

Chemical Constitution and Activity of Bipyridylium Herbicides.  
Part VIII. 4-Bromo-6,7-dihydrodipyrido[1,2-*a*:2',1'-*c*]-  
pyrazinediium Dibromide and Related Compounds.

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6-Chloro-2,2'-bipyridyl reacts with sodium alkoxides to afford the corresponding 6-alkoxy-2,2'-bipyridyls, which form 6,7-dihydro-4-oxodipyrido[1,2-*a*:2',1'-*c*]pyrazinium bromide on treatment with 1,2-dibromoethane. 6-Chloro-2,2'-bipyridyl with this reagent gives 4-bromo-6,7-dihydrodipyrido[1,2-*a*:2',1'-*c*]pyrazinediium dibromide.

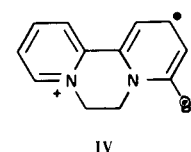
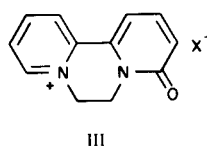
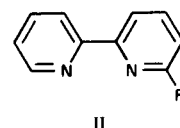
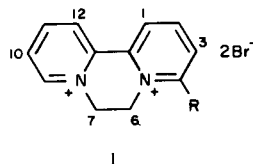
Although several analogues of the herbicide diquat dibromide (I; R = H) containing one or more substituents on the ethylene bridge have been prepared (1-10) and examined as herbicides (1,9,10) there has been little investigation of derivatives of diquat containing substituents in the pyridine rings only. Only one mono-substituted compound of this type has so far been prepared (11), namely 6,7-dihydro-4-(2'-pyridyl)dipyrido[1,2-*a*:2',1'-*c*]pyrazinediium dibromide (I; R = 2-pyridyl), although a few dimethyl (12-16), diethyl (14,15) and benzo (17) substituted compounds have been described. In view of the high herbicidal activity of (I; R = 2-pyridyl) (11) further study of derivatives of diquat containing one aromatic ring substituent only is clearly of importance. This paper is concerned with the preparation of 4-bromo-6,7-dihydrodipyrido[1,2-*a*:2',1'-*c*]pyrazinediium dibromide (I; R = Br) and related compounds.

6-Chloro-2,2'-bipyridyl (II; R = Cl), prepared by the method of Case (18), was chosen as starting material for the investigation. The reactive chlorine in (II; R = Cl) was replaced by methoxyl by reaction of (II; R = Cl) with sodium methoxide at elevated temperature to afford the new derivative 6-methoxy-2,2'-bipyridyl (II; R = OCH<sub>3</sub>). By similar means the 6-ethoxy-, 6-propoxy- and 6-isopropoxy-2,2'-bipyridyls were obtained.

The five compounds (II; R = Cl), (II; R = OCH<sub>3</sub>), (II; R = OC<sub>2</sub>H<sub>5</sub>), (II; R = OCH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>) and (II; R = OCH(CH<sub>3</sub>)<sub>2</sub>) were each in turn refluxed with excess 1,2-dibromoethane. With (II; R = Cl) the product obtained was the diquaternary salt, 4-bromo-6,7-dihydrodipyrido[1,2-*a*:2',1'-*c*]pyrazinediium dibromide (I; R = Br), the ring chlorine being replaced by bromine in addition to quaternisation. This displacement of a reactive chlorine during quaternisation has ample precedence (19). With the compounds (II; R = OCH<sub>3</sub>), (II; R = OC<sub>2</sub>H<sub>5</sub>), (II;

R = OCH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>) and (II; R = OCH(CH<sub>3</sub>)<sub>2</sub>) the product obtained in each case was the pyridone, 6,7-dihydro-4-oxodipyrido[1,2-*a*:2',1'-*c*]pyrazinium bromide (III; X = Br) rather than the appropriate alkoxy substituted diquat. Pyridone formation from attempted quaternisation of 2-alkoxypyridines and related compounds has been observed previously (19,20). The structure of the product was consistent with elemental analyses and with its spectral properties (uv, ir, nmr). The uv spectrum closely resembled that reported for the corresponding iodide salt (III; X = I) prepared by another route (21).

4-Bromo-6,7-dihydrodipyrido[1,2-*a*:2',1'-*c*]pyrazinediium dibromide (I; R = Br) was a reactive substance. In aqueous solution it was stable only at pH values below about 4.5. Above this pH it decomposed to the pyridone (III; X = Br) Like diquat dibromide (1) (I; R = H), the salt (I; R = Br) was reduced in aqueous solution by zinc dust by the transfer of one electron to give a stable green radical cation of which IV is one canonical form. In keeping with these results, (I; R = Br), on polarographic examination in the pH range 1.9-4.5, gave a typical symmetrical one electron reduction wave independent



of pH and concentration with a half-wave potential ( $E_{0}$ ) of -0.01 volts. At pH 5.9 the wave height was smaller while at pH 7.0 it was no longer present. Diquat dibromide (I; R = H) had, as noted previously (1), a half-wave potential of -0.36 volts. The higher reduction potential observed with (I; R = Br) compared with diquat dibromide is clearly due to the effect of the electron-attracting bromo substituent.

The salt (I; R = Br) was inactive as a herbicide at 8 lbs/acre. This is in agreement with the instability of (I; R = Br) at physiological pH values and with its high reduction potential (*cf.* references 1,17). The pyridone (III; X = Br) was also inactive.

#### EXPERIMENTAL

Microanalyses were performed by the Australian Micro-analytical Service, Melbourne. Uv absorption measurements were taken with 0.0005 *M* solutions. Nmr spectra (60 MHz) were determined for 10% w/v solutions using tetramethylsilane or sodium 3-trimethylsilylpropane-1-sulphonate as the internal standard. Britton and Robinson (pH 1.9, 4.5) and Sorensen (pH 5.9, 7.0) buffers were used in the polarography experiments which were conducted at 20° with a standard calomel electrode and 0.001 *M* and 0.0015 *M* solutions. Experimental error in half-wave potential was  $\pm 0.02$  volts. Light petroleum had b.p. 60°-80°.

#### 6-Methoxy-2,2'-bipyridyl (II; R = OCH<sub>3</sub>).

6-Chloro-2,2'-bipyridyl (18) (1.0 g.) in dry methanol (20 ml.) and sodium methoxide, from sodium (0.2 g.) and methanol (25 ml.), were heated in a sealed tube at 110° for 20 hours. The solvent was removed and the residue extracted with dichloromethane (20 ml.). The extract was dried (sodium sulfate) and the solvent evaporated off. The residual pale yellow oil on distillation afforded 6-methoxy-2,2'-bipyridyl, b.p. 110-113°/0.2 m.m., as a colorless liquid (yield 75%).

*Anal.* Calcd. for C<sub>11</sub>H<sub>10</sub>N<sub>2</sub>O: C, 71.0; H, 5.4; N, 15.05. Found: C, 71.0; H, 5.6; N, 15.1. The uv spectrum (ethanol) showed  $\lambda$  max 235 and 300 nm (log  $\epsilon$  4.11, 4.22). The nmr spectrum (deuteriochloroform) consisted of a singlet at  $\delta$  4.06 (CH<sub>3</sub>) and a complex group of signals from 6.72-8.75 ppm (aromatic).

#### 6-Ethoxy-2,2'-bipyridyl (II; R = OC<sub>2</sub>H<sub>5</sub>).

This compound was prepared similarly using sodium ethoxide in ethanol. It distilled to give a colorless liquid, b.p. 120°/0.45 mm. The uv spectrum (ethanol) showed  $\lambda$  max 234 and 300 nm (log  $\epsilon$  4.11, 4.21). The nmr spectrum (deuteriochloroform) consisted of a triplet at  $\delta$  1.32-1.56 (CH<sub>3</sub>), a quartet at 4.33-4.70 (CH<sub>2</sub>) and a complex group of signals from 6.70-8.75 ppm (aromatic).

*Anal.* Calcd. for C<sub>12</sub>H<sub>12</sub>N<sub>2</sub>O: C, 72.0; H, 6.0; N, 14.0. Found: C, 71.9; H, 6.2; N, 14.2.

#### 6-Propoxy-2,2'-bipyridyl (II; R = OCH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>).

This compound was obtained likewise using sodium propoxide in propanol. The residual oil was chromatographed on alumina

using ether/light petroleum (1:1) as eluent and was then distilled to give a colorless liquid, b.p. 120°/0.1 mm. The uv spectrum (ethanol) showed  $\lambda$  max 235 and 300 nm (log  $\epsilon$  4.08, 4.18). The nmr spectrum (deuteriochloroform) consisted of a triplet at  $\delta$  0.91-1.17 (CH<sub>3</sub>), a multiplet at 1.56-2.16 (C-CH<sub>2</sub>-C), a triplet at 4.30-4.51 (OCH<sub>2</sub>) and a complex group of signals from 6.71-8.74 ppm (aromatic).

*Anal.* Calcd. for C<sub>13</sub>H<sub>14</sub>N<sub>2</sub>O: C, 72.9; H, 6.55; N, 13.1. Found: C, 73.2; H, 6.8; N, 13.4.

#### 6-Isopropoxy-2,2'-bipyridyl (II; R = OCH(CH<sub>3</sub>)<sub>2</sub>).

This compound was obtained similarly using sodium isopropoxide in 2-propanol. The residual oil was chromatographed on alumina using light petroleum/ether (99:1) as eluent and was then distilled to give a colorless liquid, b.p. 100°/0.14 mm. The nmr spectrum (deuteriochloroform) consisted of a doublet at 1.36-1.47 (CH<sub>3</sub>), a multiplet at 5.30-5.72 (CH) and a complex group of signals from 6.72-8.79 ppm (aromatic).

*Anal.* Calcd. for C<sub>13</sub>H<sub>14</sub>N<sub>2</sub>O: C, 72.9; H, 6.55; N, 13.1. Found: C, 73.0; H, 6.5; N, 12.9.

#### 4-Bromo-6,7-dihydrodipyrido[1,2-*a*:2',1'-*c*]pyrazinediium Dibromide (I; R = Br).

6-Chloro-2,2'-bipyridyl was heated under reflux with excess 1,2-dibromoethane for 5 hours. The precipitate was collected and washed with dry acetone and then chloroform. It was crystallised from acetone with a trace of aqueous hydrobromic acid to afford 4-bromo-6,7-dihydrodipyrido[1,2-*a*:2',1'-*c*]pyrazinediium dibromide as a greenish solid, m.p. 310° dec. (yield 70%). The nmr spectrum (deuterium oxide) consisted of a singlet at 5.42 (CH<sub>2</sub>) and a multiplet at 8.28-9.31 ppm (aromatic).

*Anal.* Calcd. for C<sub>12</sub>H<sub>11</sub>N<sub>2</sub>Br<sub>3</sub>: C, 34.05; H, 2.8; N, 6.6; Cl, 0.0; Br (total), 56.8; Br (ionic), 37.8. Found: C, 34.3; H, 2.9; N, 6.3; Cl, 0.0; Br (total), 56.5; Br (ionic), 38.3.

#### 6,7-Dihydro-4-oxodipyrido[1,2-*a*:2',1'-*c*]pyrazinium Bromide (III; X = Br).

This compound was prepared in the following ways:

(a) 4-Bromo-6,7-dihydrodipyrido[1,2-*a*:2',1'-*c*]pyrazinediium dibromide (1.2 g.) was dissolved in aqueous ethanol (1:1) and the solvent evaporated in a stream of nitrogen. The residue was crystallised from ethanol to give yellowish needles of 6,7-dihydro-4-oxodipyrido[1,2-*a*:2',1'-*c*]pyrazinium bromide, m.p. 287-288° dec. (yield 90%). The nmr spectrum (DMSO-d<sub>6</sub>) consisted of a multiplet at  $\delta$  4.40-4.60 (CH<sub>2</sub>-N), a multiplet at 4.95-5.15 (CH<sub>2</sub>-N<sup>+</sup>) and a complex group of signals from 6.72-9.30 ppm (seven aromatic type protons). The ir spectrum (potassium bromide disc) showed a band at 1650 cm<sup>-1</sup> (CO). The uv spectrum (water) showed  $\lambda$  max 260 and 361 nm (log  $\epsilon$  3.77, 4.12). Calderbank, Charlton, Farrington and James (21) give  $\lambda$  max 262 and 357 nm (log  $\epsilon$  3.83, 4.17) for 6,7-dihydro-4-oxodipyrido[1,2-*a*:2',1'-*c*]pyrazinium iodide.

*Anal.* Calcd. for C<sub>12</sub>H<sub>11</sub>BrN<sub>2</sub>O: C, 51.6; H, 3.9; N, 10.0; Br, 28.7. Found: C, 51.5; H, 3.9; N, 9.8; Br, 28.8.

(b) 6-Methoxy-2,2'-bipyridyl (0.2 g.) was heated under reflux with 1,2-dibromoethane (6 ml.) for 30 minutes. The precipitate (0.1 g.) was collected. Its m.p. and ir and nmr spectra were identical to those of 6,7-dihydro-4-oxodipyrido[1,2-*a*:2',1'-*c*]pyrazinium bromide prepared in (a) above. Similar results were obtained with 6-ethoxy-, 6-propoxy- and 6-isopropoxy-2,2'-bipyridyls.

## Acknowledgements

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## REFERENCES

- (1) Part VII, A. L. Black and L. A. Summers, *J. Heterocyclic Chem.*, **8**, 29 (1971).
- (2) D. J. Fry and B. A. Lea, British Patent 940,152 (1963); *Chem. Abstr.*, **60**, 155 (1964).
- (3) D. R. Douglas and G. F. Duffin, British Patent 946,476 (1964); *Chem. Abstr.*, **60**, 10102 (1964).
- (4) D. H. Corr and E. E. Glover, *Chem. Ind. (London)*, 847 (1965).
- (5) D. H. Corr and E. E. Glover, *J. Chem. Soc.*, 5816 (1965).
- (6) I. C. Calder and W. H. F. Sasse, *Tetrahedron Letters*, 1465 (1965).
- (7) I. C. Calder and W. H. F. Sasse, *ibid.*, 3871 (1964).
- (8) I. C. Calder and W. H. F. Sasse, *Aust. J. Chem.*, **21**, 2951 (1968).
- (9) Imperial Chemical Industries Ltd., Netherlands Patent App. 6,406,225 (1964); *Chem. Abstr.*, **63**, 13292 (1965).
- (10) Imperial Chemical Industries Ltd., Belgian Patent 658,519 (1965); *Chem. Abstr.*, **64**, 9691 (1966).
- (11) J. E. Dickeson and L. A. Summers, *Experientia*, **25**, 1247 (1969).
- (12) R. F. Homer and T. E. Tomlinson, *J. Chem. Soc.*, 2498 (1960).
- (13) R. F. Homer, G. C. Mees and T. E. Tomlinson, *J. Sci. Food Agr.*, **11**, 309 (1960).
- (14) R. F. Homer, British Patent 857,501 (1960); *Chem. Abstr.*, **55**, 12430 (1961).
- (15) R. F. Homer, U.S. Patent 3,202,500 (1965); *Chem. Abstr.*, **63**, 16368 (1965).
- (16) T. M. Spotswood and C. I. Tanzer, *Aust. J. Chem.*, **20**, 1213 (1967).
- (17) A. L. Black and L. A. Summers, *J. Chem. Soc. (C)*, 2271 (1971).
- (18) F. H. Case, *J. Org. Chem.*, **31**, 2398 (1966).
- (19) E. N. Shaw, "The Chemistry of Heterocyclic Compounds. Pyridine and Its Derivatives", E. Klingsberg, Ed., Part 2, p. 1, Interscience, New York 1961.
- (20) G. F. Duffin, *Adv. Heterocyclic Chem.*, **3**, 1 (1964).
- (21) A. Calderbank, D. F. Charlton, J. A. Farrington and R. James, *J. Chem. Soc. Perkin I*, 138 (1972).