}$ = 7 Hz, $J_{4,6}$ =1 Hz, H-4), 7.30 (dd, 1 H, $J_{4,5}$ = 7 Hz, $J_{5,6}$ = 5 Hz, H-5), 7.03 (d, 1 H, J_{AB} = 9 Hz, H_A).

Anal. Calcd for $C_{11}H_7ClN_2O_3$: C, 52.70; H, 2.82. Found: C, 52.74; H, 2.83.

The ethanol filtrate was chromatographed on a column of silica gel. Elution with $CHCl_3$ gave *p*-nitrophenol (3.2%), identical (mp, mmp, IR) with an authentic sample. No other product was isolated.

Rearrangement of 3-Bromo-1-(*p*-nitrophenoxy)-pyridinium Tetrafluoroborate. A solution of the salt (2.30 g) was rearranged as above for the chloro compound. The product (1.47 g) was chromatographed on a silica gel column. Elution with light petroleum (bp 30–60 °C)–benzene (1:1, v/v) gave 5-bromo-2-(2-hydroxy-5-nitrophenyl)pyridine (4 mg, <1%): mp 225 °C (EtOH); IR (KBr) 2600 ($^+$NH=), 1520, 1350 cm^{-1} (NO_2); ^{1}H NMR ($CDCl_3$) δ 9.00 (d, 1 H, $J_{4,6}$ = 2 Hz, H-6), 8.80 (m, 2 H, H-4 and H_C), 8.45 (m, 2 H, H-3 and H-8), 7.34 (d, 1 H, J_{AB} = 9 Hz, H_A); mass spectrum, *m/e* 296, 294 ($M^{+\cdot}$), 266, 264 ($M^{+\cdot}$ – NO), 250, 248 ($M^{+\cdot}$ – NO_2).

Anal. Calcd for $C_{11}H_7BrN_2O_3$: C, 44.75; H, 2.38. Found: C, 44.80; H, 2.47.

Elution with benzene (300 mL) gave 3-bromo-2-(2-hydroxy-5-nitrophenyl)pyridine (1.06 g, 60%): mp 165 °C (EtOH); IR (KBr) 2600 ($^+$NH=), 1520, 1350 cm^{-1} (NO_2); ^{1}H NMR ($CDCl_3$) δ 9.24 (d, 1 H, J_{BC} = 3 Hz, H_C), 8.52 (dd, 1 H, $J_{5,6}$ = 5.5 Hz, $J_{4,6}$ = 1.6 Hz, H-6), 8.17 (dd, 1 H, J_{AB} = 9 Hz, J_{BC} = 3 Hz, H_B), 8.10 (dd, 1 H, $J_{4,6}$ = 1.6 Hz, $J_{4,5}$ = 7 Hz, H-4), 7.22 (dd, 1 H, $J_{4,5}$ = 7 Hz, $J_{5,6}$ = 5.5 Hz, H-5), 7.05 (d, 1 H, J_{AB} = 9 Hz, H_A); mass spectrum, *m/e* 296, 294 ($M^{+\cdot}$), 280, 278 ($M^{+\cdot}$ – O), 266, 264 ($M^{+\cdot}$ – NO), 250, 248 ($M^{+\cdot}$ – NO_2), 222, 220 ($M^{+\cdot}$ – NO_2 – CO).

Anal. Calcd for $C_{11}H_7BrN_2O_3$: C, 44.75; H, 2.38. Found: C, 44.69; H, 2.44.

3-Bromo-2-(5-cyano-2-hydroxyphenyl)pyridine (6, X = Br, R = CN). The reaction was carried out as above, using 3-bromo-1-(*p*-cyanophenoxy)pyridinium tetrafluoroborate (1.82 g) and potassium phenoxide (0.79 g). The acidified mixture was stirred with hot chloroform (70 mL), the layers separated, and the aqueous layer was extracted with $CHCl_3$ (2 × 50 mL). The dried ($MgSO_4$) combined organic extracts were evaporated to give the product (1.1 g, 82%), mp 176–179 °C. Recrystallization from ethanol gave pure 3-bromo-2-(5-cyano-2-hydroxyphenyl)pyridine (0.84 g, 68%): mp 178–180 °C; IR (KBr) 2600 ($^+$NH=), 2245 cm^{-1} (C≡N); ^{1}H NMR ($CDCl_3$) δ 8.65 (dd, 1 H, $J_{5,6}$ = 5 Hz, $J_{4,6}$ = 2 Hz, H_6), 8.60 (d, 1 H, J_{BC} = 2.5 Hz, H_C), 8.28 (dd, 1 H, $J_{4,5}$ = 8 Hz, $J_{4,6}$ = 2 Hz, H-4), 7.68 (dd, 1 H, J_{BC} = 2.5 Hz, J_{AB} = 9 Hz, H_B), 7.30 (dd, 1 H, $J_{4,5}$ = 8 Hz, $J_{5,6}$ = 5 Hz, H-5), 7.18 (d, 1 H, J_{AB} = 9 Hz, H_A).

Anal. Calcd for $C_{12}H_7BrN_2O$: C, 52.37; H, 2.55. Found: C, 52.26; H, 2.68.

3-Bromo-2-(4,6-dinitro-2-hydroxyphenyl)pyridine. The oily product, obtained from 3-bromo-1-(3,5-dinitrophenoxy)pyridinium tetrafluoroborate (1.07 g) in the usual manner, was chromatographed on a column of silica gel (60 g). Elution with benzene–chloroform (30:70, v/v) gave a dark yellow oil (0.46 g), which was dissolved in ethyl acetate (4 mL), decolorized with charcoal, and added dropwise with vigorous stirring to petroleum ether (bp 30–60 °C, 30 mL). The yellow solid was filtered and recrystallized from ether–petroleum ether (bp 30–60 °C, 1:1, v/v) to give the product (0.42 g, 49%): mp 98.5–99.5 °C: IR (KBr) 2600 (=N$^+$H), 1525, 1340 cm^{-1} (NO_2); ^{1}H NMR (CH_3OD) δ 8.76 (dd, 1 H, $J_{5,6}$ = 5 Hz, $J_{4,6}$ = 1.4 Hz, H-6), 8.58 (d, 1 H, J_{AB} = 2.8 Hz, H_B), 8.35 (dd, 1 H , $J_{4,6}$ = 1.4 Hz, H-4), 8.22 (d, 1 H, J_{AB} = 2.8 Hz, H_A), 7.55 (dd, 1 H, $J_{4,5}$ = 8 Hz, $J_{5,6}$ = 5 Hz, H-5).

Anal. Calcd for $C_{11}H_6BrN_3O_5$: C, 38.83; H, 1.77. Found: C, 38.94; H, 1.84.

2-(2-Hydroxy-5-nitrophenyl)-3-iodopyridine (6, X = I, R = NO_2). The pyridinium salt (6.45 g) was rearranged as before, the acidic solution extracted wtih chloroform (3 × 100 mL), and the dried ($MgSO_4$) solution evaporated. The residue was chromatographed on a column of silica gel. Elution with benzene–ether (1:2, v/v) gave 2-(2-hydroxy-5-nitrophenyl)-3-iodopyridine (0.93 g, 24%), mp 157–158 °C.

Anal. Calcd for $C_{11}H_7IN_2O_3$: C, 38.63; H, 2.06. Found: C, 38.43; H, 2.10.

The acetate was prepared by treating the above phenol with acetic anhydride (60 °C, 2 h) and obtained as colorless crystals (50.5%): mp 94–95 °C (petroleum ether); IR (KBr) 1775 (C=O), 1530, 1353 cm^{-1} (NO_2); ^{1}H NMR ($CDCl_3$) δ 8.65 (dd, 1 H, $J_{5,6}$ = 4 Hz, $J_{4,6}$= 2 Hz, H-6).

Anal. Calcd for $C_{13}H_9IN_2O_4$: C, 40.66; H, 2.36. Found: C, 40.68; H, 2.36.

Further elution gave 2-(2-hydroxy-5-nitrophenyl)pyridine (0.027 g, 1%), identical with an authentic sample.[2] The acetate has mp 92–93 °C.

Anal. Calcd for $C_{13}H_{10}N_2O_4$: C, 60.52; H, 3.91. Found: C, 60.45; H, 3.90.

Rearrangement of 3-Carbomethoxy-1-(*p*-nitrophenoxy)-pyridinium Tetrafluoroborate. The salt (1.09 g) was rearranged as usual. After extraction of the acidic solution with $CHCl_3$, the pH of the aqueous layer was adjusted to 10–11 and the solution extracted with $CHCl_3$ (3 × 20 ml). The combined extracts were dried ($MgSO_4$) and evaporated. The residue was chromatographed on a silica gel column. Elution with ethanol gave 6-nitropyrido[3,2-*d*]coumarin (**8a**) (0.367 g, 50.5%): mp 186–187 °C; IR (KBr) 1755 (C=O), 1525, 1340 cm^{-1} (NO_2); NMR (Me_2SO-d_6) δ

9.10 (dd, 1 H, $J_{5,6}$ = 4.6 Hz, $J_{4,6}$ = 1.3 Hz, H-6), 9.03 (d, 1 H, J_{BC} = 3 Hz, H_C), 8.54 (dd, 1 H, $J_{4,6}$ = 1.3 Hz, $J_{4,5}$ = 7.8 Hz, H-4), 8.40 (dd, 1 H, J_{AB} = 9 Hz, J_{BC} = 3 Hz, H_B), 7.78 (dd, 1 H, $J_{5,6}$ = 4.6 Hz, $J_{4,5}$ = 7.8 Hz, H-5), 7.60 (d, 1 H, J_{AB} = 9 Hz, H_A).

Anal. Calcd for $C_{12}H_6N_2O_4$: C, 59.50; H, 2.48. Found: C, 59.49; H, 2.56.

When the above rearrangement was carried out with 2,2,6,6-tetramethylpiperidine (1 equiv) instead of potassium phenoxide as base, but under otherwise identical conditions, **8a** was obtained together with much tar.

6-Cyanopyrido[3,2-*d*]coumarin. 3-Carbomethoxy-(1-*p*-cyanophenoxy)pyridinium tetrafluoroborate (0.684 g) was rearranged as above to give 6-cyanopyrido[3,2-*d*]coumarin (0.221 g, 49.2%): mp 212–214 °C ($CHCl_3$); IR (KBr) 2225 (C≡N), 1730 cm^{-1} (C=O); ^1H NMR (CH_3NO_2 + 5 drops of CF_3CO_2H) δ 9.53–9.30 (m, 2 H, H_4, H_6), 9.02 (d, 1 H, J_{BC} = 2 Hz, H_C), 8.63–8.12 (m, 2 H, H-5, H_B), 7.70 (d, 1 H, J_{AB} = 9 Hz, H_A).

Anal. Calcd for $C_{13}H_6N_2O_2$: C, 70.27, H, 2.72. Found: C, 70.24; H, 2.72.

10-Hydroxy-10-methyl-6-nitropyrido[3,2-*d*]benzopyran (9). 3-Acetyl-1-(*p*-nitrophenoxy)pyridinium tetrafluoroborate (1.73 g) was rearranged as usual. The acidic solution was extracted with chloroform (2 × 50 mL), and the extract was dried ($MgSO_4$) and evaporated. The residue was cooled at 0 °C overnight and washed with ether to give **9** (0.14 g, 10.8%): mp 178–179 °C; IR ($CHCl_3$) 3520 (s), 3400–3020 (br, OH), 1520, 1360 cm^{-1} (NO_2); ^1H NMR (Me_2SO-d_6) δ 9.10 (d, 1 H, J_{BC} = 3 Hz, H_C), 8.80 (dd, 1 H, $J_{5,6}$ = 5 Hz, $J_{4,6}$ = 1 Hz, H-6), 8.30 (dd, 1 H, J_{AB} = 9 Hz, J_{BC} = 3 Hz, H_B), 8.10 (dd, 1 H, $J_{4,5}$ = 8 Hz, $J_{4,6}$ = 1 Hz, H-4), 7.85 (s, 1 H, OH, exchangeable with D_2O), 7.56 (dd, $J_{4,5}$ = 8 Hz, $J_{5,6}$ = 5 Hz, H-5), 7.26 (d, 1 H, J_{AB} = 9 Hz, H_A), CH_3 band overlaps band of Me_2SO.

Anal. Calcd for $C_{13}H_{10}N_2O_4$: C, 60.46; H, 3.87; N, 10.85. Found: C, 60.20; H, 3.95; N, 10.61.

7-Nitrobenzofuro[3,2-*b*]pyridine (10). A finely ground mixture of 3-bromo-2-(2-hydroxy-5-nitrophenyl)pyridine (0.443 g) and potassium hydroxide (0.084 g) was heated under vacuum at 100 °C for 3 h. Copper powder (0.10 g, 150 mesh) was added, and the mixture was heated in a Fischer-Porter tube at 200 °C for 12 h. Aqueous potassium carbonate (5%, 20 mL) was added and the mixture extracted with chloroform. Evaporation of the dried ($MgSO_4$) chloroform extracts gave 7-nitrobenzofuro[3,2-*b*]pyridine (0.225 g, 70%): mp 224–225 °C (EtOH); IR (KBr) 1525, 1355 cm^{-1} (NO_2); ^1H NMR (Me_2SO-d_6) δ 8.90 (d, 1 H, J_{BC} = 2.4 Hz, H_C), 8.70 (d, 1 H, $J_{5,6}$ = 5 Hz, H_6), 8.50 (dd, 1 H, J_{AB} = 9 Hz, J_{BC} = 2.4 Hz, H_B), 8.28 (d,1 H, $J_{4,5}$ = 7.5 Hz, H-4), 8.00 (d, 1 H, J_{AB} = 9 Hz, H_A), 7.60 (dd, 1 H, $J_{4,5}$ = 7.5 Hz, $J_{5,6}$ = 5 Hz, H-5); mass spectrum, *m/e* 214 ($M^{+\cdot}$), 198 ($M^{+\cdot}$ – O), 184 ($M^{+\cdot}$ – NO), 168 ($M^{+\cdot}$ – NO_2).

Anal. Calcd for $C_{11}H_6N_2O_3$: C, 61.69; H, 2.82. Found: C, 61.65; H, 2.87.

The same product was obtained from either the 3-chloro or the 3-iodo compound under essentially the same conditions.

7-Aminobenzofuro[3,2-*b*]pyridine (11). 7-Nitrobenzofuro-[3,2-*b*]pyridine (0.428 g), stannous chloride (2 g), and dilute HCl (20 mL) were heated under reflux for 2 h. The clear reaction mixture was cooled and made alkaline with 30% aqueous NaOH solution (100 mL). Extraction with ether (3 × 100 mL) and evaporation of the dried ($MgSO_4$) ethereal extracts afforded a yellow residue, which on recrystallization from ethyl acetate (10 mL) yielded 7-aminobenzofuro[3,2-*b*]pyridine as pale yellow needles (0.248 g, 67.3%): mp 164–165.5 °C; IR (KBr) 3340, 3200 cm^{-1} (NH_2); ^1H NMR ($CDCl_3$) δ 8.61 (dd, 1 H, $J_{5,6}$ = 5 Hz, $J_{4,6}$ = 1.1 Hz, H-6), 7.80 (dd, 1 H, $J_{4,6}$ = 1.1 Hz, $J_{4,5}$ = 7.8 Hz, H-4), 7.55–7.25 (m, 3 H, H-5, H_A, H_C), 6.94 (dd, 1 H, J_{AB} = 9.5 Hz, J_{BC} = 2.5 Hz, H_B), 4.3–3.5 (br s, 2 H, NH_2); mass spectrum, *m/e* 184 ($M^{+\cdot}$), 183 ($M^{+\cdot}$ – H), 168 ($M^{+\cdot}$ – O).

Anal. Calcd for $C_{11}H_8N_2O$: C, 71.75; H, 4.35. Found: C, 71.78; H, 4.42.

Benzofuro[3,2-*b*]pyridine by Deamination of 11. 7-Aminobenzofuro[3,2-*b*]pyridine (0.147 g) was diazotized with 5 N hydrochloric acid (1 mL) and sodium nitrite (0.069 g), and the orange solution was added dropwise into 50% hypophosphorus acid (5 mL). Immediate evolution of nitrogen occurred, and the flask was stoppered loosely and placed in the refrigerator overnight. The mixture was made alkaline with sodium carbonate and extracted with ether (3 × 25 mL). The ethereal extracts were dried (Na_2SO_4) and evaporated under reduced pressure at room temperature to give benzofuro[3,2-*b*]pyridine (**12**), mp 58–60 °C. Recrystallization from light petroleum (bp 30–60 °C) afforded pale yellow needles (0.109 g, 79.7%): mp 61 °C; ^1H NMR (CCl_4) δ 8.64 (dd, 1, $J_{4,6}$ = 1.4 Hz, $J_{5,6}$ = 4.8 Hz, H-6), 8.34 (dd, 1, J_{BD} = 1.5 Hz, J_{CD} = 5.1 Hz, H_D), 7.82 (dd, 1, $J_{4,5}$ = 8.5 Hz, $J_{4,6}$ = 1.4 Hz, H-4), 7.59 (m, 3, H_A, H_B, H_C), 7.31 (dd, 1, $J_{4,5}$ = 8.5 Hz, $J_{5,6}$ = 4.8 Hz, H-5); mass spectrum, *m/e* 169 ($M^{+\cdot}$); picrate mp 190.5–192 °C. The compound was identical with the sample made by the Pschorr cyclization as described below.

3-(*o*-Nitrophenoxy)pyridine. 3-Hydroxypyridine (5 g) and potassium hydroxide (3 g) were dissolved in water, and the solution was evaporated to dryness. *o*-Bromonitrobenzene (15 g) was added, and the mixture was heated at 140 °C (oil bath, air condenser). After 30 min a vigorous reaction took place that caused the mixture to boil. Heating at 140 °C was continued for a further 2.5 h, and the temperature was then raised to 180 °C and kept there for 2 h. The cooled mass was transferred to a Soxhlet thimble and extracted continuously with ether. The extract was dried ($MgSO_4$), evaporated, and distilled under vacuum, the fraction with bp 148–152 °C (0.42 mmHg) being collected as 3-(*o*-nitrophenoxy)pyridine (2.7 g). The picrate (EtOH) had mp 156–157 °C.

Anal. Calcd for $C_{11}H_8N_2O_3 \cdot C_6H_3N_3O_7$: C, 45.84; H, 2.49. Found: C, 46.06, H, 2.44.

3-(*o*-Aminophenoxy)pyridine (14). This was prepared by catalytic reduction of the nitro compound (5 g) with H_2 over Raney Ni: bp 108–110 °C (0.03 mm).

Anal. Calcd for $C_{11}H_{10}NO$: C, 70.55; H, 5.41. Found: C, 70.76; H, 5.55.

Benzofuro[3,2-*b*]pyridine from 14. The amine (5.9 g) in concentrated sulfuric acid (10 mL) and water (60 mL) was diazotized at 0–5 °C with sodium nitrite (5.5 g) in water (20 mL). Stirring at 0 °C was continued for a further 0.5 h, urea (3 g) was then added, and the solution was filtered from a small amount of tar. The filtrate was boiled under reflux for 4 h, cooled, and extracted with ether, and the aqueous layer was basified and extracted with ether again. This latter extract was dried ($MgSO_4$) and evaporated, and the residual oil (2.3 g) was chromatographed on a column of basic alumina (60 g). Elution with benzene gave a colorless, pleasant smelling oil (0.47 g), which solidified. Recrystallization from petroleum ether (bp 40–60 °C) gave **12**, mp 61–62 °C. The picrate had mp 196–197 °C (EtOH).

Anal. Calcd for $C_{11}H_7NO$: C, 78.09; H, 4.17. Found: C, 78.48; H, 4.11.

Anal. Calcd for $C_{11}H_7NO \cdot C_6H_3N_3O_7$: C, 51.25; H, 2.51. Found: C, 51.35; H, 2.75.

Further elution with benzene gave benzofuro[2,3-*c*]pyridine (0.38 g): mp 69–70 °C; bp 94 °C (0.1 mmHg). The picrate (benzene) had mp 240–241 °C.

Anal. Calcd for $C_{11}H_7NO \cdot C_6H_3N_3O_7$: C, 51.25; H, 2.51. Found: C, 51.60; H, 2.83.

Elution with benzene–ether (2:1, v/v) gave a number of oils that were not characterized further.

7-Cyanobenzofuro[3,2-*b*]pyridine (15). A solution of 3-bromo-2-(5-cyano-2-hydroxyphenyl)pyridine (0.275 g) and potassium hydroxide (0.051 g) in methanol (20 mL) was heated under reflux for 1 h and the solvent removed under reduced pressure. Dry tetrahydrofuran (15 mL) was added to the residue, and again the solvent was removed under reduced pressure. Addition of dry THF and evaporation was repeated twice more to give an amorphous powder, which was transferred to a Fischer-Porter tube and heated to 200 °C with copper powder (0.040 g, 150 mesh) for 1 h. Aqueous potassium carbonate (5%, 50 mL) was added and the mixture extracted with chloroform (3 × 50 mL). The combined chloroform extracts were dried ($MgSO_4$) and evaporated to give a pale yellow residue, which was sublimed under low pressure (100–105 °C (2 mmHg)). The sublimate was recrystallized from ethanol to give 7-cyanobenzofuro[3,2-*b*]pyridine: mp 202–203 °C (0.116 g, 60%); IR (KBr) 2245 cm^{-1} (C≡N); ^1H NMR ($CDCl_3$) δ 8.80 (dd, 1 H, $J_{5,6}$ = 5 Hz, H-6), 8.62 (d, 1 H, J_{BC} = 2 Hz, H_C), 7.95–7.80 (m, 3 H, H_A, H_B, H-4), 7.50 (dd, 1 H, $J_{5,6}$ = 5 Hz, $J_{4,5}$ = 8 Hz, H-5); mass spectrum, *m/e* 194 ($M^{+\cdot}$), 167 ($M^{+\cdot}$ – HCN), 149 ($M^{+\cdot}$ – HCN – H_2O).

Anal. Calcd for $C_{12}H_6N_2O$: C, 74.22; H, 3.14. Found: C, 74.30; H, 3.12.

***N*-Methyl-7-cyanobenzofuro[3,2-*b*]pyridinium Iodide (16).** 7-Cyanobenzofuro[3,2-*b*]pyridine (0.097 g) and methyl iodide (0.213 g) were dissolved in benzene (30 mL) and heated in a Fischer-Porter tube at 100 °C for 3 days. The yellow crystals were filtered (0.165 g, 98%) and recrystallized from methanol (15 mL) to give yellow needles of *N*-methyl-7-cyanobenzofuro[3,2-*b*]-pyridinium iodide (0.147 g, 85.7%): mp 285–287 °C dec; IR (KBr) 2242 cm^{-1} (C≡N); ^1H NMR (CF_3COOH) δ 9.2–8.1 (m, 6 H), 5.03 (s, 3 H, CH_3); mass spectrum, *m/e* 194 ($M^{+\cdot} - CH_3I$).

Anal. Calcd for $C_{13}H_9IN_2O$: C, 46.43; H, 2.68. Found: C, 46.29; H, 2.74.

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Registry No. **5** (X = Me; R = NO_2), 69593-46-0; **5** (X = Cl; R = NO_2), 84499-14-9; **5** (X = Br; R = NO_2), 69593-44-8; **5** (X = Br; R = CN), 84499-16-1; **5** (X = Br; R = 3,5-$(NO_2)_2$), 84499-18-3; **5** (X = I; R = NO_2), 84499-20-7; **5** (X = OMe; R = NO_2), 84499-22-9; **5** (X = CO_2Me; R = NO_2), 63801-86-5; **5** (X = CO_2Me; R = CN), 84499-24-1; **5** (X = COMe; R = NO_2), 84499-26-3; **6** (X = Cl; R = NO_2), 84499-27-4; **6** (X = Br; R = NO_2), 83702-39-0; **6** (X = Br; R = CN), 84499-28-5; **6** (X = Br; R = 4,6-$(NO_2)_2$), 84520-42-3; **6** (X = I; R = NO_2), 84499-29-6; **6** (X = I; R = NO_2) acetate, 84499-30-9; **6** (X = OMe; R = NO_2), 84499-31-0; **6** (X = H; R = NO_2), 33400-82-7; **6** (X = H; R = NO_2) acetate, 84499-32-1; **7** (X = Me; R = NO_2), 84499-33-2; **7** (X = Br; R = NO_2), 84499-34-3; **8a**, 84499-35-4; **8b**, 84499-36-5; **9**, 84499-37-6; **10**, 67274-82-2; **11**, 84499-38-7; **12**, 54499-49-9; **12** picrate, 84499-39-8; **13**, 244-80-4; **13** picrate, 84558-13-4; **14**, 76167-49-2; **15**, 84499-40-1; **16**, 84499-41-2; 2,2,6,6-tetramethylpyridine, 768-66-1; *p*-nitrobenzenediazonium tetrafluoroborate, 456-27-9; *p*-cyanobenzenediazonium tetrafluoroborate, 2252-32-6; potassium phenoxide, 100-67-4; 3-hydroxypyridine, 109-00-2; *o*-bromonitrobenzene, 577-19-5; benzofuro[3,2-*b*]pyridine-7-diazonium cation, 84499-42-3; 3-(*o*-nitrophenoxy)pyridine, 76167-50-5; 3-(*o*-nitrophenoxy)-pyridine picrate, 84499-43-4; potassium 3-bromo-2-(5-cyano-2-hydroxyphenyl)pyridine, 84499-44-5.

Aza Cope Rearrangements in the Cyclopropenyl- and Allyl-Substituted Δ^2-Oxazolinone Systems

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The scope of the thermal and photochemical reorganization reactions of a number of cyclopropenyl- and allyl-substituted oxazolinones has been examined. These systems undergo a facile sigmatropic rearrangement in accord with orbital symmetry predictions. 2-Methyl-4-allyl-Δ^2-oxazolinones were found to undergo a 3,3 sigmatropic allyl shift on thermolysis to give the Δ^3-oxazolinone isomer. In contrast, on direct irradiation the 2-methyl-4-allyl-Δ^3-oxazolinones undergo a 1,3 allyl shift to give the Δ^2 isomer. The 4,4-disubstituted Δ^2-oxazolinones undergo decarbonylation either on irradiation or by flash vacuum pyrolysis to give acetimides. The acetimides formed were easily hydrolyzed to give the corresponding ketones. The excited-state behavior of the 2-phenyl-4-methyl-Δ^2-oxazolinone system was found to be markedly different from that encountered with the 2-methyl-4-phenyl-substituted isomer. The rationale for the difference in behavior is discussed.

Together with nitrile imines, oxides, sulfides and selenides, nitrile ylides belong to a class of 1,3-dipoles to which the general name nitrilium betaines has been given.[1] These reactive species have been known for over 20 years[2] and continue to elicit the interest of both experimental[3] and theoretical chemists.[4] 1,3-Dipolar cycloaddition of this class of 1,3-dipoles has led to the synthesis of a variety of interesting heterocyclic compounds.[5,6] Recently, it has been shown that 1,1 intramolecular cycloaddition of nitrile ylides can compete with the normal 1,3-addition when certain geometric constraints are imposed.[7,8] In these cases, the reactions have been formulated in terms of the carbene form of the dipole.[4,8] Beside the Huisgen procedure which involves the elimination of hydrogen chloride from imidoyl chlorides,[9] other accesses to nitrile ylides include (a) elimination of phosphoric acid ester from 2,3-dihydro-1,4-Δ^5-oxazaphospholes,[10] (b) photolysis of 2*H*-azirines,[5,6] and (c) thermal elimination of carbon dioxide from oxazolinones.[11] The thermolysis of trisubstituted Δ^3-oxazolinones (**1**) has been studied in some detail by Steglich and co-workers.[11–16] These compounds readily lose carbon dioxide at moderate temperatures and form products expected from nitrile ylides. If the dipole contains groups capable of conjugation, 1,5-dipolar electrocyclization is observed.[13] When alkyl groups are present on the nitrile ylide carbon centers, the dipole can be trapped with various dipolarophiles.[14–16]

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