

Chemical Constitution and Activity of Bipyridylum Herbicides.  
Part IX. *N*-Alkoxy Quaternary Salts of 4,4'-Bipyridyl.

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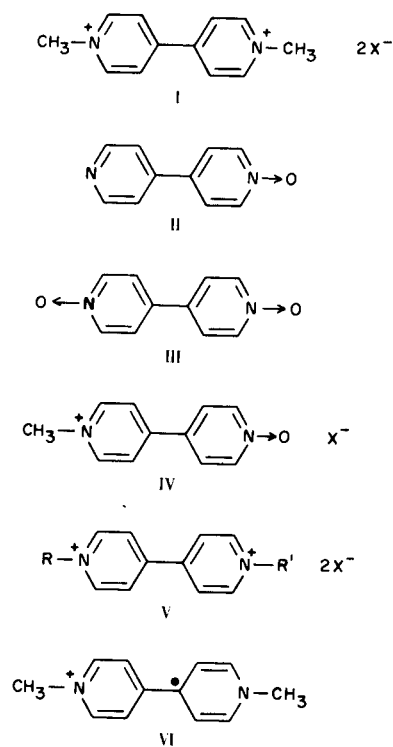
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4,4'-Bipyridyl *N*-oxide and 4,4'-bipyridyl *N,N'*-dioxide react with alkylating agents to afford *N*-alkoxy *N'*-alkyl and *N,N'*-dialkoxy diquaternary salts of 4,4'-bipyridyl respectively. The diquaternary salts were very much less active as herbicides than paraquat. Unlike paraquat they cannot be regarded as reversible one electron transfer systems.

Although there are reports of the preparation and herbicidal activity of many *N,N'*-dialkyl (1-9) and *N,N'*-diamino (10,11) diquaternary salts of 4,4'-bipyridyl related to the herbicide paraquat (I), there has been no investigation of *N*-alkoxy quaternary salts of 4,4'-bipyridyl. This paper is concerned with their synthesis.

*N*-Alkoxy quaternary salts of aromatic nitrogen heterocycles are prepared from the corresponding *N*-oxides by reaction with alkylating agents (12,13). 4,4'-Bipyridyl *N*-oxide (II) was therefore synthesised by reacting 4,4'-bipyridyl with hydrogen peroxide in acetic acid. With excess of the oxidising agent the previously reported (14-16) 4,4'-bipyridyl *N,N'*-dioxide (III) was obtained. The *N*-oxide (II) was characterised by conversion to the quaternary *N*-methyl salt (IV; X = I) with methyl iodide in boiling ethanol and to the corresponding methosulphate (IV; X = CH<sub>3</sub>SO<sub>4</sub>) with dimethyl sulphate at 30°. At 120°, the *N*-oxide (II) reacted with excess dimethyl sulphate to afford the *N*-methoxy *N'*-methyl diquaternary salt (V; R = CH<sub>3</sub>; R' = OCH<sub>3</sub>; X = ClO<sub>4</sub>) which was conveniently isolated and purified as the bisperchlorate. The salt (IV; X = CH<sub>3</sub>SO<sub>4</sub>) with diethyl sulphate at 130° afforded *N*-ethoxy-*N'*-methyl-4,4'-bipyridylum bisperchlorate (V; R = CH<sub>3</sub>; R' = OC<sub>2</sub>H<sub>5</sub>; X = ClO<sub>4</sub>). Similarly, 4,4'-bipyridyl *N,N'*-dioxide (III) with dimethyl sulphate and diethyl sulphate gave the *N,N'*-dimethoxy (V; R = R' = OCH<sub>3</sub>; X = ClO<sub>4</sub>) and *N,N'*-diethoxy (V; R = R' = OC<sub>2</sub>H<sub>5</sub>; X = ClO<sub>4</sub>) diquaternary salts respectively. The structures of the quaternary salts were confirmed by elemental analyses and by their nmr spectra.

The salts (V; R = CH<sub>3</sub>; R' = OCH<sub>3</sub>; X = ClO<sub>4</sub>), (V; R = CH<sub>3</sub>, R' = OC<sub>2</sub>H<sub>5</sub>; X = ClO<sub>4</sub>), (V; R = R' = OCH<sub>3</sub>; X = ClO<sub>4</sub>) and (V; R = R' = OC<sub>2</sub>H<sub>5</sub>; X = ClO<sub>4</sub>) were stable in aqueous solution up to a pH of about 9.0 but were, as expected, decomposed by stronger base.



Paraquat (I) in aqueous solution is reduced, for example, by zinc powder to the stable violet radical cation of which (VI) is one canonical form (1). The one electron transfer which is completely reversed by air is closely involved in the biological mode of action of paraquat (1). In contrast the alkoxy diquaternary salts (V; R = CH<sub>3</sub>; R' = OCH<sub>3</sub>; X = ClO<sub>4</sub>), (V; R = CH<sub>3</sub>; R' = OC<sub>2</sub>H<sub>5</sub>; X = ClO<sub>4</sub>), (V; R = R' = OCH<sub>3</sub>; X = ClO<sub>4</sub>) and (V; R = R' = OC<sub>2</sub>H<sub>5</sub>; X = ClO<sub>4</sub>) rapidly decomposed on treatment with zinc dust in

aqueous solution possibly by way of the corresponding radical cations which are unstable. The nature of the products of the decomposition and the mechanism involved are not yet completely clear but from NMR evidence it was apparent that among the products were the *N*-methyl-4,4'-bipyridylium cation from (V; R = CH<sub>3</sub>; R' = OCH<sub>3</sub>; X = ClO<sub>4</sub>) and (V; R = CH<sub>3</sub>; R' = OC<sub>2</sub>H<sub>5</sub>; X = ClO<sub>4</sub>) and 4,4'-bipyridyl from (V; R = R' = OCH<sub>3</sub>; X = ClO<sub>4</sub>) and (V; R = R' = OC<sub>2</sub>H<sub>5</sub>; X = ClO<sub>4</sub>) along with aldehydes and alcohols derived from the breakdown of the *N*-alkoxy groups. *N*-Alkoxy quaternary salts are known to decompose readily to the corresponding aldehyde and free base (12). The four *N*-alkoxy diquaternary salts were examined by polarography at pH values of 4.6, 7.2 and 8.0 in an attempt to obtain evidence for the formation of radical cations on their reduction (*cf.* ref. 17). The polarographic waves, however, were complex and have not been fully interpreted. They showed wave maxima which could not be suppressed with the addition of gelatine to the solution.

The diquaternary salts (V; R = CH<sub>3</sub>; R' = OCH<sub>3</sub>; X = ClO<sub>4</sub>), (V; R = CH<sub>3</sub>; R' = OC<sub>2</sub>H<sub>5</sub>; X = ClO<sub>4</sub>), (V; R = R' = OCH<sub>3</sub>; X = ClO<sub>4</sub>) and (V; R = R' = OC<sub>2</sub>H<sub>5</sub>; X = ClO<sub>4</sub>) were very much less active as post-emergent herbicides than paraquat (I; X = CH<sub>3</sub>SO<sub>4</sub>). This result is in accordance with the evidence that the diquaternary salts are much more reactive than paraquat and that they cannot be regarded as the oxidised forms of reversible one electron transfer systems.

#### EXPERIMENTAL

Britton and Robinson (pH 4.6) and Sorensen (pH 7.2 and 8.0) buffers were used in the polarography experiments, which were conducted at 20° with a standard calomel electrode and 0.001 M solutions containing 1% gelatine in an attempt to suppress wave maxima. Nmr spectra were determined at 60 Mc/sec. with tetramethyl silane or sodium 3-trimethylsilylpropane-1-sulphonate as internal standard. Similar solutions were used for the zinc powder reduction experiments. Microanalyses were performed by the Australian Microanalytical Service, Melbourne.

#### 4,4'-Bipyridyl *N*-Oxide (II).

4,4'-Bipyridyl (5.2 g.) was dissolved in glacial acetic acid (25 ml.) and to this solution there was added hydrogen peroxide solution (27.5%; 4 g.). The mixture was left 24 hours at 70° and was then poured into water (200 ml.). The solution was made alkaline by the addition of solid sodium carbonate and was then repeatedly extracted with chloroform (1 litre). The chloroform layer was dried and the solvent evaporated. The residue was dissolved in ethyl acetate and was then chromatographed on an alumina column. The column was eluted first with ethyl acetate to remove unreacted 4,4'-bipyridyl and then with chloroform. On evaporation of the chloroform extracts a white solid was obtained which was crystallised from acetone containing a trace of water to afford 4,4'-bipyridyl *N*-oxide (3.4 g.) as white needles, m.p. 180°, after drying *in vacuo* at 80°.

The nmr spectrum (deuterium oxide) showed two doublets at  $\delta$  7.60-7.91 ppm (3,5,3',5' protons) and two doublets at 8.38-8.68 (2,6,2',6' protons).

*Anal.* Calcd. for C<sub>10</sub>H<sub>8</sub>N<sub>2</sub>O: C, 69.8; H, 4.6; N, 16.3: Found: C, 70.1; H, 4.7; N, 16.3.

#### 4,4'-Bipyridyl *N,N'*-Dioxide (III).

4,4'-Bipyridyl (5.2 g.) was dissolved in glacial acetic acid (25 ml.) and heated to 70°. Hydrogen peroxide solution (27.5%; 4 g.) was added. After 7 hours another 4 g. of 27.5% hydrogen peroxide was added to the solution which was kept at 70° for 48 hours. The mixture was poured into water (200 ml.) and the solution made alkaline by the addition of solid sodium carbonate. The alkaline solution was continuously extracted with chloroform for 4 days. Evaporation of the chloroform extract gave a white solid which crystallised from ethanol to give 3.3 g. of 4,4'-bipyridyl-*N,N'*-dioxide hemihydrate, m.p. 335°. Tolstikov *et al.* (16) give m.p. 305-306°. The nmr spectrum (deuterium oxide) showed a doublet at  $\delta$  7.95-8.05 ppm (3,5,3',5' protons) and a doublet at 8.42-8.55 (2,6,2',6' protons).

*Anal.* Calcd. for C<sub>10</sub>H<sub>8</sub>N<sub>2</sub>O<sub>2</sub>·0.5 H<sub>2</sub>O: C, 60.9; H, 4.6; N, 14.2. Found: C, 61.2; H, 4.8; N, 14.0.

#### *N'*-Methyl-4,4'-bipyridylium Iodide *N*-Oxide (IV; X = I).

4,4'-Bipyridyl *N*-oxide (0.5 g.) and methyl iodide (2 ml.) were refluxed in ethanol for 30 minutes. On cooling, golden crystals were obtained which on recrystallisation from ethanol gave the product, m.p. 234°. The nmr spectrum (deuterium oxide) showed a singlet at  $\delta$  4.60 ppm (3 methyl H), a doublet at 8.21-8.35 (3,5 protons), two overlapping doublets at 8.51-8.71 (2,6,3',5' protons) and a doublet at 9.05-9.16 (2',6' protons).

*Anal.* Calcd. for C<sub>11</sub>H<sub>11</sub>IN<sub>2</sub>O: C, 42.0; H, 3.5; N, 8.9. Found: C, 42.1; H, 3.4; N, 8.9.

#### *N'*-Methyl-4,4'-bipyridylium Methosulphate *N*-Oxide (IV; X = CH<sub>3</sub>SO<sub>4</sub>).

To 4,4'-bipyridyl *N*-oxide (1 mole) in chloroform solution at 30° there was added gradually dimethyl sulphate (1 mole) over 3 hours. The mixture was stirred at 30° for 24 hours. The white solid which precipitated was collected and crystallized from ethanol to give the product, m.p. 208° (yield 90%). The nmr spectrum (deuterium oxide) showed a singlet at  $\delta$  3.80 (3 methosulphate H), a singlet at 4.59 (3 *N*-methyl H), a doublet at 8.20-8.30 (3,5 protons), two overlapping doublets at 8.49-8.70 (2,6,3',5' protons) and a doublet at 9.00-9.11 (2',6' protons).

*Anal.* Calcd. for C<sub>12</sub>H<sub>14</sub>N<sub>2</sub>SO<sub>5</sub>: C, 48.3; H, 4.7; N, 9.4. Found: C, 48.4; H, 4.7; N, 9.2.

#### *N*-Methoxy-*N'*-methyl-4,4'-bipyridylium Bisperchlorate (V; R = CH<sub>3</sub>; R' = OCH<sub>3</sub>; X = ClO<sub>4</sub>).

4,4'-Bipyridyl *N*-oxide (0.8 g.) in dimethyl sulphate (5 ml.) was heated to 120° for 15 minutes. The mixture was then poured into ethanol and excess concentrated perchloric acid was added. The white precipitate was crystallised from aqueous ethanol to afford the product, m.p. 226° (yield 95%). The nmr spectrum (deuterium oxide) showed singlets at 4.59 and 4.62 ppm (3 *N*-methoxy and 3 *N*-methyl protons), two overlapping doublets at 8.55-8.80 (3,5,3',5' protons), a doublet at 9.10-9.22 (2',6' protons) and a doublet at 9.46-9.58 (2,6 protons).

*Anal.* Calcd. for C<sub>12</sub>H<sub>14</sub>Cl<sub>2</sub>N<sub>2</sub>O<sub>9</sub>: C, 35.9; H, 3.5; N, 7.0. Found: C, 35.65; H, 3.5; N, 6.8.

#### *N*-Ethoxy-*N'*-methyl-4,4'-bipyridylium Bisperchlorate (V; R = CH<sub>3</sub>; R' = OC<sub>2</sub>H<sub>5</sub>; X = ClO<sub>4</sub>).

*N'*-Methyl-4,4'-bipyridylium methosulphate *N*-oxide (IV; X = CH<sub>3</sub>SO<sub>4</sub>) (1 mole) was heated to 130° with diethyl sulphate for 30 minutes. The mixture was then poured into ethanol and excess

concentrated perchloric acid was added. The white precipitate was crystallised from aqueous ethanol to afford the product, m.p. 174° (yield 85%). The nmr spectrum (deuterium oxide) showed a triplet at 1.40-1.65 ppm (3 C-methyl protons), a singlet at 4.58 (3 N-methyl protons), a quartet at 4.70-5.05 (2 methylene protons), two overlapping doublets at 8.52-8.76 (3,5,3',5' protons), a doublet at 9.08-9.19 (2',6' protons) and a doublet at 9.40-9.51 (2,6 protons).

*Anal.* Calcd. for C<sub>13</sub>H<sub>16</sub>Cl<sub>2</sub>N<sub>2</sub>O<sub>9</sub>: C, 37.6; H, 3.9; N, 6.7. Found: C, 37.4; H, 3.65; N, 6.7.

*N,N'*-Dimethoxy-4,4'-bipyridylum Bisperchlorate (V; R = R' = OCH<sub>3</sub>; X = ClO<sub>4</sub>).

4,4'-Bipyridyl *N,N'*-dioxide (0.5 g.) and dimethyl sulphate (3 ml.) were heated at 150° with stirring for 30 minutes. The cooled mixture was poured into ethanol and excess concentrated perchloric acid was added. The white precipitate was crystallised from aqueous ethanol to afford the product, m.p. 252°, (yield 95%). The nmr spectrum (deuterium oxide) showed a singlet at 4.60 (6 N-methoxy protons), a doublet at 8.62-8.75 (3,5,3',5' protons) and a doublet at 9.42-9.55 (2,6,2',6' protons).

*Anal.* Calcd. for C<sub>12</sub>H<sub>14</sub>Cl<sub>2</sub>N<sub>2</sub>O<sub>10</sub>: C, 34.5; H, 3.4; N, 6.7. Found: C, 34.6; H, 3.3; N, 6.7.

*N,N'*-Diethoxy-4,4'-bipyridylum Bisperchlorate (V; R = R' = OC<sub>2</sub>H<sub>5</sub>; X = ClO<sub>4</sub>).

By similar means from 4,4'-bipyridyl *N,N'*-dioxide and diethyl sulphate the product was obtained as white needles, m.p. 218° dec. from aqueous ethanol. The nmr spectrum (deuterium oxide) showed a triplet at 1.45-1.68 ppm (6 methyl protons), a quartet at 4.72-5.08 (4 methylene protons), a doublet at 8.65-8.76 (3,5,3',5' protons) and a doublet at 9.40-9.52 (2,6,2',6' protons).

*Anal.* Calcd. for C<sub>14</sub>H<sub>18</sub>Cl<sub>2</sub>N<sub>2</sub>O<sub>10</sub>: C, 37.8; H, 4.0; N, 6.3. Found: C, 37.5; H, 3.8; N, 6.3.

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