Pyridylethyl: A Versatile Protecting Group. Part II [1]. The Protection of Heterocyclic N-H Groups

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Pyrrole, indole, carbazole and imidazole have been protected as *N*-[2-(4-pyridyl)ethyl] derivatives. Deprotection occurred under mild conditions after quaternisation. 3-Bromoindole was prepared by bromination of the protected parent indole.

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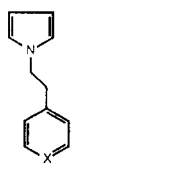
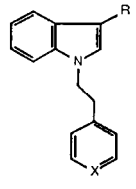
An earlier paper from this laboratory demonstrated the promising potential of the 2-(2- or 4-pyridyl)ethyl group in the protection of a group possessing an active hydrogen. Thus, carboxylic acids, thiols and sulphinic acids can be protected as 2-(2- or 4-pyridyl)ethyl esters, followed by deprotection upon treatment with methyl iodide under neutral or weakly basic conditions [1]. Other workers have reported the use of the 2-(2- or 4-pyridyl)ethyl group in the form of the 2-(2- or 4-pyridyl)ethoxycarbonyl protecting group [2,3].



1, X = N

2, X = $\overset{+}{N}$Me I^-

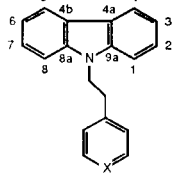


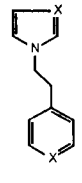
3, R = H, X = N

4, R = Br, X = N

5, R = H, X = $\overset{+}{N}$Me I^-

6, R = Br, X = $\overset{+}{N}$Me I^-





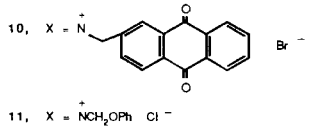
7, X = N

8, X = NMe I

9, X = $\overset{+}{N}$CHPh$_2$ Br^-

12, X = N

13, X = $\overset{+}{N}$Me I^-



10, X = $\overset{+}{N}$ Br^-

11, X = $\overset{+}{N}$CH$_2$OPh Cl^-

We are seeking to develop the potential of the 2-(4-pyridyl)ethyl group as a protective group. The present paper describes work in which we explore its application to the NH groups of *N*-heterocycles. A variety of existing methods of protection are available for such compounds and some of the more useful ones include: *t*-butyloxycarbonyl for pyrroles [4] (deprotection by TFA, 20°, 2 minutes), *N,N*-dimethylsulphamoyl for imidazoles [5] (2*N* hydrochloric acid, 4 hours reflux), and [2-(trimethylsilyl)-ethoxy]methyl for pyrroles and indoles [6] boron trifluoride etherate, 20°). However all the previous reported methods suffer from lack of generality, or require relatively forcing conditions for deprotection. 2- and 4-Pyridylethyl groups have previously been used for benzimidazoles [7], but the conditions employed for deprotection (aluminum chloride, 140°, 5 hours) were severe. Efficient protection of heterocyclic N-H groups has been required in a variety of applications, *e.g.* in directed metalations, [8,9] in the incorporation of histidine [10] and tryptophan [11,12] residues in polypeptide synthesis, and in Friedel-Crafts acylations [13,14].

Conjugate addition (of NH containing compounds) to 2-and 4-vinylpyridines was established by Doering and Weil [15]. There are numerous efficient procedures for preparing pyridylethylated *N,N*-dialkylamines [7,16-20]. Pyridylethylations of pyrrole [16], indole [21,22], carbazole [23], imidazole [24] and benzimidazole [25] have been achieved. We have now investigated the deprotection of such pyridylethylated derivatives by quaternisation with a variety of deprotecting agents: methyl iodide, benzhydryl bromide, chloromethoxybenzene, aluminum chloride and (2-bromomethyl)anthraquinone, followed by treatment with a variety of bases under mild conditions. Our objective was to achieve flexibility in selecting suitable conditions for deprotection.

Pyrrole underwent pyridylethylation with 4-vinylpyridine and sodium metal, giving 4-[2-(4-pyrrolyl)ethyl]pyridine **1**, as previously reported [16]. The pyridine **1** reacted smoothly with MeI in acetone at 25°, affording the pyridinium iodide **2** in 80% yield. When the salt **2** was stirred with one equivalent of NaOH in aqueous acetone, quantitative deprotection occurred at 25° and pyrrole was easily separated from 1-methyl-4-vinylpyridinium iodide by extraction of the former with anhydrous ethyl ether.

Indole underwent pyridylethylation with 4-vinylpyridine at 140°, using sodium ethoxide/ethanol and cupric sulfate,

according to the method of Gray and Archer [22]. The resulting 4-[2-(1-indolyl)ethyl]pyridine was alkylated quantitatively by MeI in acetone at 25°, affording the pyridinium iodide **5**. Deprotection of the latter led to the quantitative recovery of indole.

It was demonstrated that the protected indole **3** could undergo reaction before subsequent deprotection. Thus, bromination of the indole **3** with NBS at 25° afforded the protected 3-bromoindole **4** in 95% yield. The latter underwent quantitative alkylation with methyl iodide in acetone at 25°, to give the pyridinium iodide **6**. Deprotection of **6** afforded 3-bromoindole in quantitative yield.

Pyridylethylation of carbazole using 4-vinylpyridine and sodium by the method of Dressler and Baum [23] afforded the protected carbazole **7**. Alkylation of pyridylethylcarbazole **7** with methyl iodide afforded the pyridinium iodide **8** in 92% yield. Quaternisation of the carbazole **7** was also achieved with diphenylmethyl bromide (24 hours reflux in benzene, 56%), with 2-(bromomethyl)anthraquinone (1 hour reflux in acetone, 80%), and with (chloromethoxy)-benzene (4 hours reflux in acetonitrile, 76%), giving the respective salts **9**, **10** and **11**. The ^{1}H- and ^{13}C-nmr spectra of the above three salts were consistent with their structures; in particular, the signals at δ 7.78, 6.12 and 6.63 in the ^{1}H nmr spectra, and those at 74.8, 61.5 and 83.8 ppm in the ^{13}C nmr spectra of the pyridinium salts **9**, **10** and **11**, reflect the respective fragments CH-N$^+$, CH_2-N$^+$ and CH_2-N$^+$ found in those salts.

Deprotection of the *N*-(diphenylmethyl)pyridinium bromide **9** was achieved by refluxing in ethanol with 2.5 molar equivalents of collidine; the yield of carbazole was quantitative. An alternative method of deprotection employed refluxing acetonitrile with 0.5 molar equivalents of sodium; the yield of carbazole was 78%. One equivalent of aqueous sodium hydroxide proved less satisfactory for deprotection, since some pyridylethylcarbazole **7** was formed along with the main product, carbazole.

Deprotection of the 1-(2-anthraquinonylmethyl)pyridinium bromide **10** with 2*N* ethanolic sodium ethoxide at 20° gave a mixture of carbazole and 4-[2-(9-carbazolyl)-ethyl]pyridine, as shown by ^{1}H nmr spectroscopy; when the salt **10** was refluxed in collidine for 11 hours, no reaction occurred. Attempts to deprotect the pyridinium chloride **11** using aqueous sodium hydroxide (1.25 equivalents) at 25° and triethylamine (1.5 equivalents) at 25° also gave mixtures. Consequently, the 1-(2-anthraquinonylmethyl) and the 1-phenoxymethyl groups were considered unsuitable for cleavage of the 2-(4-pyridyl)ethyl moiety.

Imidazole underwent pyridylethylation to give the pyridine **12** when heated under reflux in glacial acetic acid with 4-vinylpyridine, according to the method of Profft and Georgi [24]. It was confirmed that deprotection of **12** could be accomplished by refluxing in 1,1,2,2-tetrachloroethane with aluminum chloride, the method used by Ichikawa, Yamamoto and Hisano [25] to remove pyridylethyl groups from protected benzimidazoles. 'Deprotection' of the pyridine **12**, with the formation of 1-methylimidazole, was achieved by alkylation with excess methyl iodide, to give the diiodide **13** in 63% yield, followed by treatment of the latter with 2 moles of potassium carbonate in aqueous acetone. The 1-methylimidazole so obtained was isolated as the picrate.

In conclusion we have demonstrated that several heterocyclic NH groups can conveniently be protected by *N*-[2-(4-pyridyl)ethylation] and that deprotection follows under very mild conditions, after quaternisation. The method would appear to be that of choice for many applications, and its feasibility has been tested by applying it to the bromination of indole.

EXPERIMENTAL

Melting points were determined with a Thomas-Hoover capillary apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 283B spectrophotometer. 60 MHz ^{1}H nmr spectra were recorded on a Varian EM 360L spectrometer and 25 MHz ^{13}C nmr spectra on a JEOL JNM FX 100 spectrometer; in all cases deuterated dimethylsulfoxide was the solvent. Mass spectra were obtained on an AEI MS 30 instrument. Evaporation refers to removal of solvent under reduced pressure. Anhydrous magnesium sulphate was used as the drying agent unless otherwise stated.

The following compounds were prepared by literature methods: 4-[2-(1-pyrrolyl)ethyl]pyridine, mp 88-90° (lit [16], mp 90-91°); 4-[2-(1-indolyl)-ethyl]pyridine, mp 48-49° (lit [22], mp 41-45°); 4-[2-(9-carbazolyl)ethyl]-pyridine, mp 170-172° (lit [23], mp 173-174°); 4-[2-(imidazol-1-yl)ethyl]-pyridine, mp 88-90°; ν max (bromoform): 1590, 1555, and 1490 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 3.00 (2H, t, J = 7 Hz, CH_2-pyridine), 4.22 (2H, t, J = 7 Hz, CH_2-N), 6.87-7.27 (4H, m), 8.60 (2H, d, J = 5 Hz, pyridine α-H); ^{13}C nmr (deuteriochloroform): 148.5 (C-2, 6, pyridine), 145.6 (C-4, pyridine), 135.8 (C-2, imidazole, 127.8 (C-4, imidazole), 122.8 (C-3, 5, pyridine) and 117.7 (C-5, imidazole); (lit [24], bp 184-186° at 1 mm Hg); 2-(bromomethyl)anthraquinone, mp 188-191° (lit [26], mp 190-194°); diphenylmethyl bromide, mp 40-42° (lit [27], mp 42°).

Anal. Calcd. for $C_{10}H_{11}N_3$: C, 69.34; H, 6.40; N, 24.26. Found: C, 68.99; H, 6.53; N, 24.04.

4-[2-(3-Bromo-1-indolyl)ethyl]pyridine (**4**).

A mixture of 4-[2-(1-indolyl)ethyl]pyridine (0.444 g, 2.0 mmole), *N*-bromosuccinimide (0.356 g, 2.0 mmoles) and THF (10 ml) was stirred at 25° for 24 hours. The reaction mixture was poured onto a mixture of ice, water and sodium sulphite (1.0 g), followed by extraction with ether. The aqueous layer was further extracted with methylene chloride (2 x 50 ml) and the combined ethereal extracts dried and evaporated to give 4-[2-(3-bromo-1-indolyl)ethyl]pyridine (0.57 g, 95%), as a reddish brown viscous oil; ir (bromoform): ν max 1600, 1550, and 1500 cm^{-1}; ^{1}H nmr: δ 2.90 (2H, t, CH_2-py), 4.20 (2H, t, CH_2-N), 6.8-7.8 (7H, m), and 8.5 (2H, d, J = 6 Hz, pyridine α-H); ^{13}C nmr: δ 149.6 (C-2, pyridine), 146.9 (C-4, pyridine), 135.0 (C-9, indole), 126.8 (C-8, indole), 126.2 (C-2, indole), 124.2 (C-3, 5, pyridine), 122.3 (C-5, indole), 119.9 (C-4, indole), 118.8 (C-6, indole), 109.0 (C-7, indole), and 89.3 (C-3, indole), 35.2 (CH_2-pyridine) and 46.2 (CH_2-N).

The structure of the pyridine **4** was further confirmed by the elemental analysis of its hydrochloride obtained by passing hydrogen chloride gas through its solution in carbon tetrachloride, followed by recrystallising the precipitate from ethanol/ether.

Anal. Calcd. for $C_{15}H_{14}BrClN_2.0.5\ H_2O$: C, 51.97; H, 4.36; N, 8.08. Found: C, 51.92; H, 4.12; N, 8.01.

1-Methyl-4-[2-(1-pyrrolyl)ethyl]pyridinium Iodide (**2**).

4[2-(1-Pyrrolyl)ethyl]pyridine (0.86 g, 5.0 mmoles) was treated with methyl iodide (0.83 g, 5.8 mmoles) in acetone (5 ml) at 25° for 24 hours. Addition of ether and filtration afforded a solid which on recrystallisation from acetone-ether gave the pyridinium iodide **2** (1.25 g, 80%) as prisms, mp 130-132°; ir (bromoform): ν max 1635, 1600, 1565, and 1500 cm^{-1}; ^1H nmr: δ 3.38 (2H, t, J = 6 Hz, CH_2-pyridinium), 4.36 (2H, t, J = 6 Hz, CH_2-N), 4.48 (3H, s, N-CH_3), 6.05 (2H, t, J = 2 Hz), 6.83 (2H, t, J = 2 Hz), 8.00 (2H, d, J = 6 Hz, pyridinium β-H), and 9.00 (2H, d, J = 6 Hz, pyridinium); ^{13}C nmr: δ 158.2 (C-4, pyridinium), 144.5 (C-2, 6, pyridinium), 127.5 (C-3, 5, pyridinium), 120.5 (C-2, pyrrole), 107.6 (C-3, pyrrole), 47.5 (CH_2-N), 47.3 (CH_3-N), and 36.5 (CH_2-pyridinium); ms: 186 (M^+-HI, 1.5%), 172 (M^+-MeI, 20), 80 (100).

Anal. Calcd. for $C_{12}H_{15}IN_2.0.25\ H_2O$: C, 45.22; H, 5.06; N, 8.79. Found: C, 45.23; H, 4.76; N, 8.61.

1-Methyl-4-[2-(1-indolyl)ethyl]pyridinium Iodide (**5**).

4[2-(1-Indolyl)ethyl]pyridine (**3**) (0.834 g, 3.76 mmoles) was stirred with methyl iodide (1.0 g, 0.70 mmole) in acetone (12 ml) at 25° for 24 hours. Addition of anhydrous ether (100 ml) and filtration afforded the pyridinium iodide **5** (1.34 g, 96%), crystallising from ethanol-ether as prisms, mp 217-219°; ir (bromoform): ν max 1640, 1600, 1565, and 1500 cm^{-1}; ^1H nmr: δ (2H, t, J = 7 Hz, CH_2-pyridinium), 4.67 (2H, t, J = 7 Hz, CH_2-N), 4.35 (3H, s, N^+-CH_3), 6.47 (1H, d, J = 3 Hz, indole 3-H), 7.0-7.9 (5H, m), 8.08 (2H, d, J = 6 Hz, pyridinium β-H), and 9.00 (2H, d, J = 6 Hz, pyridinium α-H); ^{13}C nmr: δ 158.4 (C-4, pyridinium), 144.7 (C-2, 6, pyridinium), 135.7 (C-9, indole), 128.7 (C-3, 5, pyridinium), 128.5 (C-8, indole), 128.0 (C-2, indole), 121.3 (C-5, indole), 120.6 (C-4, indole), 119.3 (C-6, indole), 109.5 (C-7, indole), 101.1 (C-3, indole), 47.5 (CH_3-N^+), 45.0 (CH_2-N), and 35.5 (CH_2-pyridinium).

Anal. Calcd. for $C_{16}H_{17}IN_2.0.5\ H_2O$: C, 51.49; H, 4.86; N, 7.51. Found: C, 51.35; H, 4.66; N, 7.31.

1-Methyl-4-[2-(3-bromo-1-indolyl)]pyridinium Iodide (**6**).

3-Bromo-1-[2-(4-pyridyl)ethyl]indole (1.33 g, 4.42 mmoles) was stirred with methyl iodide (0.627 g, 4.42 mmoles) in acetone (15 ml) at 25° for 24 hours. Addition of anhydrous ether (100 ml) and filtration afforded the pyridinium iodide **6** (1.85 g, 95%), crystallising from ethanol-ether as prisms, mp 179-181°; ir (bromoform): ν max 1640, 1605, 1570, and 1510 cm^{-1}; ^1H nmr: δ 3.50 (2H, t, J = 7 Hz, CH_2-pyridinium), 4.40 (3H, s, N^+-CH_3, 4.70 (2H, t, J = 7 Hz, CH_2-N), 7.2-7.9 (5H, m), 8.20 (2H, d, J = 6 Hz, pyridinium β-H), and 9.00 (2H, d, J = 6 Hz pyridinium α-H), ^{13}C nmr: δ 157.9 (C-4, pyridinium), 144.7 (C-2, 6, pyridinium), 135.2 (C-9, indole), 127.8 (C-3, 5, pyridinium), 127.4 (C-2, indole), 126.4 (C-8, indole), 122.5 (C-5, indole), 120.3 (C-4, indole), 118.3 (C-6, indole), 110.6 (C-7, indole), 88.5 (C-3, indole), 47.3 (CH_3-N^+), 45.0 (CH_2-N), and 35.2 (CH_2-pyridinium).

Anal. Calcd. for $C_{16}H_{16}BrIN_2.0.5\ H_2O$: C, 42.50; H, 3.79; N, 6.20. Found: C, 42.84; H, 3.57; N, 6.12.

1-Methyl-4-[2-(9-carbazolyl)ethyl]pyridinium Iodide (**8**).

A mixture of 4-[2-(9-carbazolyl)ethyl]pyridine (0.554 g, 2.04 mmoles), methyl iodide (0.385 g, 2.71 mmoles) and acetone (20 ml) was stirred at room temperature for 54 hours. Addition of anhydrous ether (100 ml) and filtration afforded the pyridinium iodide **8** (0.770 g, 92%) which crystallised from methanol as needles, mp 153-154°; ir (bromoform): ν max 1640, 1590, 1580 and 1510 cm^{-1}; ^1H nmr: δ 3.33 (2H, t, J = 7 Hz, CH_2-pyridinium), 4.30 (3H, s, N-CH_3), 4.80 (2H, t, J = 7 Hz, CH_2-N), 7.07-7.87 (6H, m), 8.20 (4H, m), and 8.96 (2H, d, J = 5 Hz, pyridinium α-H); ^{13}C nmr (deuteriochloroform-trifluoroacetic acid): δ 159.2 (C-4, pyridinium), 143.8 (C-2, 6, pyridinium), 139.5 (C-8a, 9a, carbazole), 128.7 (C-3, 5, pyridinium), 126.0 (C-2, 7, carbazole), 122.7 (C-4a, 4b, carbazole), 120.5 (C-4, 5, carbazole), 119.6 (C-3, 6, carbazole), 108.5 (C-1, 8, carbazole), 48.3 (CH_3-N^+), 42.3 (CH_2-N), and 34.6 (CH_2-pyridinium).

Anal. Calcd. for $C_{20}H_{19}IN_2.0.5\ H_2O$: C, 56.75; H, 4.76; N, 6.62. Found: C, 56.86; H, 4.60; N, 6.49.

1-Diphenylmethyl-4-[2-(9-carbazolyl)ethyl]pyridinium Bromide (**9**).

A mixture of 4-[2-(9-carbazolyl)ethyl]pyridine (1.36 g, 5.0 mmoles), diphenylmethyl bromide (1.24 g, 5.0 moles) and benzene (9 ml) was heated under reflux for 24 hours. Addition of anhydrous ether (100 ml) and filtration afforded the pyridinium bromide **9** (1.50 g, 56%), crystallising from ethanol-ether as needles, mp 163-165°; ir (bromoform): δ 1640, 1590, 1560, and 1500 cm^{-1}; ^1H nmr: δ 3.45 (2H, t, J = 7 Hz, CH_2-pyridinium), 4.89 (2H, t, J = 7 Hz, CH_2-N), 7.1-7.6 (16H, m), 7.78 (1H, s, N^+-CH), 7.96 (2H, d, J = 6 Hz pyridinium β-H), 8.13 (2H, d, J = 8 Hz, carbazole (1-H and 8-H), and 8.92 (2H, d, J = 6 Hz pyridinium α-H); ^{13}C nmr: δ 160.4 (C-4, pyridinium) 143.3 (C-2, 6, pyridinium), 139.5 (C-8a, 9a, carbazole), 128.4 (C-3, 5, pyridinium), 125.6 (C-2, 7, carbazole), 122.0 (C-4a, 4b, carbazole), 120.3 (C-4, 5, carabazole), 119.0 (C-3, 6, carbazole), 109.3 (C-1, 8, carbazole), 74.8 (CH-N^+), 42.1 (CH_2-N), and 34.3 (CH_2-pyridinium).

Anal. Calcd. for $C_{32}H_{27}BrN_2.H_2O$: C, 71.50; H, 5.44; N, 5.21. Found: C, 71.22; H, 5.22; N, 5.05.

1-(2-Anthraquinonylmethyl)-4-[2-(9-carbazolyl)ethyl]pyridinium Bromide (**10**).

A mixture of 4-[2-(9-carbazolyl)ethyl]pyridine (0.544 g, 2 mmoles), 2-(bromomethyl)anthraquinone (0.602 g, 2 mmoles) and acetone (10 ml) was heated under reflux for 1 hour and then stirred at 25° for 24 hours. A yellow product which had precipitated was filtered and recrystallised from methanol-ether to give the pyridinium bromide **10** (0.987 g, 80%) as prisms, mp 160-163°; ir (bromoform): δ 1675, 1635, 1590, and 1570 cm^{-1}; ^1H nmr: δ 3.45 (2H, t, J = 7 Hz, CH_2-pyridinium), 4.90 (2H, t, J = 7 Hz, CH_2-N), 6.12 (2H, s, CH_2-N^+), 6.9-8.6 (17H, m), and 9.30 (2H, d, J = 6 Hz pyridinium α-H); ^{13}C nmr: δ 159.5 (C-4, pyridinium), 143.9 (C-2, 6, pyridinium), 139.5 (C-8a, 9a, carbazole), 129.0 (C-3, 5, pyridinium), 125.5 (C-2, 7, carbazole), 122.0 (C-4a, 8b, carbazole), 120.2 (C-4, 5, carbazole), 118.9 (C-3, 6, carbazole), 109.3 (C-1, 8, carbazole), 61.5 (CH_2-N^+), 42.2 (CH_2-N), and 34.2 (CH_2-pyridinium); ms: 493 (M^+-Br, 0.4%), 272 (10.0), 180 (100).

Anal. Calcd. for $C_{34}H_{25}BrN_2O_2.2.5\ H_2O$: C, 66.02; H, 4.89; N, 4.53. Found: C, 65.80; H, 4.61; N, 4.42.

1-Phenoxymethyl-4-[2-(9-carbazolyl)ethyl]pyridinium Chloride (**11**).

A mixture of 4-[2-(9-carbazolyl)ethyl]pyridine (0.408 g, 1.5 mmoles), (chloromethoxy)benzene (0.255 g, 1.79 mmoles) and acetonitrile (5 ml) was heated under reflux for 4 hours. Evaporation of the solvent gave a residue which was recrystallised from methanol-ether to give the pyridinium chloride **11** (0.484 g, 76%) as needles, mp 166-167°; ir (bromoform): ν max 1640, 1595, 1590, 1560, and 1500 cm^{-1}; ^1H nmr: δ 3.45 (2H, t, J = 7 Hz, CH_2-pyridinium), 4.85 (2H, t, J = 7 Hz, CH_2-N), 6.63 (2H, s, CH_2-N^+), 7.0-7.8 (11H, m), 8.2 (4H, m, carbazole 1-H and 8-H, and pyridinium β-H), and 9.3 (2H, d, J = 7 Hz, pyridinium α-H); ^{13}C nmr: δ 154.5 (C-4, pyridinium), 143.0 (C-2, 6, pyridinium), 139.6 (C-8a, 9a, carbazole), 128.5 (C-3, 5, pyridinium), 125.6 (C-2, 7, carbazole), 122.1 (C-4a, 4b, carbazole), 120.2 (C-4, 5, carbazole), 119.0 (C-3, 6 carbazole), 109.3 (C-1, 8, carbazole), 83.8 (CH_2-N^+), 42.1 (CH_2-N), and 34.3 (CH_2-pyridinium).

Anal. Calcd. for $C_{26}H_{23}ClN_2O.0.5\ H_2O$: C, 73.66; H, 5.71; N, 6.61. Found: C, 73.71; H, 5.63; N, 6.49.

Reaction of 1-Methyl-4-[2-(1-pyrrolyl)ethyl]pyridinium Iodide (**2**) with Sodium Hydroxide.

A mixture of 1-methyl-4-[2-(1-pyrroyl)ethyl]pyridinium iodide (0.157 g, 0.5 mmole), sodium hydroxide (0.020 g, 0.5 mmole), acetone (5 ml) and water (0.5 ml) was stirred at 25° for 24 hours. Addition of anhydrous ether precipitated 1-methyl-4-vinylpyridinium iodide; the filtrate was dried and evaporated to give pyrrole (28 mg, 84%), identified by its ^1H nmr spectrum.

Reaction of 1-Methyl-4-[2-(1-indolyl)ethyl]pyridinium Iodide (**5**) with Sodium Hydroxide.

1-Methyl-4-[2-(1-indolyl)ethyl]pyridinium iodide (0.364 g, 1.0 mmole), sodium hydroxide (0.040 g, 1.0 mmole), acetone (10 ml) and water (1 ml) was stirred at 25° for 24 hours. Addition of anhydrous ether precipitated 1-methyl-4-vinylpyridinium iodide; the filtrate was dried and evaporated to give indole (0.102 g, 87%), mp 51-53° (lit [28], mp 51-53°), identified

by its ^{1}H nmr spectrum.

Reaction of 1-Methyl-4-[2-(3-bromo-1-indolyl)ethyl]pyridinium Iodide (**6**) with Sodium Hydroxide.

1-Methyl-4-[2-(3-bromo-1-indolyl)ethyl]pyridinium iodide (0.511 g, 1.15 mmoles), sodium hydroxide (50 mg, 1.25 mmoles), acetone (15 ml) and water (1 ml) was stirred at 25° for 24 hours. Addition of anhydrous ether (100 ml) precipitated 1-methyl-4-vinylpyridinium iodide; the filtrate was dried and evaporated to give 3-bromoindole (0.192 g, 85%) as prisms, mp 65-66° (lit [29], mp 65-66° dec), identified by its ^{1}H nmr spectrum.

Reaction of 1-Methyl-4-[2-(9-carbazolyl)ethyl]pyridinium Iodide (**8**) with Sodium Hydroxide.

1-Methyl-4-[2-(9-carbazolyl)ethyl]pyridinium iodide (0.207 g, 0.5 mmole), sodium hydroxide (0.020 g, 0.5 mmole), acetone (10 ml) and water (1 ml) were stirred at 25° for 2 hours. Addition of anhydrous ether precipitated 1-methyl-4-vinylpyridinium iodide; the filtrate was dried and evaporated to give carbazole (0.068 g, 82%) as plates, mp 242-244° (lit [30], mp 246°), identified by its ^{1}H- and ^{13}C-nmr spectra.

Reaction of 1-Diphenylmethyl-4-[2-(9-carbazolyl)ethyl]pyridinium Bromide (**9**) with Bases. With Sodium and Pyridine.

A mixture of 1-diphenylmethyl-4-[2-(9-carbazolyl)ethyl]pyridinium bromide (0.120 g, 0.23 mmole), sodium (5 mg, 0.125 mmole), pyridine (50 mg) and acetonitrile (10 ml) was heated under reflux for 4.5 hours; monitoring by tlc (ether-benzene, 1:1 v/v) showed that complete deprotection at the 9-position of carbazole had occurred. Ethanol (5 ml) was added, the mixture poured onto ice-water (50 ml) and neutralised by careful addition of aqueous 70% perchloric acid. The neutral suspension was extracted with ether (2 x 50 ml), the ethereal extracts combined, dried (potassium carbonate) and evaporated to give carbazole (30 mg, 78%), as plates, mp 240-242° (lit [30], mp 246°), identified by its ^{1}H- and ^{13}C-nmr spectra.

B. With Collidine.

A mixture of 1-diphenylmethyl-4-(2-(9-carbazolyl)ethyl]pyridinium bromide (200 mg, 0.385 mmole) collidine (80 mg, 0.66 mmole) and ethanol (11 ml) was heated under reflux for 29 hours. The mixture was brought to *p*H 8.0 with aqueous 70% perchloric acid, the yellow precipitate filtered off, and the filtrate brought to *p*H 5.0 with 70% perchloric acid. The resulting brown precipitate was treated with aqueous 10% sodium hydroxide until the suspension was neutral; extraction with ether (2 x 50 ml), combining of the ethereal layers, drying and evaporation afforded carbazole (60 mg, 93%), as plates, mp 242-244° (lit [30], mp 246°), identified by its ^{1}H- and ^{13}C-nmr spectra.

1-Methyl-4-[2-(3-methylimidazolium-1-yl)ethyl]pyridinium Diiodide (**13**).

4-[2-[1-Imidazolyl)ethyl]pyridine (0.519 g, 3.0 mmoles), methyl iodide (1.23 g, 8.6 mmoles) and dry benzene (15 ml) were stirred at 20° for 28 hours. Benzene was removed by decantation and the precipitate repeatedly washed with anhydrous ether; residual benzene-ether was evaporated. The residue was recrystallised from methanol-ether, filtered, and dried over phosphorus pentoxide to give the pyridinium diiodide **13** (0.87 g, 63%) as needles, mp 188-190°; ir (bromoform): ν max 1640, 1600, 1565, 1515 and 1465 cm^{-1}; ^{1}H nmr (deuterium oxide-dioxane): δ 3.20 (2H, t, J = 7 Hz, CH_2-pyridinium), 3.75 (3H, s, CH_3-Nim) 4.02 (3H, s, N$^+$ Py CH_3), 4.20 (2H, t, J = 7 Hz, N-CH_2), 7.84 (2H, m, imidazolium H-4 and H-5), 7.92 (2H, d, J = 5 Hz, pyridinium β-H), 8.70 (2H, d, J = 5 Hz, pyridinium α-H), 8.90 (1H, s, imidazolium H-2, integration smaller due to deuterium exchange); ^{13}C nmr (deuterium oxide-dioxane ref): δ 157.2 (C-4, pyridinium), 143.9 (C-2, 6, pyridinium), 136.6 (C-2, imidazolium), 129.0 (C-4 or 5, imidazolium) 129.0 (C-3, 5, pyridinium), 123.6 (C-4 or 5, imidazolium), 49.4 (*p*-CH_3N$^+$py), 48.8 (N-CH_2), 36.0 (CH_3-Nim) and 35.9 (CH_2-pyridinium).

Reaction of 1-Methyl-4-[2-(3-methylimidazolium-1-yl)ethyl]pyridinium Diiodide (**13**) with Potassium Carbonate.

A mixture of pyridinium diiodide **13** (0.519 g, 1.14 mmoles), potassium carbonate (0.321 g, 2.33 mmoles), acetone (20 ml) and water (1 ml) was stirred at 20° for 36 hours. Addition of anhydrous ether (200 ml) precipitated 1-methyl-4-vinylpyridinium iodide; the mixture was filtered and the filtrate dried and evaporated to give crude 1-methylimidazole, identified by its ^{1}H-nmr and ^{13}C-nmr spectral data. Addition of a solution picric acid (0.129 g in 5 ml methanol) to a solution of 1-methylimidazole in methanol (5 ml) gave a yellow solution which was concentrated to 2 ml. Dropwise addition of ether gave a solution which on standing afforded 1-methylimidazole picrate as needles, mp 156-158° (lit [31], mp 156.5-158°).

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