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ONE ELECTRON TRANSFER PROPERTIES AND HERBICIDAL ACTIVITY OF DIQUATERNARY SALTS OF 2,4-DI-(4-PYRIDYL)-1,3,5-TRIAZINES

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Abstract—Diquaternary salts of 2,4-di-(4-pyridyl)-1,3,5-triazines have been prepared. The salts can be regarded as reversible one electron transfer systems with redox potentials (E_0) of about $-0{\cdot}44$ V in the pH range 7·0–8·5. 2,4-*Bis*-(4-methyl-4-pyridinio)-1,3,5-triazinediium dihalides are effective post-emergent herbicides at application rates of 4–6 kg/hectare.

The mode of action of the bipyridylium herbicides diquat (**1**) and paraquat (**2**) is connected with their ability to be rapidly reduced in aqueous solution to stable radical cations (e.g. **3**) at a potential (E_0) of about $-0{\cdot}35$ to $-0{\cdot}45$ V by a one electron transfer which is rapidly and quantitatively reversed by oxygen.[1] The stability of the radical cations is due to the delocalisation of the odd electron over both pyridine rings which are essentially co-planar. The effect on herbicidal activity of the introduction between the pyridine rings of an atom or group which is capable of acting as an electron transfer bridge has received some attention. For instance, the introduction of a S atom[2,3] (e.g. **4**, X=S) or an O atom[4] results in loss of herbicidal activity since the resultant radical cations are unstable. Diquaternary salts of 4,4′-iminodipyridine (**4**; X=NH) are also inactive.[3] They are not reduced to radical cations at least at potentials attainable in aqueous solution. Diquaternary salts of *trans*-1,2-di-(4-pyridyl)ethylene (**4**; X=CH=CH) show slight activity.[5] Their derived radical cations are much more reactive than those from diquat and paraquat. Diquaternary salts of di-2-pyridyl ketone (e.g. **5**; X=O) give stable radical cations but at potentials much higher than diquat[6] and the one electron transfer is not reversible. Moreover the salts are rather unstable at physiological pH values. Consequently they show only mediocre or no activity. Related diquaternary salts of 2,2′-vinylidene-dipyridine (e.g. **5**; X=CH_2) are not reduced to radical cations in aqueous solution and are inactive.[7] So far there has been no report of the investigation of salts containing a planar aromatic ring appropriately placed between the two pyridine rings although diquaternary salts of 2,5-di-(4-pyridyl)-1,3,4-thiadiazole and related heterocycles have been claimed as herbicides in a patent.[8] Compounds of this type might give stable radical cations on reduction due to the delocalisation of the odd electron over the three aromatic rings (cf. Ref. 9). Of particular interest is the influence of the electron withdrawing 1,3,5-triazine ring system placed between the pyridine rings. This paper is concerned with the synthesis, properties and herbicidal activity of diquaternary salts (**6**) of 2,4-di-(4-pyridyl)-1,3,5-triazines (**7**). Parts of the work are the subject of a patent specification.[10]

2,4-Di-(4-pyridyl)-1,3,5-triazine (**7**; R=H) was readily synthesised by reacting the imino-methyl ether obtained from 4-cyanopyridine with formamidine hydrochloride or by reacting isonicotinamidine hydrochloride with formamidine hydrochloride.[11] These methods gave much better yields of **7** (R=H) than the route used by Yasumoto *et al.*[12] 2,4-Di-(4-pyridyl)-6-methyl-1,3,5-triazine (**7**; R=CH_3) was prepared by treating isonicotinamidine with acetic anhydride (cf. Ref. 11).

Compounds **7** (R=H and R=CH_3) were converted into the diquaternary salts, **6**; (R=H; X=Br and R=CH_3; X=Br) respectively by reaction with methyl bromide in dimethylformamide. Compound **7** (R=H) was also converted into the corresponding dichloride **6**; (R=H; X=Cl) by similar treatment with methyl chloride. Data on the salts are given in Tables 1 and 2.

Like paraquat,[1,13] the three salts **6** (R=H; X=Br and R=H; X=Cl) and **6** (R=CH_3; X=Br) in aqueous solution gave red-violet solutions on treatment with zinc dust attributed to the presence of the corresponding radical cations of which (**8**), for example, is one canonical form. The presence of a high concentration of a stable radical was confirmed in each case by the observation that the intensely coloured solutions gave no NMR spectrum (cf. Refs. 14, 15). This suggests that the odd electron is delocalised over the three aromatic rings. When the reducing agent was removed and the solutions were shaken for about 15 sec in air the deep colour substantially discharged. The NMR spectrum obtained then was the same as that of the original diquaternary salt, thus demonstrating that the one electron transfer is, like paraquat,[1,13] completely reversible.

The three salts **6** (R=H; X=Cl and R=H; X=Br) and **6** (R=CH_3; X=Br) were examined by polarography (Table 3) in the pH range 3·2–10·0 at two concentrations. As expected the salts **6** (R=H; X=Cl and R=H; X=Br), which differ only in the nature of the anion, gave almost identical polarographic waves. In the pH range 7·0–8·5 the three salts all gave typical one electron reduction waves with half-wave potentials (E_0) of about $-0{\cdot}44$ V essentially independent of pH and concentration, thus confirming that the reduction of the salts involves one electron and not hydrogen. Their reduction potentials are close to that

Table 1. Analytical data of diquaternary salts (**6**)

Compound	M.p.	Yield %	Solvent	Formula	Analyses	C	H	N	Br
(**6**; R=H; X=Cl)	313-315°	90	dimethylformamide	$C_{15}H_{15}Cl_2N_5$	Calcd.	53.6	4.5	-	-
					Found	53.0	4.4	-	-
(**6**; R=H; X=Br)	322-323°	98.5	dimethylformamide	$C_{15}H_{15}Br_2N_5$	Calcd.	42.4	3.5	16.5	37.7
					Found	42.2	3.7	16.3	37.3
(**6**; R=CH$_3$; X=Br)	309-311	96	dimethylformamide	$C_{16}H_{17}Br_2N_5$	Calcd.	43.7	3.9	15.9	36.4
					Found	43.2	4.1	15.7	36.4

Table 2. UV and NMR spectra of diquaternary salts (**6**)

Compound	U.V. in H_2O, pH 7.0 λ_{max} nm (log ε)	N.M.R. in D_2O (δ values, ppm)
(**6**; R=H; X=Cl)	247, 283 sh (4.56, 3.97)	4.58 (s, 6H, CH$_3$); 9.19 (s, 8H, pyridine H); 9.85 (s, 1H, triazine H).
(**6**. R=H; X=Br)	247, 282 sh (4.64, 4.00)	4.58 (s, 6H, CH$_3$); 9.15 (s, 8H, pyridine H); 9.80 (s, 1H, triazine H).
(**6**; R=CH$_3$; X=Br)	246, 282 sh (4.48, 3.90)	3.04 (s, 3H, C-CH$_3$); 4.58 (s, 6H, N-CH$_3$); 9.12 (s, 8H, pyridine H).

Table 3. Polarography of 0·001 M* aqueous solutions of diquaternary salts (**6**). Half-wave potentials (E_0) in volts

		pH									
		3.2	4.0	5.0	6.0	7.0	7.5	8.1	8.5	9.2	10.0
(**6**; R=H; X=Cl)	1st wave[b]		-0.28		-0.38	-0.43		-0.45	-0.45	a	a
	2nd wave[c]		-		-	-0.73		-0.72	-0.75		
(**6**; R=H; X=Br)	1st wave[b]	-0.23	-0.27	-0.32	-0.38	-0.43	-0.45	-0.45	-0.45	a	a
	2nd wave[c]	-	-	-	-	-0.73	-0.72	-0.72	-0.77		
(**6**; R=CH$_3$; X=Br)	1st wave[b]		-0.32		-0.40	-0.43		-0.45	-0.45	a	a
	2nd wave		-		-	-		-	-		

* Similar results were obtained with 0.0015M solutions

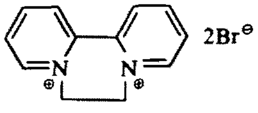
a Unstable

b One electron wave

c Approximately one electron wave

of paraquat which has an E_0 value of $-0{\cdot}45$ V.[1,13] In this pH range the salts **6** (R=H; X=Cl and R=H; X=Br) also gave a second one electron reduction wave at lower potential ($E_0 \sim -0{\cdot}73$ V) presumably due to the formation of betaine structures such as **9** (cf. Ref. 16). Above about pH 9 the salts decomposed. Between pH 3·5 and pH 6·0 the salts also gave a one electron reduction wave but it was pH dependent presumably due to protonation of the triazine ring in acid solution. In this pH range a second reduction wave was not present. It is clear from these results that at physiological pH values the three triazine salts can be considered to be the oxidised forms of reversible one electron transfer systems with redox potentials close to that of paraquat.

In post-emergent herbicidal tests against ten plant species at CIBA-GEIGY AG, Basel, and against mixed grass flora at Newcastle the salts **6** (R=H; X=Cl and R=H; X=Br), although less active than paraquat, were nonetheless very effective herbicides giving a complete kill of most species at about 4–6 kg/hectare. It is estimated that they are on average against many plant species about one-eighth to one-sixteenth as active as paraquat. the salt **6** (R=CH$_3$; X=Br) had very low activity (<1% of that of paraquat). These results are consistent with those obtained from previous work on salts related to diquat and paraquat. The triazine salts, being reversible one electron transfer systems with redox potentials close to paraquat, would be expected to show some herbicidal activity. It is known, however, that in addition to appropriate redox properties the molecule should be of compact size for high herbicidal activity.[17] The salts **6** (R=H; X=Cl and R=H; X=Br) are much larger in size than paraquat and this would account for their lower activity. The methyl substituted salt **6** (R=CH_3; X=Br) is larger still and much less active. This recalls the similar considerable decrease in herbicidal activity noted with analogues of diquat containing methyl substituents on the ethylene bridge.[18] The salts **6** (R=H; X=Cl and R=H; X=Br) are also effective desiccants in cotton and give within 7 days greater than 90% defoliation at rates of ≥1·5 kg/ha. Regrowth is inhibited. Potato vine is completely killed at rates of 2·5–5 kg/ha.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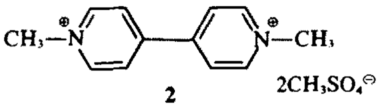
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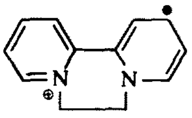
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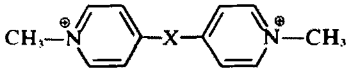
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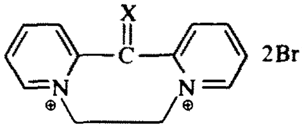
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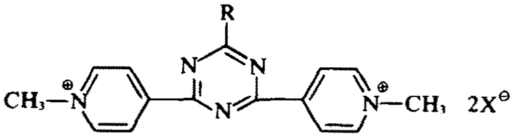
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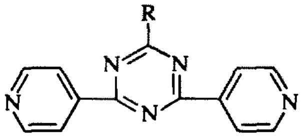
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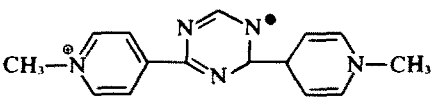
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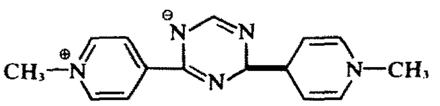
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EXPERIMENTAL

UV absorption measurements were taken with 0·0005M solns. NMR spectra (60 MHz) were determined for 10% w/v solns using TMS or sodium 3-trimethylsilylpropane-1-sulphonate as the internal standard. Britton and Robinson or Sorenson aqueous buffer solutions were used in the polarography experiments which were conducted at 20° with a standard calomel electrode and 0·001 and 0·0015 M solns. The solns contained 0·1% gelatine to suppress wave maxima. Half-wave potentials are assumed to be E_0 values and were calculated by adding 0·25 V to the $E_{1/2}$ values. Experimental error in the half-wave potentials was ±0·02 V.

2,4-*Di*-(4-*pyridyl*)-1,3,5-*triazine* (**7**; R=H)

(a) To a soln of Na (0·022 mol) in MeOH (150 ml) there was added 4-cyanopyridine (0·5 mol). The mixture was stirred for 4 hr at room temp. Formamidine hydrochloride (0·505 mol) in DMF was added. After 16 hr at room temp. the solvents were removed at 65° under vacuum. The residual semi-crystalline residue was heated for 16 hr at 125°. After cooling, the mixture was poured into water (500 ml). The ppt was collected, washed with water and dried. It crystallised from benzene to afford the product, m.p. 180–182°, yield 87·5% (Found: C, 66·1; H, 3·7; N, 29·75. $C_{13}H_9N_5$ requires: C, 66·4; H, 3·8; N, 29·8%).

(b) Isonicotinamidine hydrochloride (0·1 mol) and formamidine hydrochloride (0·13 mol) were mixed and heated for 16 hr at 185°. The mixture was poured into water (100 ml). The ppt was collected, washed with water, dried and crystallised. The yield of the product was 86%.

2,4-*Di*-(4-*pyridyl*)-6-*methyl*-1,3,5-*triazine* (**7**; R=Me)

Isonicotinamidine hydrochloride (0·5 mol) was added to a mixture of NaOAc (0·5 mol) in Ac_2O (600 ml). The suspension was heated under reflux for 2 hr. The solvent was removed under vacuum and the residue poured into water (500 ml). The ppt was filtered washed with water, dried and crystallised to give the product, m.p. 162–163°, yield 29%. Yanagiya *et al.*[19] give m.p. 127·5°. (Found: C, 67·7; H, 4·5; N, 28·1; $C_{14}H_{11}N_5$ requires: C, 67·5; H, 4·4; N, 28·1%).

2,4-*Bis*-(4-*methyl*-4-*pyridinio*)-1,3,5-*triazidinediium dihalides* **6** (Tables 1 and 2).

The appropriate 2,4-di-(4-pyridyl)-1,3,5-triazine (0·4 mol) was suspended in DMF (1·4 litres) in an autoclave. The methyl halide (1 mol) was added and the mixture heated for about 2 days at 100°. After cooling, the resultant ppt was collected, washed with acetone, dried and crystallised. The salts were hygroscopic.

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