

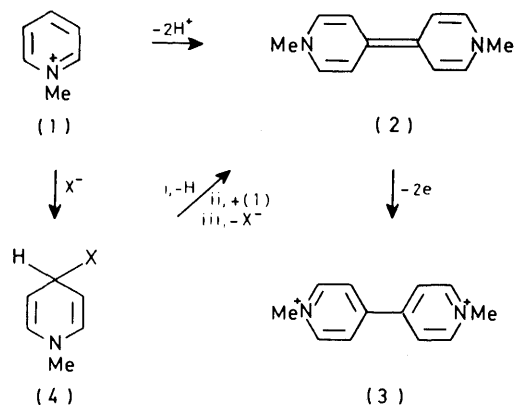
## Coupling Reactions of 1-Alkylpyridinium Salts. Part 1. With Phosphite and Phosphinite Ions †

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Dimerisation of 1-methylpyridinium ion by coupling at the 4-position can be brought about by treatment with diphenylphosphinite, diphenylthiophosphinite, and diethyl or diphenyl phosphite anions in a range of solvents. Evidence is presented for the intermediate formation of 1,1'-dimethyl-4,4'-(1*H*,1'*H*)-bipyridylium *via* addition of the phosphorus nucleophile at the 4-position of the pyridinium ring.

EXAMPLES of reactions of heterocyclic systems with nucleophiles are legion. Cyanide ion is notably versatile, affording with *N*-substituted pyridinium ions a variety of products depending on the nature of the *N*-substituent, ring substitution, and conditions such as solvent and temperature. Representative examples include addition to 3-carbamoyl-*N*-alkylpyridinium ions to form 1,2-, 1,4-, or 1,6-dihydropyridines, formation of 2- or 4-cyanopyridine from *N*-alkoxy- and *N*-amido-pyridinium salts, and the induced dimerization of *N*-alkyl- and *N*-arylpyridinium salts to the corresponding 4,4'-bipyridylidene (2).<sup>1</sup> These reactions are of theoretical<sup>2</sup> and practical interest<sup>3</sup> [*viz.* the oxidation of (2) to (3) to give the herbicidal 1,1'-dimethyl-4,4'-bipyridylium (paraquat)].

The structural features of the cyanide ion which facilitate these reactions are not unique. They are also found in the anions of phosphite diesters (RO)<sub>2</sub>POH and



X = (EtO)<sub>2</sub>P(O), (PhO)<sub>2</sub>P(O), Ph<sub>2</sub>P(O), or Ph<sub>2</sub>P(S)

phosphinous acids R<sup>2</sup>POH and their sulphur analogues.<sup>4</sup> For example Redmore<sup>5</sup> has obtained 2-pyridylphosphonic acid derivatives from diethyl phosphite ion and *N*-methoxypyridinium salts. The present paper describes the dimerization of *N*-methylpyridinium ion, (1) → (2), brought about by diphenyl phosphite anion in dimethylformamide, liquid ammonia, ethanol, or

† In this paper, the phosphorus nucleophiles are named in the form -O-PR<sub>2</sub>, although they react in the form O<sup>-</sup>P-R<sub>2</sub>.

‡ Oxidation of the dihydrobipyridyl [(2) → (3)] by sulphur dioxide is quantitative; oxidation by air, halogens, or oxidising acids is unreliable, as reported previously.<sup>6</sup>

<sup>1</sup> R. E. Lyle, 'Pyridine and its Derivatives,' Supplement Part 1, Wiley, New York, pp. 137-182 and references therein.

<sup>2</sup> U. Eisner and J. Kuthan, *Chem. Rev.*, 1972, **72**, 1.

water, so providing a further parallel between this nucleophile and cyanide.

Heating 1-methylpyridinium chloride (1) and sodium diphenyl phosphite in dimethylformamide gave 1,1'-dimethyl-4,4'-bipyridylidene (2), which on oxidation with aqueous sulphur dioxide afforded a 53% yield of 1,1'-dimethyl-4,4'-bipyridylium (3).<sup>‡</sup>

Evidence for the intermediacy of the dihydrobipyridyl (2) was obtained by u.v. spectroscopic analysis; <sup>7</sup> absorption peaks at 374 and 400 nm were observed, increasing in intensity with time. Evidence was also obtained to support the transient intermediacy of 1-methyl-1,4-dihydropyridine adducts (4): addition of sodium diphenyl phosphite to *N*-methylpyridinium ion in dimethyl formamide at ambient temperature showed initially a single, but weak u.v. band in the region 300-325 nm before the appearance of bands at 378 and 400 nm corresponding to the dimer (2).

The addition however of diethyl phosphite ion to 1-methylpyridinium ion gave much stronger absorption peaks; an initial absorption at 360 nm was rapidly replaced by one at 330 nm. The final and lower wavelength absorption may be assigned, on the basis of n.m.r. data and recorded u.v. spectra of analogues, to the 1,4-dihydropyridine adduct; the transient absorption at 360 nm belongs to the extended enamine system of the 1,2-dihydropyridine isomer.

The <sup>1</sup>H n.m.r. spectrum of the product of addition of 1-methylpyridinium ion to sodium diethyl phosphite in hexadeuteriodimethyl sulphoxide showed a downfield shift from δ 3.6 to 4.09 of the CH<sub>2</sub>O quintet [*J*(7, P) = *J*(7,8) = 7 Hz] for the phosphonate ion, showing that addition had occurred.

There were three ring CH resonances (2 : 1 : 2). That at highest field, δ 3.49, showed a large [*J*(3,P)] coupling of 15 Hz. The single proton signal, δ 4.49, was partially obscured by the CH<sub>2</sub>O resonance. The lowest field signal, δ 5.93, showed couplings of 8 Hz [*J*(2,3)] and 4 Hz [*J*(2,4), or *J*(2,P)]. The highest field signal is consistent with H(3) and H(5), and the lowest field signal with H(2) and H(6), deshielded by the nitrogen. The coupling constants of H(2) and H(6) with H(3) and

<sup>3</sup> L. J. Winters, A. L. Borrer, and N. G. Smith, *Tetrahedron Letters*, 1967, 2313; J. Beacham and J. Carey, ICI Limited, S. Afr. Pat. 7,100,256 (*Chem. Abs.*, 1972, **76**, 126,797c).

<sup>4</sup> R. Gomper, *Angew. Chem. Internat. Edn.*, 1964, **3**, 560.

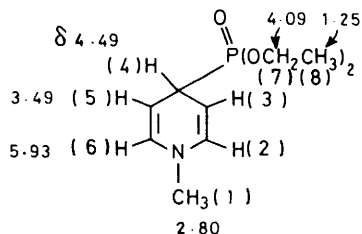
<sup>5</sup> D. Redmore, *J. Org. Chem.*, 1970, **35**, 4114.

<sup>6</sup> R. H. Reuss and L. J. Winters, *J. Org. Chem.*, 1973, **38**, 3993.

<sup>7</sup> J. G. Carey, J. F. Cairns, and J. E. Colchester, *Chem. Comm.*, 1969, 1280.

H(5) (8 Hz), together with the chemical shifts, are in agreement with the 1,4-dihydropyridine structure.

The formation of analogous kinetically (1,2-addition) and thermodynamically (1,4-addition) determined products has been reported for the addition of cyanide ion



to pyridinium salts, but only when activated by electro-negative substituents.<sup>1</sup> We have found that in the cyanide-ion-catalysed dimerization of *N*-methylpyridinium itself, only the 1,4-adduct ( $\lambda_{\max}$ , 305 nm) was detectable along with the dimer (2) ( $\lambda_{\max}$ , 378 and 400 nm). The formation of 1,4-addition products supports the outlined benzoin condensation type of mechanism [(1)  $\rightarrow$  (3)]. In neither the reaction with the phosphorous-containing nucleophiles nor the reaction with cyanide ion were any 2,4'- or 2,2'-diquaternary bipyridylium salts detected. This is in contrast to the exclusive formation of diethyl 2-pyridylphosphonate with diethyl phosphite ion,<sup>5</sup> and 2- and 4-cyanopyridines with cyanide ion<sup>1</sup> and *N*-methoxypyridinium. This selectivity could be due to steric factors and the unfavourable proximity of the nitrogen lone pair to the carbanion centre in the proposed intermediates.

The yields of dimerization of 1-methylpyridinium ion to dihydrobipyridyl (2) were highest with the diarylphosphinite, diarylthiophosphinite, and diaryl phosphite in dimethylformamide, giving respectively, after 4 h at 70–75 °C, 53, 25, and 41% yields of 1,1'-dimethyl-4,4'-bipyridylium after oxidation. Under similar conditions sodium diethyl phosphite gave only 7% yield. In ethanol as solvent diphenylphosphinite ion led to a 33% yield of bipyridylium ion whereas dimerization was not detected with diethyl or diphenyl phosphite (the latter being solvolysable to the diethyl analogue). In aqueous alkali, diphenylphosphine oxide and 1-methylpyridinium chloride gave a low yield of dimer (4%), due in part to its low solubility in water. The poorer yields obtained with diethyl phosphite ion, despite its apparently greater nucleophilicity towards *N*-methylpyridinium ion as compared to diphenyl phosphite and diphenylphosphinite, point towards significant differences in the acidity of the 4-proton in the respective 1,4-dihydropyridine adducts (4) and in the delocalization energy of the derived carbanions.

It may be that some of the phosphorus-containing nucleophiles which can participate in this reaction would be capable of catalysing other reactions known to be

induced by cyanide ion, such as the dimerization of aromatic aldehydes and Schiffs' bases.<sup>8–10</sup>

## EXPERIMENTAL

All reactions were conducted in the absence of air. U.v.–visible spectra were measured for samples obtained directly from each reaction and transferred under nitrogen to a variable path-length cell (RIK BTF9). All reactions were so examined (unless otherwise stated) and the spectra were shown to develop absorptions at  $\lambda_{\max}$  378 and 400 nm. Path lengths were generally less than 0.1 mm; hence extinction coefficients are too uncertain to be quoted. Analysis for paraquat ion was carried out by the polarographic method<sup>11</sup> or by spectrophotometric determination of the paraquat radical ion obtained upon reduction by alkaline dithionite.<sup>12</sup>

*Reactions of N-Methylpyridinium Ion.*—(a) *With sodium diethyl phosphite in dimethylformamide.* To a solution of sodium diethyl phosphite [from diethyl hydrogen phosphite (4.14 g, 0.03 mol) and sodium hydride (1.44 g)] in dry dimethylformamide (40 ml) was added *N*-methylpyridinium chloride (1.26 g, 0.01 mol). The mixture was stirred and heated for 4 h at 75 °C, then cooled and oxidised by addition of aqueous sulphur dioxide (3 g in 100 ml). The resulting solution was shown by polarographic and spectrophotometric analysis to contain 1,1'-dimethyl-4,4'-bipyridylium (62.8 mg, 69%).

(b) *With sodium diphenyl phosphite in dimethylformamide.* To a solution of sodium diphenyl phosphite [from diphenyl phosphite (7.26 g) and sodium hydride (0.72 g)] in dimethylformamide (40 ml) was added *N*-methylpyridinium chloride (1.09 g). The solution when heated to 90 °C turned from pale orange to dark green-brown. After 4 h the mixture was cooled and oxidised by aqueous sulphur dioxide as before to give a 44% yield of 1,1'-dimethyl-4,4'-bipyridylium (3) (0.35 g).

(c) *With sodium diphenylphosphinite.* (i) *In dimethyl formamide.* Diphenylphosphine oxide–acetone complex (10.4 g) was heated at 150 °C and 0.1 mmHg to remove acetone. To the cooled residue of diphenylphosphine oxide were added dimethylformamide (60 ml) and sodium (0.9 g). To the so formed solution of sodium diphenylphosphinite was added *N*-methylpyridinium chloride (1.2 g). After 4 h at 75 °C the dark red-brown solution was cooled and oxidised with aqueous sulphur dioxide as before. Analysis of the solution indicated the presence of 1,1'-dimethyl-4,4'-bipyridylium (0.645 g, 53%).

Further confirmation of the presence of paraquat ion was obtained by addition of ammonium 4,4'-diaminostilbene-2,2'-disulphonate to the solution to afford the insoluble paraquat diaminostilbenedisulphonate (Found: C, 57.0; H, 4.95; N, 10.65; S, 11.9. Calc. for C<sub>12</sub>H<sub>14</sub>N<sub>2</sub>C<sub>14</sub>H<sub>14</sub>N<sub>2</sub>O<sub>6</sub>S<sub>2</sub>: C, 56.7; H, 5.15; N, 10.8; S, 11.65%).

(ii) *In ethanol.* To a solution of sodium ethoxide (0.02 mol) and diphenylphosphine oxide (0.02 mol) in ethanol (30 ml) was added *N*-methylpyridinium chloride (1.22 g). After 3 h at reflux the mixture was cooled and oxidised. The solution was shown by analysis to contain paraquat ion (0.3 g, 33%). A similar yield was obtained using the diphenylphosphine oxide–acetone complex directly.

<sup>11</sup> R. M. Eloffson and R. E. Edsberg, *Canad. J. Chem.*, 1957, **35**, 646.

<sup>12</sup> S. H. Yuen, J. F. Bagness, and D. Myles, *Analyst*, 1967, **92**, 375.

<sup>8</sup> H. D. Becker, *J. Org. Chem.*, 1970, **30**, 6.

<sup>9</sup> J. S. Walia, J. S. Mohinder, M. S. Cattha, and M. Satyanarayanan, *Tetrahedron Letters*, 1969, **3**, 195.

<sup>10</sup> D. Johnstone and D. M. Smith, *J.C.S. Perkin I*, 1976, 399.

(iii) *In liquid ammonia.* Diphenylphosphine oxide (0.5 g), *N*-methylpyridinium chloride (2.64 g), and liquid ammonia (10 ml), were sealed together in a Carius tube at  $-75^{\circ}\text{C}$  under nitrogen and allowed to warm to room temperature. After 72 h the tube was opened and the ammonia evaporated. The red-brown semicrystalline residue gave an ion in the mass spectrum at  $m/e$  186 ( $M^+$ ,  $\text{C}_{12}\text{H}_{14}\text{N}_2$ ) and u.v. peaks (in dimethylformamide) at 374 and 400 nm, consistent with the presence of the dihydrobipyridyl (3). On oxidation as before there was obtained a solution containing 1,1'-dimethyl-4,4'-bipyridylium (0.48 g, 25%) and *N*-methylpyridinium (0.13 g, 17.8%) (by polarography).

(iv) *In water.* To a slurry of diphenylphosphine oxide (0.01 mol) and lithium hydroxide (0.8 g) in water (15 ml) was added aqueous *N*-methylpyridinium chloride (1.35 g in 10 ml). After 3 h at  $90^{\circ}\text{C}$ , work-up as before afforded an

aqueous solution containing a low yield of paraquat ion (0.03 g, 3.5%).

(d) *With diphenylphosphine sulphide.* Sulphur (0.62 g) was added to a solution of diphenylphosphine (3.6 gm) in benzene (10 ml) to form a solution of diphenylphosphine sulphide.<sup>13</sup> To this were added dimethylformamide (30 ml) and sodium hydride (0.925 g of 50% dispersion in oil) and the mixture was stirred and heated to  $70^{\circ}\text{C}$  (15 min.) A solution of *N*-methylpyridinium chloride (1.08 g) in dimethylformamide (10 ml) was then added. After 3 h the mixture was cooled and oxidised as before. Analysis confirmed the presence of 1,1'-dimethyl-4,4'-bipyridylium (0.177 g, 23%).

[7/581 Received, 4th April, 1977]

<sup>13</sup> G. Peters, *J. Amer. Chem. Soc.*, 1960, **82**, 4751.