

## Coupling Reactions of 1-Alkylpyridinium Salts. Part 2.<sup>1</sup> Reaction of 1-Methylpyridinium-4-carboxylate with Cyanide and Diphenylphosphinite Ions

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A novel reaction between 1-methylpyridinium-4-carboxylate and cyanide ion in dipolar aprotic solvents leading to high yields of 1,1'-dimethyl-4,4'-(1*H*,1'*H*)-bipyridylidene (4) is described. Coupling is also brought about by diphenylphosphinite ion. *N*-Methylpyridinium-2-carboxylate on heating in dimethylformamide also surprisingly affords some 4,4'-coupled product, as does 1-methylpyridinium ion when heated with carbonate or fluoride ion in non-protic media.

*N*-ALKYLPYRIDINIUM salts and some simple ring-substituted derivatives having an available  $\gamma$ -proton (e.g. 2-methyl and 2,6-dimethylpyridinium salts) have been found to couple in the 4-position when treated with cyanide ion<sup>2,3</sup> and certain phosphorous nucleophiles.<sup>1</sup> In this paper the 4,4'-co-annular dimerization of a 4-substituted pyridinium salt is described.

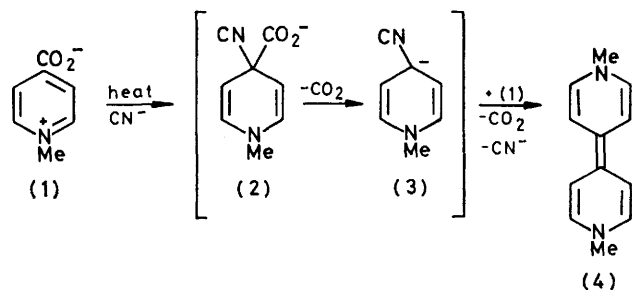
When 1-methylpyridinium-4-carboxylate (1) was heated in dimethyl sulphoxide solution above 60 °C in the presence of a catalytic amount of cyanide ion, carbon dioxide was evolved, leading to nearly quantitative

cyanide ion to the betaine (1) to give the 1,4-dihydropyridine adduct (2), which undergoes decarboxylation to afford the carbanion intermediate (3). Addition of the carbanion to a second molecule of the betaine, followed by loss of carbon dioxide and the nucleophile, leads to the bipyridylidene (4). Similar high yields have been obtained in other dipolar aprotic solvents such as dimethylformamide and hexamethylphosphoramide.

Dimeric coupling of the betaine can also be induced by sodium diphenylphosphinite under similar conditions, though the yield is lower (13%).

When pyridine-4-carboxylic acid methosulphate was employed yields of paraquat of 40–55% were obtained only when more than 1 equiv. of cyanide was used.

The intermediacy in these reactions of 1,1'-dimethyl-4,4'-(1*H*,1'*H*)-bipyridylidene (4) was indicated by absorption bands at 378 and 400 nm.<sup>4</sup> A sequence of spectra of solutions in a 1 mm quartz cell at 60 °C also shows broad absorption between 295 and 310 nm tentatively assigned to the 4-cyano-1,4-dihydropyridine-4-carboxylate adduct (2) on the basis of data for related 1,4-dihydropyridines.<sup>5</sup> The proposed intermediate carbanion (3) has also been implicated in the cyanide-catalysed dimerization of *N*-substituted pyridine quaternary salts.<sup>2</sup> We believe that a mechanism involving direct decarboxylation of the betaine at less than 100 °C



formation of 1,1'-dimethyl-4,4'-(1*H*,1'*H*)-bipyridylidene (4) as determined by its oxidation to the corresponding bipyridinium dication (paraquat ion). On the basis of u.v. and i.r. spectra and the catalytic nature of the reaction we suggest a mechanism involving addition of

<sup>1</sup> J. G. Carey and J. R. Case, preceding paper.

<sup>2</sup> L. J. Winters, N. G. Smith, and M. I. Cohen, *Chem. Comm.*, 1970, 642.

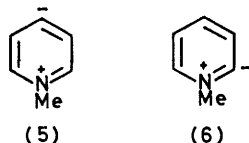
<sup>3</sup> J. G. Carey, Ger. Offen. 2,116,250 (*Chem. Abs.*, 1972, **76**, 46,097i).

<sup>4</sup> J. G. Carey, J. F. Cairns, and J. E. Colchester, *Chem. Comm.*, 1969, 1280.

<sup>5</sup> U. Eisner and J. Kuthan, *Chem. Rev.*, 1972, **72**, 1.

to afford the 1,4-dipole (5) is unlikely; \* no dimeric products were detected (mass spectra) when 1-methylpyridinium-4-carboxylate (1) was heated alone or in the presence of *N*-methylpyridinium chloride under the moderate conditions required for the cyanide-assisted reaction. Only when the betaine (1) was distilled *in vacuo* or heated in a sealed tube at *ca.* 300 °C did condensation occur leading to a complex mixture of bipyridyls, methyl- and dimethyl-bipyridyls, and methyl pyridine-4-carboxylate (mass spectra).

In contrast when the relatively unstable 1-methylpyridinium-2-carboxylate was heated alone or in aprotic solvents above 60 °C and the resulting mixture was oxidised by sulphur dioxide (or other one-electron oxidising agents) a low yield (1.5%) of paraquat ion was obtained. When the decarboxylation was performed in the presence of an excess of 1-methylpyridinium chloride there was formed a mixture of paraquat (10%) and 2,4'- (1%) and 2,2'- (1%) bipyridylium ions. The surprising predominance of the 4,4'-isomer suggests a mechanism involving participation of the 1,2-dipole (6). Similar ratios of the bipyridylium isomers [4,4' (5.3%), 2,4' (0.5%), and 2,2' (0.5%)] were obtained when *N*-methylpyridinium chloride was heated at 110 °C for 4 h with anhydrous sodium carbonate or cesium fluoride in dimethylformamide and the products then oxidised (SO<sub>2</sub>); a mechanism involving  $\alpha$ -deprotonation of the pyridinium ring to afford the same dipolar intermediate (6) is possible. In the reaction of *N*-methylpyridinium



chloride with fluoride ion the mixture was free of the dark-coloured by-product species; a u.v. spectrum then revealed the absorptions at 378 and 400 nm characteristic of the bipyridylidene (4).

#### EXPERIMENTAL

I.r. spectra were measured under nitrogen using a variable solution path cell (R1K BTF9). At the small path lengths employed extinction coefficients are uncertain and are therefore not quoted. All the reactions were carried out under nitrogen. *N*-Methylpyridinium-4-carboxylate was prepared from pyridine-4-carboxylic acid methosulphate by the ion-exchange technique<sup>7</sup> using Deacidite FF(OH<sup>-</sup> form). *N*-Methylpyridinium-2-carboxylate was prepared from ethyl pyridine-2-carboxylate methiodide.<sup>8</sup>

**Reactions of *N*-Methylpyridinium-4-carboxylate (1).**—(a) *With cyanide ion.* To a stirred solution of the betaine (1) (0.973 g, 7 mmol) in dimethylformamide (25 ml) at 80 °C was added dry sodium cyanide (0.035 g, 0.7 mmol). The solution instantly turned dark brown. A u.v. spectrum showed absorptions at 378 and 400 nm, characteristic of 1,1'-

dimethyl-4,4'(1*H*,1'*H*)-bipyridylidene (4). After 3 h at 80–90 °C the mixture was cooled and oxidised with aqueous sulphur dioxide (3 g in 100 ml). Spectroscopic analysis of the solution after reduction with alkaline sodium dithionite<sup>9</sup> showed the presence of paraquat ion (0.63 g, 96%). The absence of isomeric bipyridylium salts was confirmed by polarography.

Under similar conditions but with dimethyl sulphoxide as solvent the yield of paraquat was 86%. No reaction was observed in acetone, ethylene glycol, or water under reflux even with a 3 molar excess of cyanide ion.

(b) *With sodium diphenylphosphinite.* To a solution of sodium diphenylphosphinite (10 mmol) in dimethyl sulphoxide (30 ml) (from diphenylphosphine oxide-acetone complex and sodium hydride) was added the betaine (1) (10 mmol). After 2 h at 70 °C the red-brown mixture was cooled and oxidised as in (a) to give a 13% yield of paraquat ion.

**Reaction of Pyridine-4-carboxylic Acid Methosulphate with Cyanide Ion.**—To a stirred suspension of sodium cyanide (0.03 mol) in anhydrous dimethyl sulphoxide was added pyridine-4-carboxylic acid methosulphate (2.49 g, 0.01 mol). The solution turned yellow-green but no further reaction occurred until the mixture was heated to 70 °C, when it became red-brown. A u.v. spectrum showed peaks at 295–310, 378, and 400 nm. After 2.5 h at 70 °C the mixture was cooled and oxidised as before to give a solution containing paraquat ion (0.48 g, 52%).

**Pyrolysis of 1-Methylpyridinium-4-carboxylate (1).**—(a) The betaine (1) (3 g) in a micro-distillation flask fitted with cold traps was slowly heated at 0.1 mmHg until a final bath temperature of 300 °C was reached. The distillate (1.7 g) was found by g.l.c. and mass spectroscopy to be a complex mixture, but parent ions and fragments corresponding to bipyridyl (*m/e* 156), methylbipyridyl (*m/e* 170), dimethylbipyridyl (*m/e* 184), and methyl pyridine-4-carboxylatepyridylidene (*m/e* 152) were observed.

(b) When the betaine (1) was heated at 300 °C in a sealed tube a similar mixture of products was obtained.

**Thermal Decomposition of 1-Methylpyridinium-2-carboxylate.**—(a) *In dimethylformamide.* The betaine (1.0 g) in dry dimethylformamide (20 ml) was heated for 4 h at 90 °C, then cooled. The red-brown mixture was oxidised by addition to aqueous sulphur dioxide (3 g in 100 ml). Polarographic or spectroscopic analysis showed the presence of paraquat ion (*ca.* 1.5%).

(b) *In dimethylformamide with 1-methylpyridinium chloride.* To a stirred solution of 1-methylpyridinium chloride (1.2 g) in dimethylformamide (20 ml) at 70–80 °C was added the betaine (1.0 g) in three portions during 20 min. After 3 h the mixture was cooled and oxidised as above. Spectroscopic and polarographic analysis showed the presence of 1,1'-dimethyl-4,4'-bipyridylium (0.12 g, 10%). Polarographic analysis showed the presence also of 1,1'-dimethyl-2,4'-bipyridylium (*ca.* 0.011 g, 1%), 1,1'-dimethyl-2,2'-bipyridylium (*ca.* 0.011 g, 1%), and 1-methylpyridinium (0.66 g, 62.0%) (yields based on 1-methylpyridinium).

**Reactions of *N*-Methylpyridinium.**—(a) *With sodium carbonate.* To a solution of 1-methylpyridinium chloride

<sup>7</sup> R. W. Green and H. K. Tong, *J. Amer. Chem. Soc.*, 1956, **78**, 4806.

<sup>8</sup> E. M. Kosower and J. W. Patton, *J. Org. Chem.*, 1961, **26**, 1318.

<sup>9</sup> S. H. Yuen, J. E. Bagness, and D. Myles, *Analyst*, 1967, **92**, 375.

\* The rate constant for the loss of CO<sub>2</sub> from 1-methylpyridinium-4-carboxylate at 195 °C in ethylene glycol is 0.743 × 10<sup>-3</sup> s<sup>-1</sup>, *ca.* 10<sup>8</sup> times less than for the 2-carboxylate.<sup>6</sup>

<sup>6</sup> P. Haake and T. Mantlecon, *J. Amer. Chem. Soc.*, 1964, **86**, 5230.

(3.0 g) in dimethylformamide was added anhydrous sodium carbonate (7.0 g). The mixture was heated and stirred at 110 °C for 4 h, then was cooled and oxidised as before. The solution contained paraquat (0.16 g, 5.3%), and traces (*ca.* 0.5%) of the 2,2'- and 2,4'-isomers and 1-methylpyridinium ion (2% only) (by polarographic analysis).

(b) *With cesium fluoride.*—Methylpyridinium chloride (0.02 mol) was added to a stirred suspension of cesium

fluoride (0.1 mol) in dimethylsulphoxide (30 ml) and heated at 90 °C for 3 h. The liquid, which had assumed a wine-red colour, had u.v. bands at 378 and 400 nm, characteristic of the bipyridylidene (4). Analysis of the oxidised mixture as before showed the presence of paraquat ion (0.03 g, 1%). Pyridine was readily detected (mass spectra and g.l.c.) in the reaction vapour.

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