

Part XIV. Reduction Potential and Herbicidal Activity of
4,4'-(1,3,4-Thiadiazole-2,5-diyl)- and 4,4'-(1,3,4-Oxadiazole-
2,5-diyl)bis(1-methylpyridinium) Diiodides

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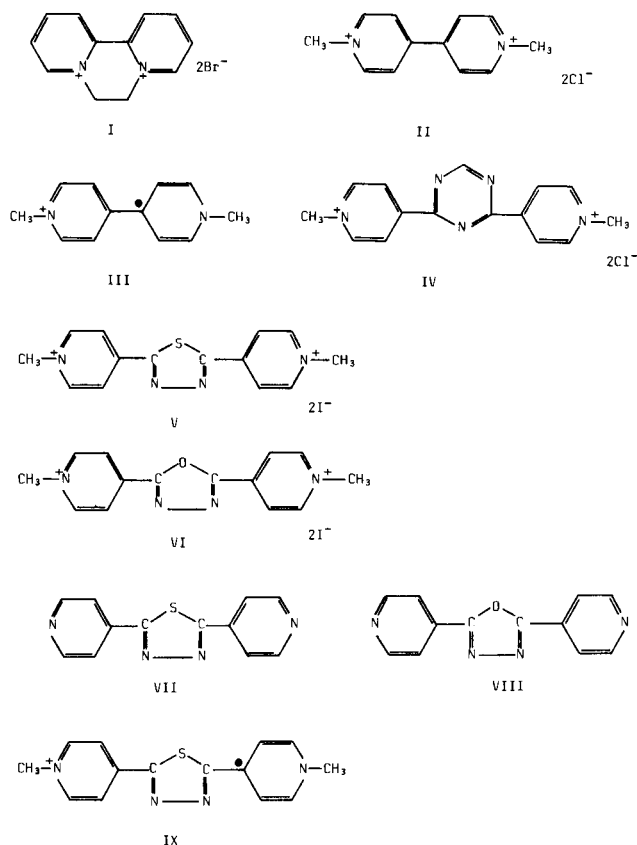
The diquaternary salts 4,4'-(1,3,4-thiadiazole-2,5-diyl)bis(1-methylpyridinium) diiodide and 4,4'-(1,3,4-oxadiazole-2,5-diyl)bis(1-methylpyridinium) diiodide are reduced in aqueous solution in the pH range 5.4-8.0 to radical cations at a potential (E_0) of -0.39 V and -0.48 V, respectively. Their activity as herbicides is reported.

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The mode of action of the bipyridinium herbicides (1,2) diquat (I) and paraquat (II) is connected with their ability to be rapidly reduced in aqueous solution to stable radical cations (*e.g.*, III) at a potential (E_0) of about -0.35 to -0.45 V by a one electron transfer which is rapidly and quantitatively reversed by oxygen. The stability of the radical cations is due to the delocalization of the odd electron over both pyridine rings which are essentially coplanar. The introduction between the pyridine rings of diquat or paraquat of an atom or group which is capable of acting as an electron transfer bridge usually results in loss of herbicidal activity since diquaternary salts of this type give, *inter alia*, unstable radical cations on reduction (3-9). Recently, however, it was found that the introduction of the planar 1,3,5-triazine ring system between the pyridine rings of paraquat gave the salt (IV) which showed very good herbicidal activity (10). The salt (IV) is reduced to a stable radical cation at a potential of -0.44 V and the one electron transfer is reversible.

Some time ago it was reported in a patent (11) that the diquaternary salts (V and VI) which contain respectively a 1,3,4-thiadiazole and a 1,3,4-oxadiazole ring between the pyridine rings of paraquat were herbicides but no further work on these compounds has been published. This paper is concerned with the results of an investigation of the ability of the salts (V and VI) to undergo reversible one electron reduction in aqueous solution in order to establish if they fit in with the criteria required for herbicidal activity of the type shown by diquat and paraquat. Research into one electron transfer agents has also received a further considerable surge of interest in the past year or two due to the utilization of paraquat and its derivatives as components of systems able to catalyse the photolysis of water to hydrogen by solar energy (*e.g.*, 12-14) and in related energy orientated electron transfer reactions (*e.g.*, 15-17).

The salt 4,4'-(1,3,4-thiadiazole-2,5-diyl)bis(1-methylpyridinium) diiodide (V) was obtained (11) by reaction of 4,4'-(1,3,4-thiadiazole-2,5-diyl)dipyridine (VII) (18) with an ex-



cess of methyl iodide in dimethylformamide. The oxadiazole salt 4,4'-(1,3,4-oxadiazole-2,5-diyl)bis(1-methylpyridinium) diiodide (VI) was formed (19) likewise by heating 4,4'-(1,3,4-oxadiazole-2,5-diyl)dipyridine (VIII) (20) with an excess of methyl iodide in nitromethane.

The salts (V and VI) are water soluble and are stable at physiological pH values. On ultraviolet spectral evidence the thiadiazole salt (V) is stable up to pH 9.5 and the oxadiazole salt (VI) to pH 8.0. Both salts are decomposed by stronger alkali.

The salts in aqueous solution gave dark green solutions on treatment with zinc dust. The deep coloration is

attributed, at least in part, to the formation of the corresponding radical cation (*e.g.*, IX) by the uptake of one electron. The uptake of one electron by the salts was confirmed by polarography. In the *pH* range 5.4-8.0 the salts gave typical one electron reduction waves with half-wave potentials (E_0) of -0.39 V for the thiadiazole salt (V) and -0.48 V for the oxadiazole salt (VI), independent of *pH* and concentration. Hydrogen was not involved in the reduction. On proton magnetic resonance spectral evidence it was apparent that the one electron transfer was substantially but not completely reversed by air.

It is evident from these results that the salts (V and VI) are reduced by a one electron transfer to radical cations at potentials very close to those of diquat and paraquat and that the one electron transfer is at least partly reversible.

In post-emergent herbicidal tests against a variety of grass flora the salts (V and VI) at high application rates of 8-16 kg./hectare desiccated green plant tissue in the manner typical of the bipyridinium herbicides. They were however, much less active than paraquat being about one thirtieth and one sixtieth as active respectively. These results are in accord with the criteria necessary for high activity in the bipyridinium series (2). The lower activity of the salts (V and VI) can be explained by the fact that the one electron transfer is not completely reversible and by the larger size of the salts compared with paraquat. Only compact molecules show high herbicidal activity.

EXPERIMENTAL

Britton and Robinson 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. The solutions contained 0.1% gelatine to suppress wave maxima. The half-wave potentials are given as E_0 values and were calculated by adding 0.25 V to the $E_{1/2}$ values.

4,4'-(1,3,4-Thiadiazole-2,5-diyl)bis(1-methylpyridinium) Diiodide (V).

4,4'-(1,3,4-Thiadiazole-2,5-diyl)dipyridine (VII) (18) was refluxed in dimethylformamide for three hours in the presence of excess methyl iodide. The salt (V) precipitated out and was recrystallized from aqueous ethanol to give orange needles of the monohydrate, m.p. 291° (yield 35%). The nmr spectrum (deuterium oxide) consisted of a singlet at δ 4.6 (6H, methyl), a doublet at 8.72-8.84 (4H, 3,5,3',5' protons), and a doublet at 9.08-9.20 ppm (4H, 2,6,2',6' protons). The literature (11) m.p. is 290° .

The uv spectrum (water) showed λ max 308 nm ($\log \epsilon$ 4.41).

Anal. Calcd. for $C_{14}H_{14}I_2N_4S \cdot H_2O$: C, 31.0; H, 3.0; N, 10.3. Found: C, 31.2; H, 2.9; N, 10.3.

4,4'-(1,3,4-Oxadiazole-2,5-diyl)bis(1-methylpyridinium) Diiodide (VI).

4,4'-(1,3,4-Oxadiazole-2,5-diyl)dipyridine (VIII) (20) was refluxed in nitromethane for three hours in the presence of excess methyl iodide. The salt (VI) precipitated out and was recrystallized from aqueous ethanol to give orange needles of the monohydrate, m.p. 279° (yield 67%). The nmr spectrum (deuterium oxide) consisted of a singlet at δ 4.61 (6H, methyl), a doublet at 8.80-8.92 (4H, 3,5,3',5' protons) and a doublet at 9.18-9.30 ppm (4H, 2,6,2',6' protons). The literature (19) m.p. is 278° . The uv spectrum (water) showed λ max 292 nm ($\log \epsilon$ 4.45).

Anal. Calcd. for $C_{14}H_{14}I_2N_4O \cdot H_2O$: C, 32.0; H, 3.1; N, 10.65. Found: C, 32.3; H, 3.1; N, 10.5.

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