Tetrahedron Vol. 35, pp. 1145 to 1149
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0040-4020/79/0501-1145/$02.00/0

A SYNTHESIS OF PYRROLO[3,4-*c*]PYRIDINES VIA PYRIDYNE INTERMEDIATES

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(*Received in the UK 12 October 1978*)

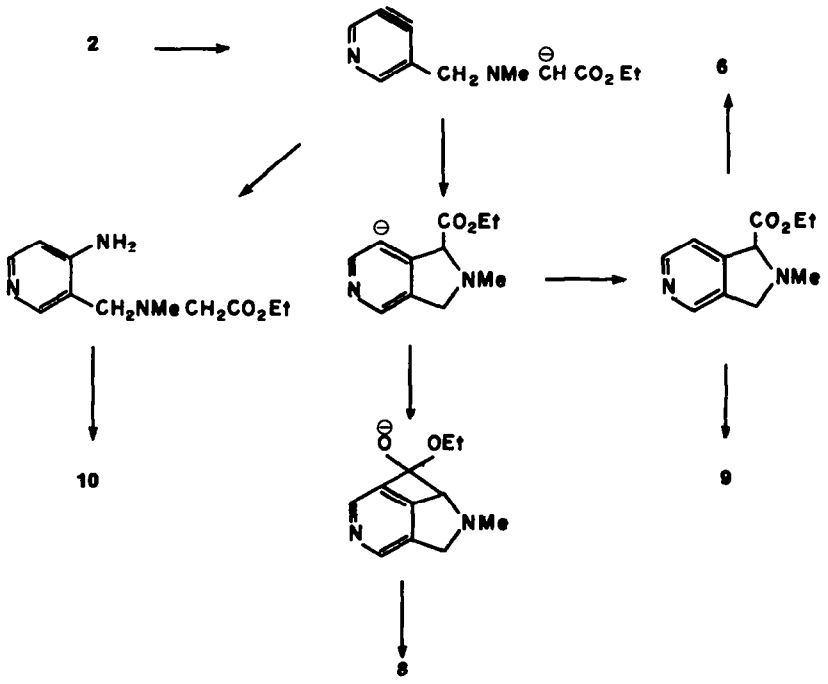
Abstract—A synthesis of pyrrolo[3,4-*c*]pyridines from pyridyne intermediates is reported together with a study of the reactions of 2-methyl-2H-pyrrolo[3,4-*c*]pyridine (5) with oxidising and reducing agents.

In continuation of our earlier work[1,2] on heterocyclic syntheses involving aryne intermediates, we now report a new synthesis of pyrrolo[3,4-*c*]pyridines. These have been prepared from 3-bromopyridines bearing a C–N–C type substituent in the 5-position. The nature of the side chain is such that under the strongly basic conditions of the reaction, a carbanion is generated which can intramolecularly attack the 3,4-didehydropyridine formed by elimination of hydrogen bromide from the 3-bromopyridine.

1. *Cyclisation reactions*

Compound 1 was prepared in 70% yield by refluxing 5-bromo-3-picolyl chloride hydrochloride[3] with N-methylaminoacetonitrile in 1,4-dioxane in the presence of triethylamine. Treatment of 1 with potassium amide in liquid ammonia furnished a product which on purification gave 2 - methyl - 2H - pyrrolo[3,4 - *c*]pyridine (5) in 69% yield. The latter compound has been previously prepared by dehydrogenation of 2,3 - dihydro - 2 - methyl - 1H - pyrrolo[3,4 - *c*]pyridine, and fully characterised by analytical and spectroscopic data and the formation of a picrate.[4] The properties of our product were closely similar to those reported in the literature; we found additionally that it formed a stable methiodide and that with Ehrlich's reagent it gave a pink colouration which changed to purple on standing. The greater quantity of material available from our experiments enabled us to carry out an investigation of the chemistry of compound 5 (see below).

When ethyl N - (5 - bromo - 3 - picolyl) - N - methylaminoacetate (2) was used as a substrate for the cyclisation reaction, a mixture of four products was obtained. The pyrrolo[3,4-*c*]pyridine esters 6 and 8, the dihydropyrrolo[3,4-*c*]pyridine carboxamide 9 and the pyridodiazepinone 10 were isolated in 6, 5, 38 and 15% yields, respectively. Compounds 6, 8, 9 and 10 were fully characterised by analytical and spectroscopic data. Possible mechanisms for the formation of the observed products are depicted in Scheme 1. The mechanism for the



Scheme 1.

formation of the rearranged ester 8 is based in analogy with the rearrangement reaction which occurs when bromobenzene is treated with diethylmalonate and sodium amide in HMPT.[5] Although diazepinone formation is depicted as involving ring amination at position 4, this could alternatively be a consequence of intramolecular cyclisation of the amide derived from the starting ester.

Cyclisation of the ketone 3 gave, as expected, the corresponding pyrrolo[3,4 - *c*]pyridine 7. Compound 7 was found to be sensitive to aerial oxidation and this may account in part for the low yield of product isolated (7%). Also isolated from this experiment was a fraction shown by spectroscopic examination to contain ring aminated products.

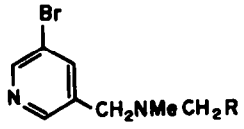
Attempted cyclisation of the picolylamine 4 failed, although we had found previously that the benzenoid derivative of analogous structure readily underwent intramolecular cyclisation to give the corresponding isoindoline in high yield.[2]

2. *Reactions of* 2-*methyl*-2H-*pyrrolo*[3,4-c]*pyridine* (5)

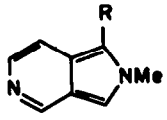
(a) *With dimethyl acetylenedicarboxylate.* Treatment of the pyrrolopyridine with the acetylene in dry ether, under N_2 at 0°, gave a 1:3-adduct. This was assigned structure 11 in analogy with the structure of the adducts obtained from pyridines[6] and isoindoles.[7,8] Attempts to purify the adduct by crystallisation were unsuccessful; however, structural assignment was supported by accurate mass measurement on the molecular ion. The observed loss of $MeO_2CC{\equiv}CCO_2Me$ on fragmentation of the molecular ion is characteristic of the 1:1-adducts of isoindoles and the ester.[8]

(b) *With* m-*chloroperbenzoic acid.* After stirring the pyrrolopyridine with *m*-chloroperbenzoic acid in chloroform solution in the dark for 90 hr, a mixture was isolated which contained approximately 60% of 2,3 - dihydro - 2 - methyl - 1 - oxo - 1H - pyrrolo[3,4 - *c*]pyridine 12 and 40% of unchanged starting material. The two components were readily separated by chromatography and the oxo compound purified by sublimation. The spectroscopic properties of the oxo compound were consistent with its structure; it had a m.p. 82–84°, which clearly indicated it was not the known isomeric 3-oxo compound which has a m.p. of 131°.[9]

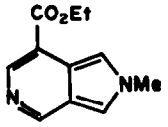
(c) *Autoxidation.* Isoindoles are known to be air-sensitive and autoxidation products of various types have



1: R = CN
2: R = CO_2Et
3: R = COPh
4: R = 4-C_5H_4N



5: R = H
6: R = CO_2Et
7: R = COPh



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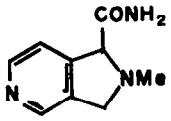

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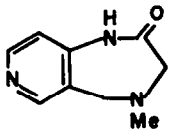

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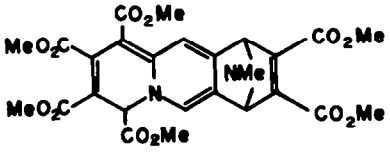

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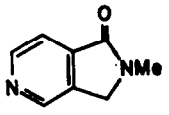

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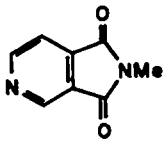

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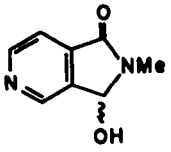

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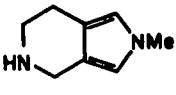

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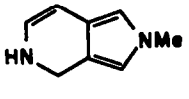

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been reported.[7,10] It had been noted earlier that compound 5 was more stable to aerial oxidation than 2-methylisoindole, and we observed that when oxygen was passed through a solution of 5 in THF at 40°, little reaction occurred. However, on irradiation of this solution, rapid oxidation occurred and starting material soon disappeared (tlc). Three main products were formed: 2,3 - dihydro - 2 - methyl - 1,3 - dioxo - 1H - pyrrolo[3,4 - *c*]pyridine (13), 2,3 - dihydro - 3 - hydroxy - 2 - methyl - 1 - oxo - 1H - pyrrolo[3,4 - *c*]pyridine (14) and 2,3 - dihydro - 2 - methyl - 1 - oxo - 1H - pyrrolo[3,4 - *c*]pyridine (12).†

The azaphthalimide 13 showed the expected CO absorptions at 1779 and 1720 cm^{-1} and the expected loss of CO_2 from the molecular ion.[10] It was converted into a hydrochloride, the m.p. of which was in agreement with the reported literature value.[9] The second product showed infrared absorptions appropriate to the presence of both CO and OH groups and PMR and mass spectral properties consistent with its proposed structure 14. The sample of 12 isolated from this experiment was identical to that obtained from *m*-chloroperbenzoic acid oxidation of 5.

(d) *Oxidation with manganese dioxide.* We were surprised to find that after stirring with manganese dioxide in boiling benzene for 8 hr, approximately 50% of starting material remained unchanged. The sole oxidation product isolated was the azaphthalimide 13.

(e) *Reduction with sodium borohydride.* Reduction of the pyrrolopyridine 5 with sodium borohydride in methanol furnished a liquid product. This gave a positive Ehrlich test, thus indicating that the pyrrole ring had not been reduced. It was characterised by spectroscopic data and by conversion into a crystalline oxalate and picrate, and found to be 4,5,6,7 - tetrahydro - 2 - methyl - 2H - pyrrolo[3,4 - *c*]pyridine 15.

(f) *Reduction with sodium bis(methoxyethoxy)aluminium hydride.* With this reagent an unstable liquid product was formed which again gave a positive Ehrlich test but which could not be converted into a crystalline derivative. Its IR spectrum showed absorptions at 3100 and 1665 cm^{-1} suggestive of the presence of a –CH=CH–NH– structural entity. We therefore tentatively suggest that the reduction product formed is 4,5 - dihydro - 2 - methyl - 2H - pyrrolo[3,4 - *c*]pyridine (16).

(g) *Miscellaneous.* Attempts to carry out various substitutions (with acetic anhydride, phenyl isocyanate, formaldehyde and morpholine) for which there was precedent in isoindole chemistry, were not successful.

EXPERIMENTAL

M.ps were determined on a Gallenkamp m.p. apparatus and are uncorrected. Tlc was performed using plates coated with Kieselgel. Visualization of tlc spots was effected by UV light, contact with iodine vapour and/or spraying with Ehrlich's reagent. Column chromatography was conducted using Merck 7734 silica. Preparative tlc was carried out using Merck silica gel $60F_{254}$ chromatography plates. IR spectra were recorded on a Unicam SP 200 spectrometer. UV spectra were taken in 96% EtOH solns on a Unicam SP 800A spectrometer. PMR spectra were taken on a Perkin–Elmer R12B spectrometer using TMS as an internal standard; chemical shifts are reported in δ units (ppm downfield from TMS). Mass spectral measurements were performed by PCMU, Harwell, U.K.

5 - *Bromo* - 3 - *picolyl chloride hydrochloride* was prepared starting from nicotinic acid according to the method described by Kauffmann and Fischer.[3]

N - (5 - *Bromo* - 3 - *picolyl*) - N - *methylaminoacetonitrile* (1). 5 - Bromo - 3 - picolyl chloride hydrochloride (24.3 g, 0.10 mol), N-methylaminoacetonitrile (7.7 g, 0.11 mol) and triethylamine (20.2 g, 0.20 mol) were heated together under reflux in dry purified 1,4-dioxane (40 ml) for 5 hr. The mixture was then poured into water (200 ml) and layered with $CHCl_3$ (50 ml). After separation, the aqueous phase was further extracted with $CHCl_3$ (4 × 50 ml). The combined extracts were washed with brine (1 × 50 ml), dried over $MgSO_4$ and concentrated. The residue was applied to a silica gel column (1:30 w/w) as an ethanolic soln. Elution with petroleum–ether 60–80/ether/ethanol (4:2:1) gave 1 (18.1 g, 75%). Attempted distillation at 116–118°/0.01 mm resulted in decomposition. IR (cm^{-1}, film): 2800s (N–Me), 2240w (CN), 1595m (C=N); PMR (CCl_4): 2.37 (s, 3, NMe), 3.52 (s, 2, CH_2), 3.60 (s, 2, CH_2CN), 7.92 (m, 1, aromatic), 8.55 (m, 1, aromatic), 8.67 (d, 1, J = 2.0 Hz, aromatic). (Found: C, 45.60; H, 4.28; N, 18.79. $C_9H_{10}BrN_3$ requires: C, 45.02; H, 4.20; N, 17.50%).

Ethyl N - (5 - *bromo* - 3 - *picolyl*) - N - *methylaminoacetate* (2). 5 - Bromo - 3 - picolyl chloride hydrochloride (24.3 g, 0.10 mol), ethyl N-methylaminoacetate (12.0 g, 0.10 mol) and triethylamine (20.2 g, 0.20 mol) were heated in refluxing 1,4-dioxane (40 ml) for 6 hr. Work up as above followed by distillation gave 2 (25.2 g, 88%, b.p. 100–102°/0.05 mm) as a colourless liquid. IR (cm^{-1}, film): 2790s (N–Me), 1725s (CO), 1582m (C=N); PMR (CCl_4): 1.25 (t, 3, J = 7.5 Hz, $CO_2CH_2\underline{CH_3}$), 2.35 (s, 3, NMe), 3.26 (s, 2, CH_2), 3.73 (s, 2, $\underline{CH_2}CO_2Et$), 4.15 (q, 2, J = 7.5 Hz, $CO_2\underline{CH_2}CH_3$), 7.97 (m, 1, aromatic), 8.54 (m, 1, aromatic), 8.63 (d, 1, J = 2.0 Hz, aromatic). (Found: C, 45.96; H, 5.16; N, 10.00. $C_{11}H_{15}BrN_2O_2$ requires: C, 46.00; H, 5.26; N, 9.76%).

N - (5 - *Bromo* - 3 - *picolyl*) - N - *methylaminoacetophenone* (3). N - (5 - Bromo - 3 - picolyl) - N - methylamine (20.2 g, 0.10 mol) (prepared by heating 5 - bromo - 3 - picolyl chloride hydrochloride and ethanolic methylamine in EtOH), freshly crystallised phenacyl bromide (19.9 g, 0.10 mol) and triethylamine (10.1 g, 0.10 mol) were stirred together at 0° in MeOH (40 ml) for 1 hr, and then heated under reflux for 0.5 hr. Work up as above gave a brown residue, which was crystallised from ether to afford 3 (20.2 g, 63%, m.p. 63–64°) as a white solid, which darkened on storage. IR (cm^{-1}, film): 2790m (NMe), 1690s (CO), 1600m, 1587m; PMR (CCl_4): 2.31 (s, 3, NMe), 3.65 (s, 2, CH_2), 3.82 (s, 2, $\underline{CH_2}COPh$), 7.4–8.03 (m, 6, aromatic), 8.45 (d, 1, J = 1.5 Hz, aromatic), 8.55 (d, 1, J = 2 Hz, aromatic). (Found: C, 56.24; H, 4.86; N, 8.45. $C_{15}H_{15}BrN_2O$ requires: C, 56.44; H, 4.74; N, 8.77%).

N - (5 - *Bromo* - 3 - *picolyl*) - N - *methyl* - N - (4 - *picolyl*)*amine* (4). 5 - Bromo - 3 - picolyl chloride hydrochloride (24.3 g, 0.10 mol), N - (4 - picolyl) - N - methylamine (13.0 g, 0.11 mol), triethylamine (20.2 g, 0.20 mol) and 1,4-dioxane (40 ml) were heated under reflux for 6 hr. The usual work up gave a residue, which was chromatographed on a silica gel column (1:30 w/w) using ether/EtOH (1:1) as eluent to give 4 (19.3 g, 66%) as a brown liquid. IR (cm^{-1}, film): 2800s (NMe), 1605s, 1572s. PMR (CCl_4): 2.17 (s, 3, NMe), 3.50 (s, 4, $2CH_2$), 7.24 (d, 2, J = 6 Hz, aromatic), 7.83 (m, 1, aromatic), 8.52 (m, 4, aromatic). Dipicrate (from ethanol): m.p. 169–171°. (Found: C, 39.82; H, 2.58; N, 16.84. $C_{25}H_{20}BrN_9O_{14}$ requires: C, 40.01; H, 2.68; N, 16.80%).

Reaction of 1 *with potassium amide in liquid ammonia.* The nitrile 1 (4.80 g, 0.02 mol) in anhyd ether (30 ml) was added to KNH_2, prepared from K (4.00 g, 0.102 g atom), in liquid ammonia (600 ml). After 35 min, ammonium nitrate (12 g) was added and the ammonia was allowed to evaporate. Water (200 ml) was added and the product extracted into CH_2Cl_2 (6 × 50 ml). The combined extracts were washed with brine, dried over $MgSO_4$ and concentrated to give a dark coloured residue, which was extracted with cyclohexane at 50–60° (8 × 50 ml). The extracts were evaporated until pale yellow needles crystallised out, which were recovered by filtration and washed with n-pentane to give 5 (2.25 g), m.p. 91–94°. The product was further purified by sublimation at 80–85°/0.10 mm (1.82 g, 69%), m.p. 95–96° (lit.,[4] m.p. 97–98). IR (cm^{-1}, Nujol): 1616m, 1543m, 1342s, 1171m, 1141s, 992m, 908s, 814s, 765s; UV (nm, λ_{max}): 261, 264sh, 271, 281.5,

†12 was shown by tlc to oxidise to 13.

341; PMR ($CDCl_3$): 3.97 (s, 3, NMe), 7.0–9.2 (m, 5, aromatic), MS (*m/e*): 132 (M^+), 131, 117, 105, 92, 91, 79, 63. (Found: C, 72.70; H, 6.01; N, 21.30. $C_8H_8N_2$ requires: C, 72.70; H, 6.10; N, 21.20%). The compound gave a pink colour with Ehrlich's reagent, which changed to purple on standing. On adding ethereal hydrogen chloride to an ethereal soln of the compound, yellowish ppt formed, which immediately went black on filtration. Picrate (from EtOH): m.p. 193–195° (lit.,[4] m.p. 194.5–195.5). The methiodide was prepared in ether and recrystallised from EtOH; it had m.p. 140° dec. (Found: C, 39.15; H, 3.93; N, 10.04. $C_9H_{11}IN_2$ requires: C, 39.43; H, 4.04; N, 10.22%).

Reaction of **2** *with potassium amide in liquid ammonia.* The ester **2** (5.74 g, 0.02 mol) in anhyd ether (20 ml) was reacted with KNH_2, prepared from K (4.00 g, 0.10 g atom), in liquid ammonia (600 ml) in the usual manner. After 35 min, ammonium nitrate (12 g) was added and the ammonia was allowed to evaporate. Water (200 ml) was added and the mixture extracted with ether (4 × 50 ml). The combined ethereal extracts were washed with brine, dried over $MgSO_4$ and concentrated to give the crude product (0.41 g). Recrystallisation from ether gave **6** (0.24 g, 6%), m.p. 109–111°. IR (cm^{-1}, Nujol): 1678s,sh, 1660s (CO), 1617s (C=N), 1456s, 1427s, 1344s, 1317s, 1273s, 1218s, 1187s, 1170s, 1103s, 1073s, 965s, 826s, 772s; UV (nm, λ_{max}): 248, 254sh, 289sh, 296, 318sh, 332, 347; PMR ($CDCl_3$): 1.49 (t, 3, J = 7.5 Hz, $CO_2CH_2\underline{CH_3}$), 4.30 (s, 3, NMe), 4.47 (q, 2, J = 7.5 Hz, $CO_2\underline{CH_2}CH_3$), 7.56 (s, 1, aromatic), 7.91 (d, 1, J = 6 Hz, aromatic), 8.30 (d, 1, J = 6 Hz, aromatic), 9.13 (s, 1, aromatic); MS (*m/e*): 205, 204.0894 (M^+ requires: 204.0899), 176, 159, 132. (Found: C, 64.38; H, 5.91; N, 13.70. $C_{11}H_{12}N_2O_2$ requires: C, 64.68; H, 5.92; N, 13.72%).

The aqueous phase, obtained after the extraction with ether, was continuously extracted with $CHCl_3$ for 5 hr. This extract was dried over $MgSO_4$ and concentrated to afford a dark coloured solid material (2.5 g). This was shown by tlc (EtOH 100%) to contain three components. It was applied to a silica gel column (100 g) in ethanolic soln and elution was continued with the same solvent. The fraction corresponding to the most mobile component gave a white solid, which on recrystallisation from EtOH afforded **9** (1.34 g, 38%), m.p. 189–191° (sublimes at 148–150°/0.1 mm). IR (cm^{-1}, Nujol): 3350s (NH), 3160m (NH), 1660s (CO), 1603w (C=N), 1580w, 1175m, 1150m, 1120m, 1098s, 1030m, 903m, 820m, 730m; UV (nm, λ_{max}): 262; PMR (DMSO-d_6): 2.54 (s, 3, NMe), 3.05–4.55 (m, 3, $\underline{CH}$–N–$\underline{CH_2}$), 7.38 (d, 1, J = 5.5 Hz, aromatic), 7.1–8.4 (br, 2, $\underline{NH_2}$, D_2O exchangeable), 8.55 (d, 1, J = 5.5 Hz, aromatic), 8.61 (s, 1, aromatic); MS (*m/e*) 176, 175.0749 (M^+–2 requires: 175.0746), 157, 133, 132, 131. (Found: C, 60.96; H, 5.98; N, 23.53. $C_9H_{11}N_3O$ requires: C, 60.99; H, 6.25; N, 23.71%).

The fraction corresponding to two slower moving spots gave a yellowish white solid (0.90 g), which was sublimed at 180°/0.01 mm to give **10** (0.51 g, 15%). Crystallization from EtOH gave a white solid m.p. 194–196°. IR (cm^{-1}, Nujol): 3180m (NH), 1660s (CO), 1583s (C=N), 1368s, 1352s, 1178s, 1063s, 995s, 885s, 865s, 781s, 673s; UV (nm, λ_{max}): 248; PMR ($CDCl_3$): 2.40 (s, 3, NMe), 3.67 (s, 2, CH_2), 3.90 (s, 2, CH_2), 6.94 (d, 1, J = 5.5 Hz, aromatic), 8.40 (s, 1, aromatic), 8.43 (d, 1, J = 5.5 Hz, aromatic), 9.58 (br, 1, NH, D_2O exchangeable), MS (*m/e*): 177.0894 (M^+ requires: 177.0902), 148, 119, 107. (Found: C, 60.79; H, 6.13; N, 23.65. $C_9H_{11}N_3O$ requires: C, 60.99; H, 6.25; N, 23.71%).

After the separation of **10** the residual solid was crystallised twice from EtOH to give **8** (0.21 g, 5%), m.p. 191–192°. IR (cm^{-1}, Nujol): 1710s (CO), 1643m, 1280s, 1105s, 845s, 772m; UV (nm, λ_{max}): 244, 249, 288sh, 297, 319sh, 334, 348; PMR (DMSO-d_6): 1.42 (t, 3, J = 7.5 Hz, $CO_2CH_2\underline{CH_3}$), 4.46 (q, 2, J = 7.5 Hz, $CO_2\underline{CH_2}CH_3$), 4.44 (s, 3, NMe), 8.40 (s, 2, aromatic), 8.96 (s, 1, aromatic), 9.96 (s, 1, aromatic); MS (*m/e*): 205, 204.0895 (M^+ requires: 204.0899), 176, 159, 132, 131. Picrate (from ethanol): m.p. 212–214°. (Found: C, 47.15; H, 3.38; N, 16.03. $C_{17}H_{15}N_5O_9$ requires: C, 47.12; H, 3.49; N, 16.16%).

Reaction of **3** *with potassium amide in liquid ammonia.* The ketone **3** (6.38 g, 0.02 mol) in anhyd ether (20 ml) and KNH_2, from K (3.40 g, 0.087 g atom), in liquid ammonia (600 ml) were reacted for 30 min in the usual manner. After the evaporation of the ammonia, ether (100 ml) and water (150 ml) were added and the aqueous phase extracted with ether (5 × 50 ml). The combined ethereal extracts were washed with brine, dried over $MgSO_4$ and concentrated to give a brown coloured sticky material. Tlc examination (100% EtOH) showed two main spots with streaking and tailing. This material was applied to a silica gel (1:30 w/w) column, as an ethanolic soln and eluted with abs EtOH under N_2. A brown coloured sticky material, obtained as the first fraction, was found to be impure showing contamination with the slower moving component. The material was crystallised from EtOH/ether to give **7** (0.34 g, 7%), m.p. 135–137° as a light yellow solid, which was found to oxidise in air. IR (cm^{-1}, Nujol): 1618s,sh, 1601s (CO), 1575m (C=N), 1423m, 1350s, 1325m, 1225s, 1079s, 1020s, 915s, 835s, 800m, 761s, 722s, 697m, 678m; UV (nm, λ_{max}): 227, 344, 358; PMR ($CDCl_3$): 4.34 (s, 3, NMe), 6.64 (d, 1, J = 6.2 Hz, aromatic), 7.35–8.00 (m, 6, aromatic), 8.04 (d, 1, J = 6.2 Hz, aromatic), 9.14 (s, 1, aromatic); MS (*m/e*): 236.0946 (M^+ requires: 236.0949), 235, 105. (Found: 24 hr after crystallization: C, 75.41; H, 5.11; N, 11.61 and 48 hr after crystallization: C, 75.00; H, 5.05; N, 11.47. $C_{15}H_{12}N_2O$ requires: C, 76.25; H, 5.12; N, 11.86%).

Further elution gave aminated product (1.14 g, 22%) as a brown coloured sticky liquid.

Reaction of **4** *with potassium amide in liquid ammonia.* The substrate **4** (5.84 g, 0.02 mol) in anhyd ether (20 ml) was reacted with KNH_2, from K (3.40 g, 0.087 g atom), in liquid ammonia in the standard method. After the evaporation of ammonia, water (150 ml) was added and the aqueous phase extracted with $CHCl_3$ (4 × 50 ml). The combined $CHCl_3$ extracts were washed with brine, dried and concentrated to give a mixture of aminated products (4.02 g). These could not be separated by chromatography.

Reaction of **5** *with dimethyl acetylenedicarboxylate.* Dimethyl acetylenedicarboxylate (0.50 g, 3.50 mmol) in ether (10 ml) was added dropwise to **5** (0.15 g, 1.10 mmol) in ether (20 ml) at 0° with stirring under N_2. After 1 hr the red coloured ppt was filtered off and washed with ether to give **11** (0.06 g, 9%) which decomposed at 140° without melting. Attempts to recrystallize the product from different organic solvents were unsuccessful. MS (*m/e*): 558.1488 (M^+ requires: 558.1491), 499, 439, 416, 395, 357.1081 ($C_{18}H_{17}N_2O_6^+$ requires: 357.1087), 274, 132. (Found: C, 54.93; H, 4.65; N, 5.80. $C_{26}H_{26}N_2O_{12}$ requires: C, 55.91; H, 4.69; N, 5.02%).

Oxidation of **5** *with m-chloroperbenzoic acid.* A soln of **5** (0.20 g, 1.50 mmol) and *m*-chloroperbenzoic acid (0.30 g, 1.70 mmol) in chloroform (40 ml) was stirred in the dark for 90 hr. The brown soln thus obtained, was washed with dil. NaOH aq, water and brine and dried over $MgSO_4$. Removal of the solvent gave a brown coloured oil (0.113 g). Tlc (EtOH/$CHCl_3$ 1:1) and PMR examination of the product showed that it contained approximately 60% of **12** and 40% of unchanged starting material. A pure sample of **12** (0.05 g, 20%) was separated from the less mobile starting material by preparative tlc (eluting with EtOH/$CHCl_3$ 3:2). An analytical sample of m.p. 82–84° was obtained by sublimation at 70°/0.1 mm. IR (cm^{-1}, $CDCl_3$): 1690s(CO), 1615m, 1585m, 1427s, 1404s; UV(nm, λ_{max}): 265, 272sh, 283; PMR ($CDCl_3$): 3.20 (s, 3, NMe), 4.47 (s, 2, CH_2), 7.75 (d, 1, J = 5.5 Hz, aromatic), 8.83 (d, 1, J = 5.5 Hz, aromatic), 8.88 (s, 1, aromatic); MS (*m/e*): 149, 148 (M^+), 133, 120, 105. (Found: C, 64.89; H, 5.40; N, 18.80. $C_8H_8N_2O$ requires: C, 64.85; H, 5.44; N, 18.91%).

Autoxidation of **5**. O_2 was bubbled through a soln of **5** (0.22 g, 1.60 mmol) in anhyd THF (40 ml) irradiated with a 100 watt electric bulb. The soln was kept at 40–50° for 4 hr and after removal of solvent a yellow oil was obtained. Tlc (EtOH/ether 1:1) of the crude product showed three spots and a spot at the origin covering the area of application. The material corresponding to the immobile spot was separated by dissolving the product in EtOH and precipitation with ether. The ppt was filtered off and washed with ether (3 × 15 ml). The filtrate and washings thus obtained were concentrated. The residue was applied to a silica gel column (1:30 w/w), as an ethanolic soln. Elution with ether gave **13** (0.07 g, 27%), m.p. 94–95° (with sublimation) which was sublimed at 40°/0.1 mm to obtain the sample for analysis. IR (cm^{-1}, CCl_4): 1779s (CO), 1720s (CO), 1613m, 1598s (C=N); UV (nm, λ_{max}): 280; PMR (CCl_4): 3.20 (s, 3, NMe), 7.79 (1, d, J =

5.5 Hz, aromatic), 9.14 (d, 1, J = 5.5 Hz, aromatic), 9.21 (s, 1, aromatic); MS (*m/e*): 162 (M^+), 161, 134, 133, 118. (Found: C, 59.25; H, 3.85; N, 16.99. $C_8H_6N_2O_2$ requires: C, 59.25; H, 3.73; N, 17.28%).

Elution with mixtures of ether and EtOH gave **14** (0.02 g, 8%) as a colourless oil, which changed to brown on standing and was found unstable; IR (cm^{-1}, $CDCl_3$): 3300s,br (OH), 1703s (CO), MS (*m/e*): 164 (M^+), 163, 162.0429 (M^+–2H requires 162.0429), 147, 105.

Further elution with EtOH gave **12** (0.05 g, 19%), m.p. 82–84°.

Oxidation of **5** *with manganese dioxide.* The pyrrolopyridine (0.20 g, 1.5 mmol) and MnO_2 (0.80 g) were refluxed with stirring in dry benzene (20 ml) in the dark for 8 hr. After filtration, the residue was washed with EtOH (8 × 25 ml). The combined washings and the filtrate were concentrated to afford a dark coloured product, which was shown by tlc and PMR to contain about 50% of starting material. The residue was applied to a preparative tlc plate and eluted with ether to give **13** (0.02 g, 8%), m.p. 94–95° (with sublimation). The hydrochloride was crystallised from EtOH and sublimed at 80°/0.01 mm and had m.p. 205–207° dec (lit.,[9] 202–204°). (Found: C, 49.00; H, 3.57; N, 14.04. $C_8H_7ClN_2O_2$ requires: C, 48.90; H, 3.55; N, 14.10%).

Reduction of **5** *with sodium borohydride.* The compound **5** (0.20 g, 1.5 mmol) in MeOH (10 ml) was added to a soln of $NaBH_4$ (0.20 g, 5.3 mmol) in MeOH (20 ml) and the mixture was refluxed for 6 hr. After cooling, the mixture was poured into water (50 ml) and extracted with $CHCl_3$ (4 × 30 ml). The combined extracts were washed with water (2 × 20 ml) and brine and dried over $MgSO_4$. Removal of the solvent gave **15** (0.18 g, 85%) which gave a positive Ehrlich test and which was characterised as its oxalate (from EtOH), m.p. 172–173° dec. (Found: C, 53.03; H, 6.09; N, 12.18. $C_{10}H_{14}N_2O_4$ requires: C, 53.14; H, 6.24; N, 12.38%). Picrate (from EtOH): m.p. 161–163° dec. (Found: C, 46.51; H, 3.66; N, 19.10. $C_{14}H_{15}N_5O_7$ requires: C, 46.03; H, 4.14; N, 19.17%).

Reduction of **5** *with sodium bis(methoxyethoxy)aluminium hydride.* To a stirred soln of sodium bis(methoxyethoxy)aluminium hydride (2.2 g, of 70% w/w soln in benzene, 7.0 mmol) in benzene (10 ml) was added a soln of **5** (0.30 g, 2.3 mmol) in benzene (20 ml). The mixture was refluxed for 2 hr. After cooling, water was added, the ppt of aluminium hydroxide was dissolved in 15% NaOH aq and the soln was extracted with $CHCl_3$ (5 × 30 ml). The combined extracts were dried over $MgSO_4$, filtered and concentrated to give an unstable material (0.2 g) which gave a positive Ehrlich's test. The IR and PMR spectra suggested the product to be **16**. It was found to streak on a tlc plate and attempts to make an oxalate, picrate or methiodide were unsuccessful.

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