Azafluorenes Containing Two Bridgehead Nitrogen Atoms

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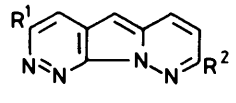
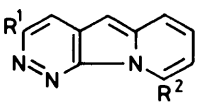
Four new tricyclic cationic ring systems containing two bridgehead nitrogen atoms have been synthesised: pyrido[1′,2′:3,4]imidazo[1,2-*a*]pyrimidinium, pyrido[1′,2′:3,4]imidazo[1,2-*c*]pyrimidinium, pyrido[1′,2′:3,4]imidazo[1,2-*a*]pyrazinium, and pyrido[1′,2′:3,4]imidazo[2,1-*b*]thiazolium. In the case of the first named system the parent heterocycle has been prepared. A new, efficient synthesis of the previously described imidazo[*a*,*c*]dipyridinium cation is also noted. The synthetic route to these compounds involved *N*-alkylation of an azinol with 2-chloromethylpyridine and ring closure of the resulting lactam with phosphoryl chloride. In the case of uracil and 6-methyluracil *N*-alkylation was proved to have occurred at N-1 by unambiguous synthesis. Nucleophilic attack by hydroxide ion upon the 1,3-dimethylpyrido[1′,2′:3,4]imidazo[1,2-*c*]pyrimidinium cation led to 3-(2-acetylaminoprop-1-enyl)imidazo[1,5-*a*]pyridine the structure of which was confirmed by unambiguous synthesis of its hydrolysis product.

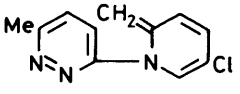
Earlier work in this series has been concerned with the synthesis of tricyclic systems such as (**1**) and (**2**), carrying two or more ring nitrogen atoms, one of which occupied the bridgehead position shown. Compounds of the former class were available[1] by self-condensation, for example, of two molecules of 3-chloro-6-methylpyridazine to give the heterocycle (**1a**). It was supposed that the methine (**3**) was an intermediate. Compound (**2a**), belonging to the latter class, was prepared[2] by a related route that required the initial synthesis of the methylene-bridged heterocycle (**4**) which was then treated with phosphoryl chloride. The intermediate (**4**) was one of several products arising from the interacton of 2-methylpyridine *N*-oxide and 3,6-dichloropyridazine. Another such product was the isomer (**5**), which with phosphoryl chloride yielded the cationic system (**6**). Structural assignment was based on n.m.r. observations, and on the similarity of the u.v. spectrum with that of a related dipyrido derivative (**8**).[3] Few substances containing two bridgehead nitrogens arranged in this manner are described in the literature, one of the most notable being the so-called Besthorn's Red prepared[4] in 1904 by heating quinoline-2-carboxylic acid in acetic anhydride. Its structure (**7**) was not confirmed until some 30 years later.[5] More recently Brown and his associates have studied the parent heterocycle (**8**) which they isolated in low yield as its bromide from condensation of 2-bromopyridine with 2-bromomethylpyridine.[3] Other publications concerning the parent system and its substitution products, benzologues and azalogues, and reduced derivatives are given in reference 6. The present paper concerns a new route to such compounds, which is capable of greater flexibility and higher yields. It is based on the cyclisation of lactams



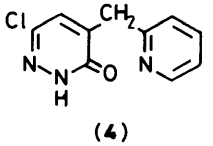
(**1**) a; R^1 = Me, R^2 = Cl



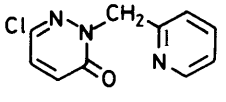
(**2**) a; R^1 = Cl, R^2 = H



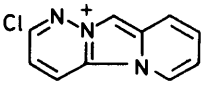
(**3**)



(**4**)



(**5**)



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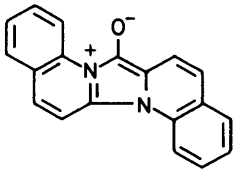
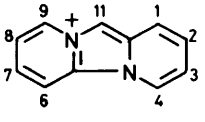
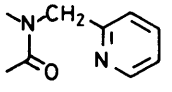


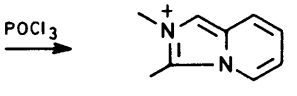
(**7**)

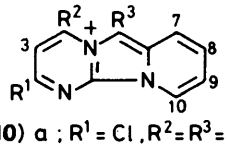


(**8**)

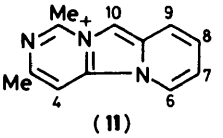


(**9**)

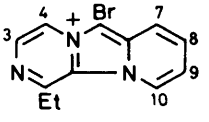




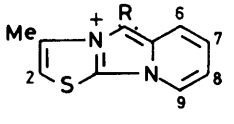
(**10**) a ; R^1 = Cl, R^2 = R^3 = H
b ; R^1 = Cl, R^2 = H, R^3 = Br
c ; R^1 = Cl, R^2 = Me, R^3 = H
d ; R^1 = R^2 = Me, R^3 = H
e ; R^1 = R^2 = R^3 = H



(**11**)



(**12**)



(**13**) a ; R = H
b ; R = Br

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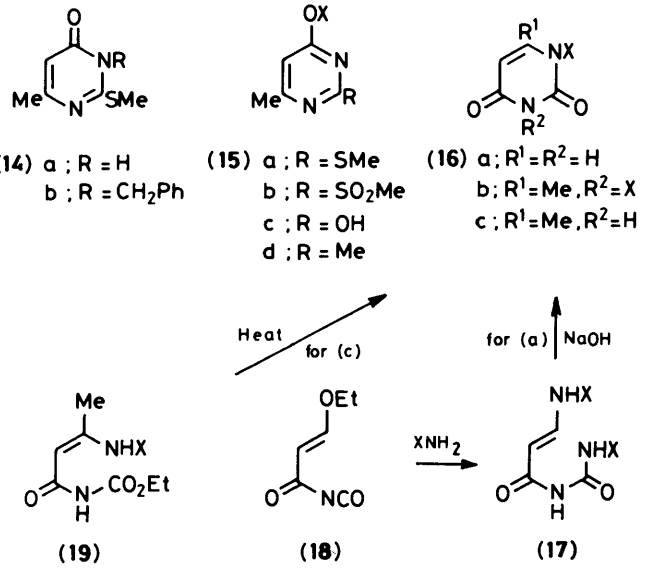
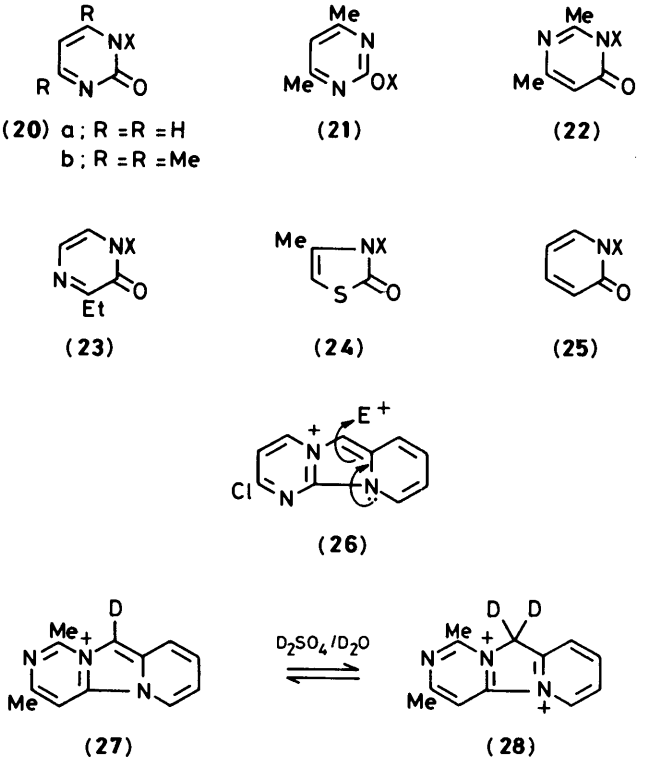
of generalised structure (**9**), prepared by the action of 2-chloromethylpyridine on the appropriate hydroxyazine. In this way, four new ring systems have been exemplified. Systems (**10**) and (**11**) were based on pyrimidinols, system (**12**) on pyrazinol, and the fourth (**13**) on a thiazolol.

Our first study began with the easily accessible pyrimidine (**14a**), particularly since it had been reported[7] to react with benzyl chloride to give the 3-benzyl derivative (**14b**). However, with us, the analogous reaction using 2-pyridylmethyl chloride, under either of two experimental conditions, failed to yield the required product, giving instead the ether (**15a**). The structure



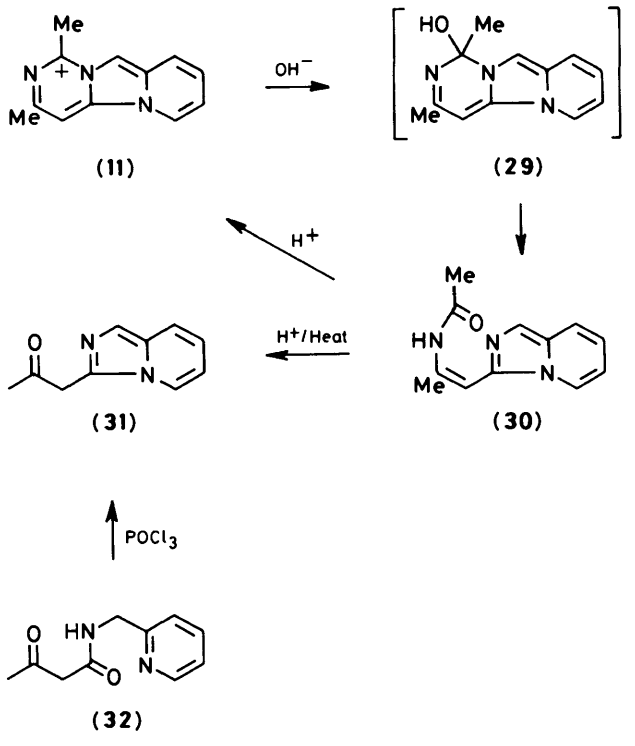
of the latter was confirmed by unequivocal synthesis from 2-pyridylmethanol and 4-chloro-6-methyl-2-methylthiopyrimidine. The thermally induced migration of the *O*-alkyl group to a ring nitrogen with heterocyclic ethers is well known[8] but our attempt (200 °C) at the thermal rearrangement of the ether (**15a**) was unsuccessful, returning only starting material. Similar results were obtained with every other 2-pyridylmethyl ether described in this paper, for example the related methyluracil derivative (**15c**). This compound was prepared by the sequential action of aqueous chlorine and sodium hydroxide on the sulphide; the intermediate sulphone (**15b**) was isolated. An interesting by-product isolated from the alkaline hydrolysis of (**15b**) was the original sulphide (**15a**) formed in a yield of 24%, evidently by some reductive process. By contrast the sodium salt of uracil in dimethylformamide treated with 2-chloromethylpyridine gave only the 1-substituted product (**16a**). Evidence based on the n.m.r. and i.r. spectra supported substitution at a ring nitrogen. Structural proof depended on the unequivocal synthesis of the uracil (**16a**) from the dipyridyl derivative (**17**) by the route shown, using essentially the method to 1-substituted uracils developed by Shaw and Warrener.[9] The replacement of the ethoxy group of the ethoxyacryloyl isocyanate (**18**) by the pyridylmethylamine residue was unexpected, but this residue was easily eliminated at the ring closure stage. Similar treatment of the sodium salt of 6-methyluracil with 2-chloromethylpyridine gave two products. The microanalysis of the first indicated a bispyridylmethyl derivative. The i.r. spectrum showed no absorption corresponding to either N–H or ether function, while the chemical shifts (δ 5.09) and (δ 5.17) attributed to the methylene groups were close to that (δ 5.01) found in compound (**16a**) and lower than that (δ 5.39) found for the methylene residue in the ether (**15c**). Structure (**16b**) was, therefore, assigned to this substance. All the related evidence for the second compound favoured the substitution of one *N*-pyridylmethyl residue into the methyluracil. The structure was eventually confirmed as (**16c**) by unequivocal synthesis starting from *N*-acetoacetylurethane[10] which was converted into the aminocrotonoyl derivative (**19**). Thermal extrusion of ethanol from the latter delivered the pyrimidine (**16c**). Alkylation of pyrimidin-2-ol gave only the *N*-substituted derivative (**20a**) whereas the 4,6-dimethyl homologue formed both the corresponding pyrimidone (**20b**) and the ether (**21**). The isomeric 2,6-dimethylpyrimidin-4-ol also yielded two products, the ether (**15d**) and the 3-substituted pyrimidone (**22**). The ability of the latter to give a tricyclic condensation product with phosphoryl chloride excluded the alternative 1-substituted pyrimidone structure. The availability of a specimen of 2-ethylpyrazin-3-ol led to its alkylation to give exclusively the *N*-substituted derivative (**23**), and a similar reaction starting with 4-methylthiazol-2-ol likewise gave only the thiazolone (**24**). Lastly, pyridin-2-ol was alkylated to give the pyridone (**25**) as previously described.[11]



Treatment of the uracil (**16a**) with an excess of refluxing phosphoryl chloride gave a dichroic solution displaying intense green fluorescence under u.v. light. The product was isolated as its sparingly soluble iodide. Elemental analysis showed the presence of a chlorine atom, indicating that replacement of the second oxygen had occurred and that the product was the triazafluorene cation (**10a**). The n.m.r. spectrum was contained in the region δ 7.35—9.80 and was completely interpretable in terms of the structure assigned. In one canonical form (**26**), the cation (**10a**) has a positively charged nitrogen of the pyrimidinium type but it also has a nitrogen lone pair as found in indolizine. The cation is at once π-deficient and π-excessive.

Electrophilic attack on the basis of the formulation (**26**) was expected to occur at C-6. It was found that treatment of a cold solution of the iodide (**10a**) in acetic acid solution with bromine yielded an immediate precipitate. Elemental analysis, showing the presence of three bromine atoms, and the loss of the strong i.r. band at 913 cm^{-1} assigned to the out of plane bend of the isolated C-6 hydrogen atom indicated that the monobromocation (**10b**) had been obtained as its dibromoiodide. The insolubility of this salt in any solvent precluded determination of the n.m.r. spectrum. Accordingly, the crude mixture obtained from the reaction of the lactam (**16a**) with phosphoryl chloride and containing the cation (**10a**) (but not in association with iodide ion) was treated with bromine as before to obtain the cation (**10b**) with bromide now as counterion. However, the insolubility of this salt also prevented an n.m.r. spectrum from being taken. Similar treatment of the 6-methyluracil (**16c**) with phosphoryl chloride gave the 2-chloro-4-methylpyrido[1′,2′:3,4]imidazo[1,2-*a*]pyrimidinium cation (**10c**) which too was isolated as its iodide. However, cyclisation of the pyrimidone (**20a**) in refluxing phosphoryl chloride was, for unknown reason, troublesome since black tars were formed. Perchloric acid was used to precipitate the crude product which was recrystallised to afford a low yield of pyrido[1′,2′ : 3,4]imidazo[1,2-*a*]pyrimidinium perchorate (**10e**), representing a new parent ring system. Phosphoryl chloride treatment of the 4,6-dimethyl-2-pyrimidone (**20b**) proceeded better and the perchlorate salt of the cation (**10d**) was obtained in good yield. The isomeric dimethylpyrimidone (**22**) also cyclised cleanly to give the 1,3-dimethylpyrido[1′,2′:3,4]imidazo[1,2-*c*]pyrimidinium cation (**11**) which was isolated as the perchlorate hydroperchlorate. This salt did not melt but detonated instead. The n.m.r. spectrum was consistent with the formulation (**11**) indicating that, in the $(CD_3)_2SO$ solution, protonation at position 10 had not occurred and that the perchloric acid was not covalently bound. However, a second n.m.r. spectrum determined in D_2SO_4–D_2O clearly showed the absence of the 10-H indicating that the equilibrium (**27**) ⇌ (**28**) had been established.

A cold, aqueous solution of the compound (**11**) when treated with alkali gave an immediate yellow precipitate, purified as microneedles from ethanol. Under u.v. light this new, neutral compound retained the fluorescence of the starting material, although the colour was considerably greener. Elemental analysis, which indicated the formula $C_{12}H_{13}N_3O$, coupled with i.r. and n.m.r. evidence enabled assignment of the imidazo[1,5-*a*]pyridine structure (**30**), it having arisen by nucleophilic attack of hydroxide ion on the cation at C-1 with the presumed formation of the neutral tricyclic species (**29**) as an intermediate. It was interesting that the u.v. spectrum of the amide (**30**) determined in methanol and in dilute hydrochloric acid solution were different. Moreover, the latter spectrum was identical with the spectrum of the cation (**11**) taken in methanol solution. Evidently in acid media the amide (**30**) recyclises to the cation (**11**). However, compound (**30**) was unmasked as an enamine since a brief treatment of it with hot, dilute hydrochloric acid yielded a new substance separating from light petroleum as white microneedles. This product was readily characterised as a ketone and the 3-acetonylimidazo[1,5-*a*]pyridine structure (**31**) was assigned, lending considerable support for the structure (**30**) originally assigned to its precursor. Unequivocal evidence for this degradation sequence was then obtained by synthesis of the ketone (**31**). 2-(*N*-Acetoacetylaminomethyl)pyridine (**32**) was prepared from 2-aminomethylpyridine and diketene. This product could not be cyclised with polyphosphoric acid at 180 °C as had been achieved[12] with similar but simpler amides; tars were the only products. However, boiling phosphoryl chloride brought about a smooth reaction to give the product (**31**) identical with that first obtained. An excellent precedent for the sequence of events



Scheme.

leading to the ketone (**31**) in the Scheme can be found in the earlier observations by one of us concerning the mechanism of isomerisation of 3-amino-*s*-triazolo[4,3-*c*]pyrimidines to 2-amino-*s*-triazolo[2,3-*c*]pyrimidines.[13] In contrast to the above results the isomeric cation (**10d**) was not precipitated with cold alkali.

The pyrazinone (**23**) needed treatment with refluxing phosphoryl chloride for 4 h before complete reaction was obtained (t.l.c.). Work-up yielded an intractable gum which was soluble in water to give a strongly blue fluorescent solution under u.v. light. However, trial additions of sodium iodide, sodium perchlorate, sodium bromide, oxalic acid, or picric acid failed to precipitate the product. In view of these difficulties, a solution of the gum in aqueous acetic acid was treated with bromine to yield crystals of 6-bromo-1-ethylpyrido[1′,2′:3,4]imidazo[1,2-*a*]pyrazinium bromide (**12**). Cyclisation of the thiazolone (**24**) proved troublesome, but it was eventually achieved by using a mixture of phosphoryl chloride and *N*,*N*-dimethylaniline at reflux. The product 3-methylpyrido[1′,2′:3,4]imidazo[2,1-*b*]thiazolium cation (**13a**) was isolated in good yield as its perchlorate. Treatment of it with bromine in glacial acetic acid yielded a monobromo derivative as its perbromide. The n.m.r. spectrum showed that reaction had occurred with loss of the singlet at δ8.61 previously assigned to the proton at C-5 in the substrate (**13a**). The possibility of bromine having entered at C-2 was considered, but discounted, by observing that both singlets in the spectrum of the product (a methyl and a methine) were slightly coupled (0.5 Hz) thus betraying their adjacent positions upon the ring. Hence the product must have been the tribromide salt of the cation (**13b**). Cyclisation of the pyridone (**25**) in refluxing phosphoryl chloride efficiently produced the imidazo[*a*,*c*]dipyridinium cation (**8**) isolated from aqueous solution as its previously described[3] perchlorate. The yield, after recrystallisation, was 80% and is an improvement upon previous preparations (26%,[3] 18%,[6i] 10%,[6i] and 76%[6p]) of this cation. The u.v. spectrum was identical with that published.[3]

Experimental

Organic extracts were dried with anhydrous magnesium sulphate. The silica used for chromatography was Hopkin and Williams' MFC grade. 2-Chloromethylpyridine was obtained commercially as a crude product in toluene solution and was converted into its hydrochloride for storage. The pure, free base was prepared from this salt as required. In the alkylation reactions sodium hydride was prepared *in situ* by washing a 50% oil dispersion with light petroleum (b.p. 30—40 °C). DMF is *N,N*-dimethylformamide. Analytical samples were dried *in vacuo* over phosphorus pentaoxide, at 40 °C for those with m.p. < 100 °C and at 60 °C for those with m.p. > 100 °C. Microanalyses were determined at I.C.I. Pharmaceuticals Division. I.r. spectra were determined as Nujol mulls using a Perkin-Elmer Infracord Model 137. U.v. spectra were determined using methanol solutions in a Perkin-Elmer 137 u.v. spectrophotometer, ε values are in units of $dm^3\ mol^{-1}\ cm^{-1}$. N.m.r. spectra were determined on Perkin-Elmer R12 (60 MHz) and Varian *HA*-100 (100 MHz) instruments with tetramethylsilane as internal standard except where it is stated that sodium 2,2-dimethyl-2-silapentane-5-sulphonate (DSS) was used. All compounds with a 2-pyridylmethyl substituent gave satisfactory signals for the pyridine protons. Field strengths are expressed in units of δ(p.p.m.).

6-*Methyl*-2-*methylthio*-4-(2-*pyridylmethoxy*)*pyrimidine* (**15a**).—(i) 6-Methyl-2-methylthiopyrimidin-4-ol[14] (**14a**) (1.56 g, 10 mmol) and potassium hydroxide (85%; 1.32 g, 20 mmol) were dissolved in methanol (25 ml) and 2-chloromethylpyridine hydrochloride (1.64 g, 10 mmol) added. The slurry was stirred at 25 °C for 18 h and finally heated under reflux for 7 h. The mixture was diluted with water to 150 ml, made alkaline with aqueous ammonia, and extracted with ethyl acetate (50 ml). The extract was washed with brine, dried, and evaporated under reduced pressure. The resulting brown oil (1.40 g) was applied to an aluminia column (45 g) which was eluted with benzene to give an oil (0.84 g, 34%). Recrystallisation from light petroleum (b.p. 40—60 °C) gave the *ether* as colourless microneedles, m.p. 66—66.5 °C (Found: C, 58.0; H, 5.3; N, 16.8. $C_{12}H_{13}N_3OS$ requires C, 58.3; H, 5.3; N, 17.0%); $\nu_{max.}$ 1 170 cm^{-1} (ether); δ_H (60 MHz; $CDCl_3$) 2.36 (3 H, s, Me), 2.44 (3 H, s, Me), 5.53 (2 H, s, CH_2), and 6.36 (1 H, s, 5-H). Picrate: yellow, flattened rods, m.p. 158—167 °C.

(ii) The pyrimidinol (**14a**) (1.56 g, 10 mmol) and sodium hydride (0.24 g, 10 mmol) were slurried in dry DMF (40 ml) and the mixture stirred at 25 °C for 1 h to give a clear solution of the sodium salt. 2-Chloromethylpyridine (1.27 g, 10 mmol) in DMF (15 ml) was added and the mixture stirred at 25 °C for 18 h. Water (150 ml) was added followed by aqueous ammonia to give pH 11. The solution was extracted with ethyl acetate and the extract washed with brine, dried, and evaporated to leave an oil (1.23 g, 50%) which, crystallised as above, gave white microneedles, m.p. 65—66 °C.

Unequivocal Synthesis of the Ether (**15a**).—Sodium hydride (2.40 g, 10 mmol) was slurried in dry tetrahydrofuran (50 ml) and a solution of 2-pyridylmethanol[15] (10.91 g, 10 mmol) in tetrahydrofuran added with stirring. The resulting thick, white suspension of the sodium salt was stirred for 20 h under nitrogen to complete the reaction. 4-Chloro-6-methyl-2-methylthiopyrimidine[16] (17.47 g, 10 mmol) in tetrahydrofuran (60 ml) was added during 1 h and the mixture was then stirred at 25 °C under nitrogen for a further 22 h. Water (100 ml) was added, followed by ether (200 ml). The organic layer was separated, washed with water and with brine, dried, and evaporated under reduced pressure to give a green oil (22.58 g). Crystallisation of this from light petroleum (b.p. 40—60 °C) afforded colourless microneedles (13.47 g, 54%), m.p. 65—66 °C. The melting point was undepressed upon admixture with the compounds previously isolated from the alkylation reactions.

6-*Methyl*-2-*methylsulphonyl*-4-(2-*pyridylmethoxy*]*pyrimidine* (**15b**).—Chlorine gas was passed briskly through a solution of potassium carbonate (2.76 g, 20 mmol) in water (10 ml) containing the sulphide (**15a**) (0.62 g, 2.5 mmol) in suspension. The temperature was kept at 5—10 °C. After 45 min the chlorine uptake was 0.53 g (theory 0.35 g). The solid *sulphone* was filtered off, washed well with water, and dried over P_2O_5 (0.68 g, 97%). It separated from ethyl acetate as colourless crystals, m.p. 152—157 °C (decomp.) (Found: C, 51.8; H, 4.9; N, 15.2. $C_{12}H_{13}N_3O_3S$ requires C, 51.6; H, 4.7; N, 15.0%); $\nu_{max.}$ 1 300 and 1 135 cm^{-1} (sulphone); δ_H (60 MHz; $CDCl_3$) 2.55 (3 H, s, 6-Me). 3.23 (3 H, s, SO_2Me), 5.60 (2 H, s, CH_2), and 6.85 (1 H, s, 5-H).

6-*Methyl*-4-(2-*pyridylmethoxy*)*pyrimidin*-2-*ol* (**15c**).—A mixture of the sulphone (**15b**) (8.24 g, 29.5 mmol) and aqueous sodium hydroxide (2M; 30 ml, 60 mmol) was heated on a steam-bath for 5 min. The oily solution was cooled, diluted with water (60 ml), and extracted with ether (2 × 50 ml). The extracts were combined, washed with water and with brine, dried, and evaporated under reduced pressure. The residual oil (2.07 g, 24%) crystallised from light petroleum (b.p. 40—60 °C) as colourless microneedles (m.p. 65—66 °C) found (mixed m.p. and i.r.) to be the methylthio compound (**15a**). The aqueous phase was adjusted to pH 7 (2M HCl) and extracted with chloroform (3 × 100 ml). The combined organic layers were washed once with water, dried, and evaporated to give the *pyrimidinol* (5.09 g, 75%), which separated from ethanol as white crystals, m.p. 200—202 °C (decomp.) (Found: C, 60.6; H, 5.0; N, 19.1. $C_{11}H_{11}N_3O_2$ requires C, 60.8; H, 5.1; N, 19.3%); δ_H [60 MHz; $(CD_3)_2SO$] 2.18 (3 H, s, 6-Me), 5.39 (2 H, s, CH_2), 5.87 (1 H, s, 6-H), and 11.35 (1 H, br s, lactam NH).

1-(2-*Pyridylmethyl*)*uracil* (**16a**).—Sodium hydride (0.96 g, 40 mmol) was slurried in dry DMF (50 ml). Uracil (4.48 g, 40 mmol) was added and the mixture stirred at 25 °C to complete the formation of the insoluble sodium salt. 2-Chloromethylpyridine (6.01 g, 47.2 mmol) was added and the suspension stirred at 25 °C for 23 h and then heated on a steam-bath for 5 h. Evaporation of the solvent under reduced pressure left a brown paste which was partitioned between water (50 ml) and chloroform–butanol (200 ml:100 ml). The organic layer was separated, dried, and evaporated under reduced pressure to give a buff-coloured solid (6.30 g). The latter was twice recrystallised from ethanol to give the *product* as white crystals (3.11 g, 38%), m.p. 186 °C (Found: C, 59.1; H, 4.5; N, 20.7. $C_{10}H_9N_3O_2$ requires C, 59.1; H, 4.5; N, 20.7%); $\nu_{max.}$ 1 690 and 1 640 cm^{-1} (carbonyls); δ_H [60 MHz; $(CD_3)_2SO$] 5.01 (2 H, s, CH_2), 5.63 (1 H, d, *J* 8 Hz, 5-H) 7.76 (1 H, d, *J* 8 Hz, 6-H), and 11.20 (1 H, br s, lactam NH).

1-(2-*Pyridylmethyl*)-3-[3-(2-*pyridylmethylamino*)*acryloyl*]-*urea* (**17**).—3-Ethoxyacryloyl isocyanate (prepared[9] from 3.08 g of the acid chloride) in benzene (15 ml) was added to a solution of 2-aminomethylpyridine[17] (2.41 g, 1.0 equiv.) in ether (20 ml) and the preparation set aside for 24 h. The solid which formed (0.75 g, 12.2%) was collected and washed with ether. Recrystallisation from ethanol afforded white crystals of the *acylurea*, m.p. 155—155.5 °C (Found: C, 61.7; H, 5.4; N, 22.1. $C_{16}H_{17}N_5O_2$ requires C, 61.7; H, 5.5; N, 22.5%); δ_H [100 MHz; $(CD_3)_2SO$] 4.22 (2 H, d, *J* 5.0 Hz, CH_2 of 3-substituent), 4.39 (2 H, d, *J* 5.5 Hz, CH_2 of 1-substituent), 4.87 (1 H, d, *J* 12.0 Hz, 2-H), 7.10—7.34 (4 H, m, pyridine 2-protons), 7.39—7.84 (4 H, m, pyridine 3-protons, 3-H, amino NH), 8.39 (2 H, m, pyridine 1-protons), 9.34 (1 H, t, *J* 5.5 Hz, 1-NH), and 9.53 (1 H, s, 3-NH).

1-(2-*Pyridylmethyl*)*uracil* (**16a**).—The acylurea (**17**) (0.23 g) was warmed with 1M NaOH (4.5 ml) and the resulting solution heated on a steam-bath for 1 h. The cooled solution was brought to pH 7 (2M HCl) and extracted with chloroform–butanol (10 ml:10 ml). The extract was dried and evaporated and the resulting white solid (0.27 g) recrystallised from ethanol to give the uracil, m.p. 186 °C (Found: C, 59.1; H, 4.5; N, 20.7. Calc. for $C_{10}H_9N_3O_2$: C, 59.1; H, 4.5; N, 20.7%). The melting point was undepressed by admixture with the alkylation product; the i.r. and n.m.r. spectra of the two samples were also identical.

Alkylation of 6-*Methyluracil*.—6-Methyluracil[18] (12.61 g, 100 mmol) was added to a slurry of sodium hydride (2.40 g, 100 mmol) in DMF (110 ml) and the mixture was stirred at 25 °C for 3 h. The resulting thick suspension of the sodium salt was treated with 2-chloromethylpyridine (12.8 g, 110 mmol) dissolved in DMF (100 ml), and stirring was continued for 15 h. The mixture was finally heated on a steam-bath for 4 h, and the solvent was then removed under reduced pressure. Water (200 ml) was added to the residual paste and the resulting solution was extracted with chloroform–butanol (200 ml:150 ml). The dried extract was evaporated to leave a light brown solid (17.2 g). Recrystallisation from ethanol afforded a buff-coloured solid (3.50 g; m.p. 225—235 °C) which was further recrystallised from water to give white crystals of 6-*methyl*-1-(2-*pyridylmethyl*)-*uracil* (**16c**) (2.42 g, 11%), m.p. 236—241 °C (Found: C, 60.9; H, 5.2; N, 19.0. $C_{11}H_{11}N_3O_2$ requires C, 60.8; H, 5.1; N, 19.3%); $\nu_{max.}$ 3 200—3 000 (N–H) and 1 725—1 590 cm^{-1} (carbonyls); δ_H [100 MHz; $(CD_3)_2SO$] 2.17 (3 H, s, 6-Me), 5.10 (2 H, s, CH_2), 5.53 (1 H, s, 5-H), and 16.18 (1 H, br s, lactam NH). The original ethanolic mother-liquor was evaporated to dryness and the residue recrystallised from water (carbon) to give 6-*methyl*-1,3-*bis*(2-*pyridylmethyl*)*uracil* (**16b**) as white microneedles (3.70 g, 12%), m.p. 144—146.5 °C (Found: C, 66.5; H, 5.3; N, 18.5. $C_{17}H_{16}N_4O_2$ requires C, 66.2; H, 5.2; N, 18.2%); $\nu_{max.}$ 1 695 and 1 650 cm^{-1} (carbonyls); δ_H [100 MHz; $(CD_3)_2SO$] 2.25 (3 H, s. 6-Me), 5.09 (2 H, s, CH_2), 5.17 (2 H, s, CH_2), and 5.75 (1 H, s, 5-H).

N-{3-[(2-*Pyridylmethyl*)*amino*]*crotonoyl*}*urethane* (**19**).—2-(Aminomethyl)pyridine[17] (1.08 g, 10 mmol) and *N*-acetoacetylurethane[10] (1.73 g, 10 mmol) dissolved in ethanol (10 ml) were heated together under reflux for 10 min. The cooled solution was seeded to afford the *crotonamide* as white crystals (2.04 g, 77.6%), m.p. 107.5 °C (Found: C, 59.1; H, 6.3; N, 16.0. $C_{13}H_{17}N_3O_3$ requires C, 59.3; H, 6.6; N, 16.0%); $\nu_{max.}$ 3 100 (NH) and 1 735 cm^{-1} (ester); δ_H (100 MHz; $CDCl_3$) 1.23 (3 H, t, ethyl CH_3), 1.97 (3 H, s, CH_3), 4.13 (2 H, q, ethyl CH_2), 4.57 (2 H, d. *J* 6.5 Hz, picolyl CH_2), 5.73 (1 H, s, crotonoyl 2-H), 7.85 (1 H, s, urethane NH), and 15.3 (1 H, signal not recorded, amino NH).

6-*Methyl*-1-(2-*pyridylmethyl*)*uracil* (**16c**).—The crotonamide (**19**) (1.00 g) was heated at 170 °C under nitrogen. Bubbles of gas emerged from the melt which, after 5 min, set solid. After cooling, water (25 ml) was added, followed by sodium hydroxide (2M; 2.5 ml). The product dissolved, leaving a small amount of suspended starting material which was filtered off (carbon). The filtrate, on acidification to pH 6 (2M HCl), gave a solid which, after two recrystallisations from water, afforded the *uracil* as white crystals (0.25 g, 30.3%), m.p. 238—241 °C (Found: C, 61.0; H, 5.0; N, 19.4. Calc. for $C_{11}H_{11}N_3O_2$: C, 60.8; H, 5.1; N, 19.3%). The melting point was not depressed upon admixture with the previously obtained alkylation product; the i.r. spectra of the two samples were also identical.

1-(2-*Pyridylmethyl*)*pyrimidin*-2(1 H)-*one* (**20a**).—Pyrimidin-2-ol[19] (4.24 g, 44 mmol) was dissolved in a solution of sodium (1.02 g, 44 mmol) in ethanol (700 ml). 2-Chloromethylpyridine (5.65 g, 44 mmol) in ethanol (50 ml) was added, and the mixture was heated under reflux for 5 h. Precipitated sodium chloride was filtered off and the filtrate evaporated to give residue which after recrystallisation from ethyl acetate (carbon), yielded the *pyrimidone* as light-brown crystals (4.96 g, 60%), m.p. 79.5—80 °C (Found: C, 63.9; H, 4.8; N, 22.9. $C_{10}H_9N_3O$ requires C, 64.1; H, 4.8; N, 22.5%); $\nu_{max.}$ 1 650 cm^{-1} (carbonyl); δ_H (60 MHz; $CDCl_3$) 5.09 (2 H, s, CH_2), 6.21 (1 H, dd, *J* 6.5 and 4.0 Hz, 5-H), 7.87 (1 H, dd, *J* 6.5 and 3.0 Hz, 6-H), and 8.41 (1 H, dd, *J* 4.0 and 3.0 Hz, 4-H).

Alkylation of 4,6-*Dimethylpyrimidin*-2-*ol*.—Sodium hydride (2.40 g, 100 mmol) was slurried in dry DMF (160 ml). 4,6-Dimethylpyrimidin-2-ol [prepared by dissolving the hydrochloride[20] (150 g) in warm, aqueous 1.5M sodium carbonate (250 ml) cooling the solution, collecting the product, and recrystallising it from water (70.7 g)] (12.41 g, 100 mmol) was added during 5 min, with cooling. The resulting thick, white suspension was stirred at 25 °C for 3 h until all the hydride had reacted. 2-Chloromethylpyridine (13.0 g, 102 mmol) in DMF (170 ml) was added. The mixture was stirred for 67 h at 25 °C and then for 1.5 h on a steam-bath. The solvent was removed under reduced pressure and the residue treated with water (100 ml) to form a solution which was extracted with chloroform–butanol (250 ml:100 ml). The extract was dried and the solvents evaporated under reduced pressure to leave an oil (15.80 g) which solidified with time. The solid was dissolved in benzene (20 ml) and the solution applied to a column of silica (450 g): elution with 80% ethyl acetate in benzene removed 4,6-*dimethyl*-2-(2-*pyridylmethoxy*)*pyrimidine* (**21**) (1.94 g, 9%) which separated from light petroleum (b.p. 40—60 °C) as white crystals, m.p. 55.5—58 °C (Found: C, 67.3; H, 6.0; N, 19.4%. $C_{12}H_{13}N_3O$ requires C, 67.0; H, 6.1; N, 19.5%); $\nu_{max.}$ 1 115 cm^{-1} (ether); δ_H (60 MHz; $CDCl_3$) 2.33 (6 H, s, methyls), 5.58 (2 H, s, CH_2), and 6.70 (1 H, s, 5-H). Elution with 10% ethanol in chloroform then yielded 4,6-*dimethyl*-1-(2-*pyridylmethyl*)*pyrimidin*-2-(1 H)-*one* (**20b**) (6.63 g, 31%) which separated from toluene as light-brown crystals, m.p. 145–147 °C (Found: C, 67.4; H, 6.0; N, 19.7. $C_{12}H_{13}N_3O$ requires C, 67.0; H, 6.1; N, 19.5%); $\nu_{max.}$ 1 660 cm^{-1} (carbonyl); δ_H (60 MHz; $CDCl_3$) 2.35 (3 H, s, Me), 2.47 (3 H, s, Me), 5.34 (2 H, s, CH_2), and 6.15 (1 H, s, 5-H).

Alkylation of 2,6-*Dimethylpyrimidin*-4-*ol*.—Sodium hydride (2.40 g, 100 mmol) was slurried in dry DMF (100 ml) and 2,6-dimethylpyrimidin-4-ol[21] (12.41 g, 100 mmol) was added during 10 min with ice cooling. A clear solution was obtained, to which was added 2-chloromethylpyridine (13.50 g, 106 mmol) dissolved in DMF (70 ml). The mixture was stirred at 25 °C for 168 h. Removal of the solvent under reduced pressure left a residue which was partitioned between water (100 ml) and chloroform (250 ml). Evaporation of the dried organic extracts left a green oil which eventually solidified. It was dissolved in benzene (5 ml) and the solution applied to a silica column (650 g). Elution with 10% chloroform in ethyl acetate removed 2,6-*dimethyl*-4-(2-*pyridylmethoxy*)*pyrimidine* (**15d**) (2.97 g, 13.8%). Recrystallisation from light petroleum (b.p. 40—60 °C) afforded white crystals, m.p. 35—37.5 °C (Found: C, 67.1; H, 5.9; N, 19.6. $C_{12}H_{13}N_3O$ requires C, 67.0; H, 6.1; N, 19.5%); $\nu_{max.}$ 1 170 cm^{-1} (ether); δ_H(60 MHz; $CDCl_3$) 2.43 (3 H, s, Me), 2.60 (3 H, s, Me), 5.60 (2 H, s, CH_2), and 6.57 (1 H, s, 5-H). Further elution with 30% ethanol in chloroform afforded 2,6-*dimethyl*-3-(2-*pyridylmethyl*)*pyrimidin*-4-(3 H)-*one* (**22**) isolated as a yellow solid (16.20 g, 75.3%). Recrystallisation from cyclohexane gave white microneedles, m.p. 86—87 °C, the resolidified sample melting at 92.5—93 °C (Found: C, 67.1: H, 6.1; N, 19.4. $C_{12}H_{13}N_3O$ requires C, 67.0; H, 6.1; N, 19.5%); $\nu_{max.}$ 1 680 cm^{-1} (carbonyl); δ_H (60 MHz; $CDCl_3$) 2.29 (3 H, s, Me), 2.61 (3 H, s, Me), 5.40 (2 H, s, CH_2), and 6.27 (1 H, s, 5-H).

3-*Ethyl*-1-(2-*pyridylmethyl*)*pyrazin*-2(1 H)-*one* (**23**).—3-Ethylpyrazin-2-ol (12.41 g, 100 mmol) was added during 15 min to a slurry of sodium hydride (2.40 g, 100 mmol) in dry DMF (100 ml) and the mixture stirred for 2 h to produce a clear solution of the sodium salt. 2-Chloromethylpyridine (14.0 g, 110 mmol) dissolved in DMF (50 ml) was added and stirring continued at 25 °C for 18 h. The solvent was removed under reduced pressure at 70 °C and the residual oil was partitioned between chloroform and water. Evaporation of the dried extract gave a brown oil which was dissolved in benzene (20 ml) and applied to a silica column (400 g). Elution with 35% ethyl acetate in benzene, then with ethyl acetate, gave the *pyrazinone* as a brown oil (13.36 g, 62%), which eventually solidified. An analytical sample was recrystallised from cyclohexane (Found: C, 67.6; H, 6.2; N, 19.2. $C_{12}H_{13}N_3O.0.05\,C_6H_{12}$ requires C, 67.3; H, 6.2; N, 19.1%); $\nu_{max.}$ 1 645 cm^{-1} (carbonyl); δ_H (60 MHz, $CDCl_3$) 1.23 (3 H, t, ethyl CH_3), 2.84 (2 H, q, ethyl CH_2), and 5.15 (2 H, s, CH_2).

4-*Methyl*-3-(2-*pyridylmethyl*)*thiazol*-2(3 H)-*one* (**24**).—4-Methylthiazol-2-ol (prepared[22] from ammonium thiocarbamate[23] (11.51 g, 100 mmol) was dissolved in a solution of sodium (2.30 g, 100 mmol) in ethanol (50 ml). 2-Chloromethylpyridine (13.00 g, 102 mmol) was added and the mixture heated under reflux for 2 h. The mixture was cooled and filtered to remove sodium chloride and the filtrate was evaporated to leave a brown oil. This was dissolved in benzene (10 ml) and the solution applied to a column of silica (600 g). Elution with 30% ethyl acetate in benzene removed an oil which was eventually solidified (17.95 g, 87%) Recrystallisation from ethyl acetate–light petroleum (b.p. 60—80 °C) afforded the *thiazolone* as colourless rods, m.p. 76—77 °C (Found: C, 58.2; H, 5.1; N, 13.8. $C_{10}H_{10}N_2OS$ requires C, 58.2; H, 4.9; 13.6%); $\nu_{max.}$ 1 645 cm^{-1} (carbonyl); δ_H (60 MHz; $CDCl_3$) 2.10 (3 H, d, J 1.5 Hz, CH_3), 5.04 (2 H, s, CH_2), and 5.80 (1 H, q, 5-H).

2-*Chloropyrido*[1′,2′:3,4]*imidazo*[1,2-a]*pyrimidinium Iodide* (**10a**).—A slurry of the uracil (**16a**) (3.00 g) in phosphoryl chloride (30 ml) was stirred under reflux for 1 h. A clear, yellow solution was formed which was concentrated under reduced pressure. Water (10 ml) was added, cautiously, to the oily residue followed by sodium iodide (22.8 g, 10 equiv.) dissolved in water (10 ml). A voluminous, yellow precipitate was obtained which was filtered off and washed once with water. The partially dried *product* was recrystallised from ethanol to form yellow rosettes (2.80 g, 57%), decomp. > 300 °C (Found: C, 36.1; H, 2.2; Cl, 10.7; I 38.1; N, 12.5. $C_{10}H_7ClIN_3$ requires C, 36.2; H, 2.1; Cl, 10.7; I, 38.3; N, 12.7%); $\nu_{max.}$ 913 cm^{-1} (6-H); $\lambda_{max.}$ 219 (ε 31 200), 247 (22 600), 310infl (3 600), 326 (7 300), 341 (8 000), 394 (5 100), and 412infl nm (4 700); δ_H [60 MHz; $(CD_3)_2SO$] 7.35 (1 H, ddd, $J_{9,8}$ 6.5, $J_{9,10}$ 6.5, $J_{9,7}$ 1.0 Hz, 9-H), 7.65 (1 H, ddd, $J_{8,7}$ 9.0, $J_{8,9}$ 6.5, $J_{8,10}$ 1.0 Hz, 8-H), 8.17 (1 H, dd, $J_{7,8}$ 9.0, $J_{7,9}$ 1.0 Hz, 7-H), 8.23 (1 H, d, $J_{3,4}$ 7.2 Hz, 3-H), 8.90 (1 H, s, 6-H), 9.03 (1 H, dd, $J_{10,9}$ 6.5, $J_{10,8}$ 1.0 Hz, 10-H), and 9.80 (1 H, d, $J_{4,3}$ 7.2 Hz, 4-H).

6-*Bromo*-2-*chloropyrido*[1′,2′:3,4]*imidazo*[1,2-a]*pyrimidinium Dibromoiodide* (**10b**).—Bromine (0.21 ml, 2 equiv.) in glacial acetic acid (4 ml) was added with stirring to a solution of the iodide (**10a**) (0.66 g, 2 mmol) in glacial acetic acid/water (20 ml:10 ml). A heavy yellow precipitate appeared immediately. The *product* was filtered off, washed with water, and recrystallised from methanol (containing a few drops of water) to give orange-coloured microplates (0.52 g, 46%), m.p. 179—185 °C (decomp.) (Found: C, 23.3; H, 1.6; Br, 41.6; C. 5.9; I, 18.2; N, 7.8 $C_{10}H_6Br_3ClIN_3$ requires C, 21.0; H, 1.1; Br 42.0; Cl, 6.2; I, 22.2; N, 7.4%).

6-*Bromo*-2-*chloropyrido*[1′,2′:3,4]*imidazo*[1,2-a]*pyrimidinium Iodide* (**10b**).—The uracil (**16a**) (0.75 g) was treated with phosphoryl chloride (7.5 ml) for 25 min as described above. The excess of reagent was removed and the residue was dissolved in water (15 ml); bromine (0.38 ml, 2 equiv.) dissolved in glacial acetic acid (5 ml) was then added with stirring. The precipitate of the *product* was filtered off, washed with water, and recrystallised from aqueous ethanol to yield orange-coloured crystals, decomp. > 300 °C (Found: C, 33.6; H, 1.7; Br, 44.0; Cl, 9.9; N, 11.2; $C_{10}H_6Br_2ClN_3$ requires C, 33.1; H, 1.7; Br, 44.0; Cl, 9.8; N, 11.6%); $\lambda_{max.}$ 215infl (ε 23 800), 252 (16 500), 320infl (4 000), 338 (6 000), 354 (5 900), 406 (3 200), and 430infl nm (3 000).

2-*Chloro*-4-*methylpyrido*[1′,2′:3,4]*imidazo*[1,2-a]*pyrimidinium Iodide* (**10c**).—The uracil (**16c**) (0.80 g, 3.68 mmol) and phosphoryl chloride (8 ml) were stirred under reflux for 45 min to yield an orange-coloured solution. The excess of reagent was removed under reduced pressure, and water (5 ml) was added cautiously to the residue. The resulting solution, when treated with sodium iodide (5.52 g, 36.8 mmol) in water (7 ml), immediately gave a yellow precipitate of the *product*. Recrystallisation from aqueous methanol afforded orange-coloured microneedles (0.52 g, 41%), decomp. > 300 °C (Found: C, 38.7; H, 2.7; Cl, 10.5; I, 35.8; N, 11.6. $C_{11}H_9ClIN_3$ requires C, 38.2; H, 2.6; Cl, 10.3; I, 36.7; N, 12.1%); $\nu_{max.}$ 907 cm^{-1} (6-H); $\lambda_{max.}$ 221 (ε 34 000), 239 (30 100), 247 (30 500), 299infl (5 100), 312 (8 100), 326 (8 500), 342 (4 400), 363 (3 700), 381 (3 500), and 401infl nm (2 200); δ_H (100 MHz; CF_3CO_2H) 3.05 (3 H, s, Me), 7.30 (1 H, ddd, $J_{9,10}$ 7.0, $J_{9,8}$ 7.0, $J_{9,7}$ 1.0 Hz, 9-H), 7.62 (1 H, dd, $J_{8,7}$ 9.0, $J_{8,9}$ 7.0 Hz, 8-H), 7.70 (1 H, s, 3-H), 7.89 (1 H, dd, $J_{7,8}$ 9.0, $J_{7,9}$ 1.0 Hz, 7-H), 8.27 (1 H, s, 6-H), and 8.81 (1 H, d, $J_{10,9}$ 7.0 Hz, 10-H).

Pyrido[1′,2′:3,4]*imidazo*[1,2-a]*pyrimidinium Perchlorate* (**10e**).—The finely divided lactam (**20a**) (1.50 g) was stirred with phosphoryl chloride (40 ml) at reflux. The solid coalesced into a black tar. After 45 min the excess of reagent was removed *in vacuo* and the residue was dissolved in ice–water (30 ml). Perchloric acid (60%; 2.0 ml) was added. The resulting dark green precipitate was collected and dried (2.44 g). Recrystallisation from aqueous ethanol afforded the *product* as yellow crystals (0.15 g, 7%), m.p. 238—239 °C (decomp.) (Found: C, 44.6; H, 3.3; N, 15.4. $C_{10}H_8ClN_3O_4$ requires C, 44.5; H, 3.0; N, 15.6%); $\nu_{max.}$ 907 (6-H), 805 (three adj. H), and 760 cm^{-1} (four adj. H); $\lambda_{max.}$ 219 (ε 23 300), 243 (20 600), 309 (3 800), 323 (6 900), 338 (7 600), 384 (4 650), and 402 nm (4 500); δ_H [100 MHz; $(CD_3)_2SO$] 7.27 (1 H, ddd, $J_{9,8}$ 7.0, $J_{9,10}$ 7.0, $J_{9,7}$ 1.0 Hz, 9-H), 7.59 (1 H, ddd, $J_{8,7}$ 9.0, $J_{8,9}$ 7.0, $J_{8,10}$ 1.0 Hz, 8-H), 7.97 (1 H, dd, $J_{3,4}$ 7.0, $J_{3,2}$ 4.0 Hz, 3-H), 8.03 (1 H, dd, $J_{7,8}$ 9.0, $J_{7,9}$ 1.0 Hz, 7-H), 8.71 (1 H, s, 6-H), 9.00 (1 H, dd, $J_{10,9}$ 7.0, $J_{10,8}$ 1.0 Hz, 10-H), 9.11 (1 H, dd, $J_{2,3}$ 4.0, $J_{2,4}$ 2.0 Hz, 2-H), and 9.61 (1 H, dd, $J_{4,3}$ 7.0, $J_{4,2}$ 2.0 Hz, 4-H).

2,4-*Dimethylpyrido*[1′,2′:3,4]*imidazo*[1,2-a]*pyrimidinium Perchlorate* (**10d**).—The finely divided pyrimidone (**20b**) (2.0 g) and phosphoryl chloride (30 ml) were heated together under reflux for 2 h; complete dissolution was not obtained. The excess of reagent was removed under reduced pressure and the residue was taken up in the minimum volume (130 ml) of boiling ethanol. Sodium perchlorate monohydrate (1.43 g) dissolved in ethanol (8 ml) was added, and the resulting precipitate was filtered off, washed once with ethanol, and dried (3.20 g). Recrystallisation from aqueous ethanol afforded brown crystals of the *product* (1.54 g, 55.6%), m.p. 204—209 °C (decomp.) (Found: C, 48.1; H, 4.2; N, 13.4. $C_{12}H_{12}ClN_3O_4$ requires C, 48.4; H, 4.1; N, 14.1%); $\lambda_{max.}$ 223 (ε 23 100), 239 (25 000), 245 (26 300), 307infl (5 400), 322 (8 600), 337 (9 300), 375 (4 700), and 393 nm (4 300); δ_H [100 MHz; $(CD_3)_2SO$] 2.79 (3 H, s, Me), 2.89 (3 H, s, Me), 7.19 (1 H, t, $J_{9,8}$ 7.0, $J_{9,10}$ 7.0 Hz, 9-H), 7.51 (1 H, dd, $J_{8,7}$ 9.0, $J_{8,9}$ 7.0 Hz, 8-H), 7.83 (1 H, s, 3-H), 7.90 (1 H, d, $J_{7,8}$ 9.0 Hz, 7-H), 8.65 (1 H, s, 6-H), and 8.87 (1 H, d, $J_{10,9}$ 7.0 Hz, 10-H).

1,3-*Dimethylpyrido*[1′,2′:3,4]*imidazo*[1,2-c]*pyrimidinium perchlorate Hydroperchlorate* (**11**).—The lactam (**22**) (2.0 g) was stirred under the reflux (1.5 h) with phosphoryl chloride (30 ml) to give a clear solution. Removal of the excess of reagent under reduced pressure left a brown solid to which acetone (25 ml) was added, followed by the minimum volume of methanol (6.8 ml) necessary to effect dissolution. The *product* (2.70 g) was precipitated by the addition of aqueous perchloric acid (60%, 10 ml) and was collected and washed once with acetone. It was recrystallised from glacial acetic acid–nitromethane (88 ml:90 ml) to give lime-green crystals (1.32 g, 35.7%) which detonated at 280 °C (Found: C, 36.3; H, 3.3; N, 10.5. $C_{12}H_{13}Cl_2N_3O_8$ requires C, 36.2; H, 3.3; N, 10.55%); $\lambda_{max.}$ 220 (ε 30 300), 318 (15 200), 333 (16 000), 367 (4 300), and 385 nm (3 300); δ_H [60 MHz; $(CD_3)_2SO$] 2.71 (3 H, s, Me), 3.05 (3 H, s, Me), 7.23 (1 H, dd, $J_{7,8}$ 7.0, $J_{7,6}$ 6.0 Hz, 7-H), 7.51 (1 H, dd, $J_{8,7}$ 7.0, $J_{8,9}$ 9.0 Hz, 8-H), 7.91 (1 H, d, $J_{9,8}$ 9.0 Hz, 9-H), 8.63 (1 H, s, 4-H, or 10-H), 8.75 (1 H, s, 4-H, or 10-H), and 8.99 (1 H, d, $J_{6,7}$ 6.0 Hz, 6-H); δ_H (60 MHz; D_2SO_4–D_2O; reference DSS) 3.15 (3 H, s, Me), 3.66 (3 H, s, Me), 7.53—8.03 (2 H, m, 7-H and 8-H), 8.17 (1 H, d, $J_{9,8}$ 9.0 Hz, 9-H), 8.81 (1 H, s, 4-H), and 8.89 (1 H, d, $J_{6,7}$ 6.0 Hz, 6-H).

3-[2-(*Acetylamino*)*prop*-1-*enyl*]*imidazo*[1,5-a]*pyridine* (**30**).—The perchlorate salt (**11**) (0.15 g) was dissolved in water (12 ml) and sufficient 2M sodium hydroxide added with cooling to give pH 14. A solid formed which was collected, washed with water, and recrystallised from ethanol to give the *amide* as yellow microneedles (0.077 g, 95%), m.p. 132.5—133 °C (Found: C, 66.9; H, 6.3; N, 19.5. $C_{12}H_{13}N_3O$ requires C, 67.0; H, 6.1; N, 19.5%); $\nu_{max.}$ 3 050 (NH), 1 700 (carbonyl), and 1 660 cm^{-1} (C=C); $\lambda_{max.}$ (CH_3OH) 214 (ε 16 100), 248 (14 300), 320 (19 500), 337 (25 200), and 354 nm (18 500); $\lambda_{max.}$ (0.1M HCl) 219 (ε 27 250), 319 (15 400), 333 (15 600), 369 (4 300), and 387 nm (3 100), this spectrum was identical in appearance to the above spectrum of the salt (**11**); δ_H (60 MHz; $CDCl_3$), 2.25 (3 H, s, CH_3CO), 2.57 (3 H, d, *J* 0.5 Hz, CH_3), 5.50 (1 H, d, *J* 0.5 Hz, olefinic H), 6.45—6.85 (2 H, m, 6-H, and 8-H), 7.35—7.57 (1 H, m, 7-H), 7.50 (1 H, s, 1-H), 7.85 (1 H, d, *J* 7.0 Hz, 5-H), and 12.0 (1 H, signal not recorded, N-H).

3-*Acetonylimidazo*[1,5-a]*pyridine* (**31**).—A solution of the amide (**30**) (0.1 g) in 2M HCl (5 ml) was heated on a steam-bath for 40 min. Removal of the solvent under reduced pressure left a gum which was dissolved in water (4 ml). Addition of 2M NaOH to pH 8 produced a solid which was extracted with ethyl acetate (20 ml). The extract was dried and concentrated and the residue (0.09 g) was recrystallised from light petroleum (b.p. 60—80 °C) to give the *ketone* as white microneedles (0.03 g, 37%), m.p. 73.5—74.5 °C. (Found: C, 69.2; H, 5.8; N, 15.8. $C_{10}H_{10}N_2O$ requires C, 69.0; H, 5.8; N, 16.1%); $\nu_{max.}$ 1 720 cm^{-1} (carbonyl); $\lambda_{max.}$ 217 (ε 37 000), 264 (5 050), 275 (6 950), 285.5 (5 750), and 331 nm (2 350); δ_H (100 MHz; $CDCl_3$) 2.17 (3 H, s, Me), 4.10 (2 H, s, CH_2), 6.45—6.77 (2 H, m, 6-H, and 8-H), 7.39 (1 H, s, 1-H), 7.35—7.49 (1 H, m, 7-H), and 7.71 (1 H, d, *J* 7.0 Hz, 5-H). The compound gave a dark blue colour with aqueous ferric chloride. Semicarbazone: off-white crystals from methanol, m.p. 168.5—170.5 °C.

2-(N-*Acetoacetylaminomethyl*)*pyridine* (**32**).—Diketene (8.41 g, 100 mmol), dissolved in dry toluene (30 ml), was added during 20 min to a stirred solution of 2-aminomethylpyridine[17] (10.81 g, 100 mmol), in toluene (90 ml), kept at 0 °C. Stirring was continued at 0 °C for 1 h, and then at 25 °C for 1 h. Removal of the solvent under reduced pressure left an oil (19.05 g) which was eventually obtained crystalline. Recrystallisation from ether gave the *amide* as a hygroscopic white solid (7.30 g, 38%), m.p. 43—44 °C (Found C, 62.8; H, 6.3; N, 14.9. $C_{10}H_{12}N_2O_2$ requires C, 62.5; H, 6.3; N, 14.6%); δ_H (60 MHz, $CDCl_3$) 2.25 (3 H, s, Me), 3.51 (2 H, s, CH_2), 4.60 (2 H, d, *J* 5.3 Hz, CH_2-NH), and 8.03 (1 H, br, NH). A purple colour was produced with aqueous ferric chloride. Picrate: yellow crystals from ethanol, m.p. 122.5—123 °C.

3-*Acetonylimidazo*[1,5-a]*pyridine* (**31**).—The amide (**32**) (2.0 g) was stirred with phosphoryl chloride (25 ml) under reflux for 1 min. The resulting purple solution was evaporated to dryness under reduced pressure at 40 °C, and the residue was dissolved in ice–water (50 ml). Neutralisation (10M NaOH) of the fluorescent solution precipitated a solid which was extracted with ethyl acetate (2 × 100 ml). The extract was washed with brine, dried, and evaporated and the solid residue was recrystallised from light petroleum (b.p. 60—80 °C) to give the ketone as white microneedles (0.63 g, 35%), 73.5—74.5 °C. This compound was identical (mixed m.p. and i.r.) with that obtained by degradation of the cation (**11**).

6-*Bromo*-1-*ethylpyrido*[1′,2′:3,4]*imidazo*[1,2-a]*pyrazinium Bromide* (**12**).—A suspension of the lactam (**23**) (4.0 g) in phosphoryl chloride (50 ml) was stirred under reflux for 4 h to produce a clear brown solution. The mixture was cooled and the excess of reagent was removed under reduced pressure. Water (20 ml) was added cautiously to the residue. The yellow, fluorescent solution was extracted with butanol (3 × 25 ml) and the combined organic layers were dried and the solvent removed under reduced pressure to yield a yellow gum (5.61 g). A portion of the gum (1.08 g) was dissolved in glacial acetic acid–water (20 ml:10 ml) and to it bromine (1.0 ml) was added with stirring. The precipitated yellow solid was filtered off, washed with water, and recrystallised from aqueous isopropyl alcohol to yield golden microneedles of the *product* (0.26 g, 20%), decomp. >150 °C (Found: C, 40.6; H, 3.3; Br, 44.6; N, 11.2; $C_{12}H_{11}Br_2N_3$ requires C, 40.4; H, 3.1; Br, 44.8; N, 11.8%); $\lambda_{max.}$ 212infl (ε 20 300), 243 (24 300), 275 (6 600), 286infl (4 500), 331infl (8 900), 347 (11 800), 367 (8 400), 384 (7 600), and 410infl nm (3 800); δ_H (60 MHz; D_2O; reference DSS) 1.57 (3 H, t, CH_3), 3.76 (2 H, q, CH_2), 7.69 (1 H, td, $J_{9,8}$ 7.0, $J_{9,10}$ 7.0, $J_{9,7}$ 2.0 Hz, 9-H), 7.86—8.34 (2 H, m, 7-H, and 8-H), 8.71 (1 H, d, *J* 4.5 Hz, 3-H), 8.95 (1 H, d, *J* 4.5 Hz, 4-H), and 9.33 (1 H, d, $J_{10,9}$ 7.0 Hz, 10-H).

3-*Methylpyrido*[1′,2′:3,4]*imidazo*[2,1-b]*thiazolium Perchlorate* (**13a**).—A solution of the thiazolone (**24**) (5.00 g) in a mixture of phosphoryl chloride (50 ml) and dimethylaniline (15 ml) was heated under reflux for 3 h after which the excess of phosphoryl chloride was removed under reduced pressure. The blue residue was treated with water (150 ml) and ether (100 ml) and sufficient 10M NaOH was added to adjust the solution to pH 9; the liberated dimethylaniline was taken up by the ether during this process. The aqueous layer was further extracted with ether (2 × 100 ml), and then with butanol (100 ml) to remove blue impurities. The pale yellow aqueous solution was treated with perchloric acid (60%; 7.5 ml) and the precipitated *product* collected, washed with a little chilled water, and dried (4.86 g). Recrystallisation from ethanol afforded white needles (4.12 g, 58.8%), m.p. 168.5—169.5 °C (Found: C, 41.8; H, 3.4; N, 9.5. $C_{10}H_9ClN_2O_4S$ requires C, 41.6; H, 3.1; N, 9.7%); $\lambda_{max.}$ 242 (ε 20 400), 248 (19 800), 257 (15 000), 267 (11 800), 288 (9 000), 301 (7 900), 344infl (4 000), and 359infl nm (2 100); δ_H [100 MHz; $(CD_3)_2SO$] 2.68 (3 H, d, *J* 1.0 Hz, Me), 7.19 (1 H, td, $J_{8,7}$ 7.0, $J_{8,9}$ 7.0, $J_{8,6}$ 1.0 Hz, 8-H), 7.30 (1 H, dd, $J_{7,6}$ 9.0, $J_{7,8}$ 7.0 Hz, 7-H), 7.70 (1 H, d, *J* 1.0 Hz, 2-H), 7.85 (1 H, dd, $J_{6,7}$ 9.0, $J_{6,8}$ 1.0 Hz, 6-H), 8.61 (1 H, s, 5-H), and 8.81 (1 H, d, $J_{9,8}$ 7.0 Hz, 9-H).

5-*Bromo*-3-*methylpyrido*[1′,2′:3,4]*imidazo*[2,1-b]*thiazolium Perbromide* (**13b**).—Bromine (0.10 ml, 2 equiv.) in glacial acetic acid (2 ml) was added with stirring to a solution of the

perchlorate (**13a**) (0.29 g) in glacial acetic acid–water. The resulting yellow *precipitate* was filtered off, washed with water, and dried (0.41 g). It crystallised from nitromethane as orange-coloured microneedles (0.26 g, 51%), m.p. 216 °C (Found: C, 23.9; H, 1.7; N, 5.4. $C_{10}H_8Br_4N_2S$ requires C, 23.6; H, 1.6; N, 5.5%); δ_H (60 MHz, CF_3CO_2H) 3.01 (3 H, d, *J* 0.5 Hz, Me), 7.07—7.55 (2 H, m, 7-H, and 8-H), 7.40 (1 H, d, *J* 0.5 Hz, 2-H), 7.70 (1 H, d, $J_{6,7}$ 9.0 Hz, 6-H), and 8.20 (1 H, d, $J_{9,8}$ 6.0 Hz, 9-H).

Imidazo[a,c]*dipyridinium Perchlorate* (**8**).—The pyridone (**25**)[11] (6.21 g) was stirred with refluxing phosphoryl chloride (100 ml) for 2.5 h and the resulting clear yellow solution was then concentrated under reduced pressure. Water (25 ml) was added cautiously to the residue and from the resulting solution the product was obtained as a thick crystalline precipitate by the addition of perchloric acid (60%; 15 ml). Recrystallisation from methanol afforded green–yellow microplates (7.15 g, 80%), m.p. 200—201.5 °C (Found: C, 49.6; H, 3.4; N, 10.2. Calc. for $C_{11}H_9ClN_2O_4$: C, 49.2; H, 3.4; N, 10.4%); δ_H [100 MHz; $(CD_3)_2SO$] 7.21 (1 H, ddd, $J_{3,2}$ 9.0, $J_{3,4}$ 9.0, $J_{3,1}$ 1.0 Hz, 3-H), 7.50 (1 H, dd, $J_{2,1}$ 7.0, $J_{2,3}$ 9.0 Hz, 2-H), 7.80 (1 H, ddd, $J_{8,7}$ 7.0, $J_{8,9}$ 7.0, $J_{8,6}$ 1.0 Hz, 8-H), 7.99 (1 H, dd, $J_{1,2}$ 7.0, $J_{1,3}$ 1.0 Hz, 1-H), 8.10 (1 H, ddd, $J_{7,6}$ 7.0, $J_{7,8}$ 7.0, $J_{7,9}$ 1.0 Hz, 7-H), 8.75 (1 H, s, 11-H), 8.85 (1 H, d, $J_{4,3}$ 9.0 Hz, 4-H), 9.13 (1 H, dd, $J_{6,7}$ 7.0, $J_{6,8}$ 1.0 Hz, 6-H), and 9.20 (1 H, dd, $J_{9,8}$ 7.0, $J_{9,7}$ 1.0 Hz, 9-H).

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