The Synthesis and Electrochemical Properties of Some Novel Photosynthesis Electron Acceptors

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A range of dioxathiadiaza heteropentalenes have been prepared and their electrochemical properties have been studied by cyclic voltammetry and e.s.r. spectroscopy. It has been found that these compounds form stable anion radicals in the absence of oxygen and have half-peak reduction potentials in the same range as the bypyridinium compounds such as paraquat (methyl viologen) or diquat.

In recent years, there has been considerable effort in several laboratories in the search for compounds with effects on plants similar to those shown by the bipyridinium herbicides (*e.g.*, paraquat and diquat). The mechanism of the herbicidal activity of this class of compounds is well understood.[1] They intercept the electron-transport pathway of photosynthesis by competing with a natural substrate such as ferredoxin for electrons originating from P700, the primary electron donor of Photosystem-I. In the course of a search for compounds that inhibit photosynthesis in a similar manner to the bipyridinium herbicides (*e.g.*, paraquat and diquat), we have synthesised a number of novel dioxathiadiaza heteropentalenes and studied their electrochemical properties by cyclic voltammetry and electron spin resonance (e.s.r.) spectroscopy. These heterocyclic compounds, *e.g.*, paraquat and diquat, act as Photosystem-I electron acceptors[2,3] at concentrations of the order of 10^{-6}M.

Results and Discussion

Synthesis—The general method for the preparation of compounds (**1**)—(**11**) in Table 1 is essentially the one described by Perrier and Vialle[4] and is illustrated by the synthesis of the novel thiacyclohexane derivative (**7**).

The sulphoxide (**8**) and sulphone (**9**) derivatives of (**7**) were prepared by oxidation of the sulphur in the thiacyclohexane ring with *m*-chloroperbenzoic acid. Melting points and elemental analyses of the compounds used in this study are given in Table 1.

Electrochemical Studies.—The electrochemical properties of the heteropentalenes in Table 1 were evaluated by cyclic voltammetry (scanned at 150 mV s^{-1}) of deoxygenated solutions in methanol–pH 7 buffer (3:1 v/v). Half-peak reduction potentials ($E_{p_{\frac{1}{2}}}$) are shown in Table 2. Under these conditions, all compounds are reversible and stable anion radicals are formed (Figure 1). The ratio of the anodic and cathodic peak currents are nearly equal to one. At pH values below 5, under the same solvent conditions, the reduction potential shifts to more positive values and the anion radical is irreversibly trapped on reaction with protons (Figure 2).

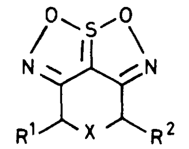
Table 2 shows that the introduction of phenyl and aromatic substituents on the cyclohexane entity of the heteropentalene system shifts the half-peak potential to a more positive value. This could partly be due to an inductive effect by these substituents. The replacement of a methylene group in the cyclohexane ring by either a sulphur atom or a sulphoxide or a sulphone group makes the corresponding heteropentalene more electron attracting. The proton chemical shifts of the methylene groups in (**1**), (**7**), (**8**), and (**9**) are linearly related to the corresponding half-peak potentials. For every 1 p.p.m. in chemical shift, $E_{p_{\frac{1}{2}}}$ moves by *ca.* 100 mV (Figure 3). This inductive effect is probably the major effect to give rise to the appreciably larger redox potentials for the sulphoxide (**8**) and the sulphone (**9**) derivatives, compared with that of the sulphur analogue (**7**). However, the possible occurrence of the enol forms (**8'**) and (**9'**) cannot be completely dismissed as these could increase the planarity of the heteropentalene, making electrochemical reduction more facile. We have carried out proton exchange experiments on (**8**) and (**9**) using n.m.r. and have found that the protons of the methylene groups exchange rapidly when a solution of either (**8**) or (**9**) in [$^2H_6$]DMSO is shaken with 0.01M-deuteriated sodium hydroxide.

The e.s.r. spectrum of $[(7)]^{-\bullet}$ generated by the electrochemical reduction at a platinum electrode of a solution of (**7**) (2.8×10^{-3} mol dm^{-3}) in methanol containing $(Me_4N)Cl$ (0.1 mol dm^{-3}) is shown in Figure 3. The anion radical was found to be stable for at least 1 h in the absence of oxygen. The spectrum of $[(7)]^{-\bullet}$ can be interpreted as a 1:4:6:4:1 quintet ($a_H = 0.18$ mT) of 1:2:3:2:1 quintets ($a_N = 0.41$ mT) and arises from coupling of the unpaired electron with two equivalent nitrogen nuclei and four equivalent hydrogen (CH_2) nuclei.

The value of a_H is approximately what would be expected for hydrogen atoms on an sp^3-hybridised carbon atom β to the nitrogen atom of a cyclic iminoxyl radical (*e.g.*, for the β hydrogen atoms of cyclohexaminoxyl, $a_H = 0.14$ mT).[5] The value of a_N is lower than that observed in a five-membered cyclic oxyaminyl radical (*e.g.*, for 2,5-dihydro-5-hydroxyisoxazol-2-yl, $a_N = 0.94$ mT)[6] presumably because the electron is delocalised over several atoms. The observation that the coupling to all four hydrogen atoms is equivalent suggests that ring flipping occurs rapidly at room temperature.

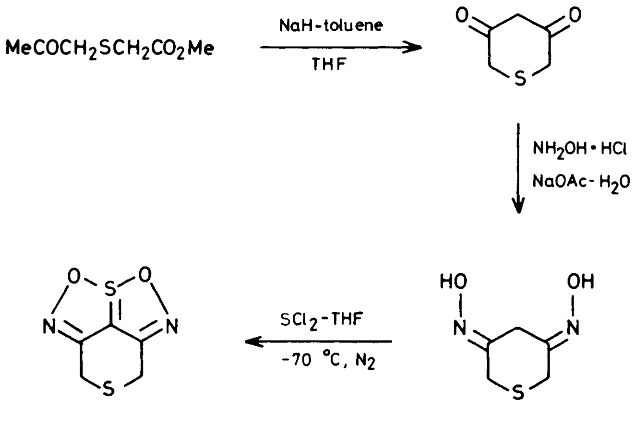
In this study, we have shown that this class of heterocycles give rise to stable radical ions at a reduction potential in the same region as the bipyridinium compounds;[7,8] the half-peak potential for methyl viologen (MV^{2+}) at neutral pH has been reported[2] as −455 mV. The lipophilicity[3] and the electrical neutrality of the heteropentalene in comparison with MV^{2+} suggest that they could be used as reduction–oxidation mediators in photoelectrochemical reductions. Indeed, we have found[9] that these molecules quench the emission of the excited state of $[Ru(bipyridyl)_3]^{2+}$ at a rate *ca.* an order of magnitude faster than MV^{2+}. Further studies in this direction are at present being pursued.

Table 1. Physical data of the compounds studied



	X	R^1	R^2	M.p. (°C) (solvent[a])	Analysis (%) Found C	Found H	Found N	Calculated C	Calculated H	Calculated N
(1)	CH_2	H	H	58—59	42.1	3.4	16.3	42.4	3.5	16.5
(2)	CH(Me)	H	H	54—55	45.7	4.3	15.2	45.65	5.1	14.1
(3)	CMe_2	H	H	65.5	48.5	5.0	14.0	48.5	5.1	14.1
(4)[b]	CH (phenyl)	H	H	158—160 (B)	58.5	4.1	11.4	58.5	4.1	11.4
(5)[b]	CH (furan)	H	H	119 (E)	50.5	3.5	11.4	50.8	3.4	11.9
(6)	CH (thiophene)	H	H	144 (E)	47.8	3.1	11.1	47.6	3.2	11.1
(7)[b]	S	H	H	97—99 (E)	31.8	2.1	14.7	31.9	2.1	14.9
(8)[b]	SO	H	H	183—184 (M)	29.4	1.8	13.8	29.4	2.0	13.7
(9)[b]	SO_2	H	H	167—168 (M)	27.3	1.7	12.6	27.3	1.8	12.7
(10)[b]	CH_2	Me	Me	97—99 (E)	48.5	5.1	14.2	48.5	5.1	14.1
(11)[b]	CH (phenyl)	H	Ph	117 (PE)	67.0	4.3	8.5	67.1	4.4	8.7
(12)[b]	CMe_2	H	Ph	126 (E)	60.9	5.3	9.9	61.3	5.1	10.2
(13)[b]	CMe_2	H	pyridine	160—163 (M)	56.6	4.6	15.0	56.7	4.7	15.3

[a] B = benzene, E = ethanol, M = methanol, PE = light petroleum. [b] New compounds.



(7) (14)

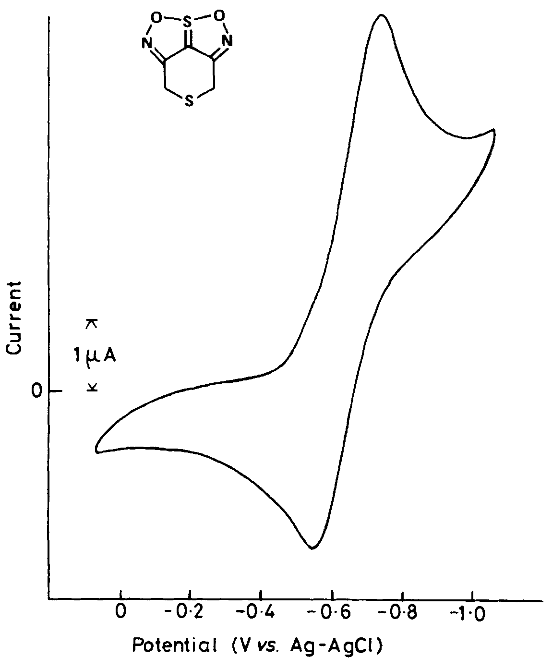


Figure 1. The cyclic voltammogram of (7) in methanol–water (3:1 v/v)

Table 2. Half-peak reduction potentials, $E_{p_{\frac{1}{2}}}$ *versus* Ag–AgCl reference electrode, for compounds (1)—(13)

Compound	$-E_{p_{\frac{1}{2}}}$/mV (±10 mV)	Compound	$-E_{p_{\frac{1}{2}}}$/mV (±10 mV)
(1)	693	(8)	573
(2)	703	(9)	523
(3)	723	(10)	713
(4)	673	(11)	683
(5)	643	(12)	663
(6)	643	(13)	673
(7)	643		

Experimental

Electrochemical Studies.—The heteropentalenes in Table 1 were dissolved in methanol (9 ml). To this solution 3 ml of 0.01M-

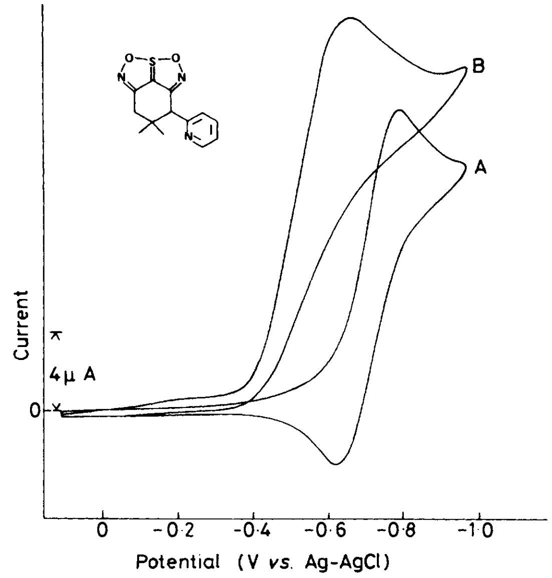


Figure 2. Cyclic voltammetry of (**13**) in A, methanol–water (3 : 1 v/v) and B, solution in A acidified with 1M-HCl to pH 2.5

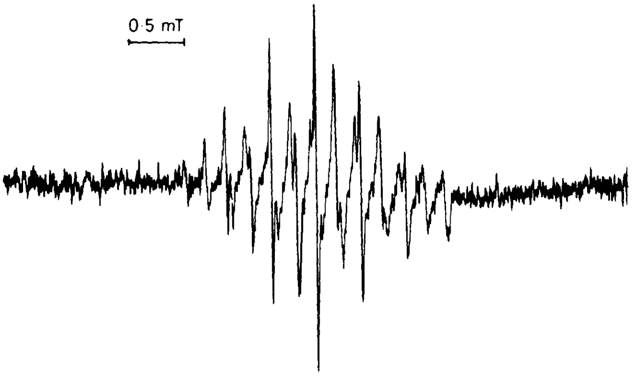
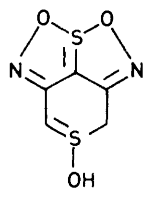
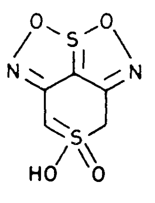


Figure 3. E.s.r. spectrum of electrolytically generated anion radical from (**7**) in methanol



(**8′**)



(**9′**)

phosphate buffer (pH 7) and 0.05M-potassium nitrate were added to give a final concentration of heteropentalene of 1.5×10^{-4} mol dm^{-3}. The cyclic voltammograms of these solutions were obtained using an electrochemical cell consisting of a carbon paste electrode (1.8 mm in diameter) as the working electrode, a platinum counter electrode, and a standard silver–silver chloride reference electrode. The electrochemical cell was connected to a cyclic voltammetry instrument (Bioloanalytical Systems Inc., Model CV-1A). Solutions were deoxygenated by the passage of a steady stream of nitrogen. Cyclic voltammograms were scanned at 150 mV s^{-1}. The e.s.r. spectrum of $[(\mathbf{7})]^{-\bullet}$ was recorded on a Varian E3 e.s.r. spectrophotometer. $[(\mathbf{7})]^{-\bullet}$ Was generated by electrochemical reduction of a solution of (**7**) (2.8×10^{-3} mol dm^{-3}) in methanol containing 0.1 mol dm^{-3} of tetramethylammonium chloride.

Chemical Synthesis.—Melting points were determined on a Kofler block and are uncorrected. ^{1}H N.m.r. spectra were recorded on a Bruker WH360 spectrometer. Chemicals were purchased from Aldrich Chemical Company. All solvents were of analytical-reagent grade.

Bis(hydroxyimino) Derivative (**14**) *of Thiacyclohexane*-3,5-*dione*.—A 60% sodium hydride dispersion in oil (80 g, 2.0 mol) was suspended in toluene (1 l) under a nitrogen blanket and then treated with tetrahydrofuran (1 l) at 20 °C. Methylacetonyl thioacetate (324 g, 2.0 mol) was slowly added until an induction period ended and then the addition was completed in 2 h. The mixture was stirred overnight at ambient temperature before cooling to 0 °C and treating with water (600 ml). The organic phase was separated and re-extracted with further portions of water (2×100 ml). The combined aqueous phases were acidified at 0 °C with concentrated HCl (180 ml) and then extracted with chloroform (3×400 ml). The combined chloroform extracts were evaporated under reduced pressure with a maximum bath temperature of 30 °C to leave a beige coloured solid. The crude thiacyclohexane-3,5-dione was dissolved in ethanol (600 ml) and the solution added to a stirred mixture of hydroxylamine hydrochloride (306 g, 4.4 mol) and sodium acetate (361 g, 4.4 mol) in water (1.6 l). The bis(hydroxyimino) compound precipitated out almost instantly. After stirring for 30 min it was stored in the cold overnight. The product was filtered, washed with ice–water, and dried to give a fine pale beige powder (216 g, 68%), m.p. 179—180 °C (decomp.); δ_H([$^2H_6$]DMSO) 10.79 (2 H, s), 3.06 (2 H, s), and 3.55 (4 H, s) (Found: C, 37.3; H, 4.7; N, 17.2. $C_5H_8N_2O_2S$ requires C, 37.5; H, 5.0; N, 17.5%).

5H,7H-2,3-*Dioxa*-2*a*,6-*dithia*(2e-S^{IV})-1,4-*diazacyclopent*-[cd]*indene* (**7**). Sulphur dichloride (681 g, 6.6 mol) was dissolved in THF (3 l), treated with iodine (3 g), and cooled to −70 °C for 2 h before adding to a stirred suspension of (**14**) (480 g, 3.0 mol) in THF (3 l) at −70 °C and under a nitrogen blanket. The temperature of the reaction mixture was allowed to rise slowly to −40 °C and was then held at this temperature overnight. Whilst still cold, water (1.5 l) was added and then the mixture was diluted with toluene (10 l) and water (15 l). The organic layer was separated, washed with water (15 l), and filtered to remove particles of sulphur. The solvent was evaporated under reduced pressure to leave 421 g of crude (**7**). This was dissolved in methylene dichloride and chromatographed on silica gel to give 298 g of purified material.

Recrystallisation of this material from a mixture of ethanol (900 ml) and toluene (120 ml) gave 258 g of yellow crystals (46%), m.p. 98—101 °C; δ_H([$^2H_6$]DMSO) 4.50 (4 H, s) (Found: C, 31.8; H, 2.1; N, 14.7. $C_5H_4N_2O_2S_2$ requires C, 31.9; H, 2.1; N, 14.9%).

Sulphoxide derivative (**8**). (**7**) (0.95 g, 5 mmol) was dissolved in dry methylene dichloride (10 ml) and a solution of *m*-chloroperbenzoic acid (1.1 g, 6 mmol) in dry methylene dichloride (10 ml) was added slowly. The reaction mixture became warm on addition and yellow crystals were deposited. After 15 min stirring at room temperature, the methylene dichloride solution was first washed with saturated sodium hydrogen carbonate solution and then dried (Na_2SO_4). Removal of the solvent under reduced pressure left an orange residue. This was recrystallised from methanol to give 0.7 g (70%) of orange needles, m.p. 183—184 °C; δ_H([$^2H_6$]DMSO) 4.62—4.67 (2 H, d, *J* 15 Hz) and 5.13—5.18 (2 H, d, *J* 15 Hz) (Found: C, 29.4; H, 1.8; N, 13.8. $C_5H_4N_2O_3S_2$ requires C, 29.4; H, 1.8; N, 13.8. $C_5H_4N_2O_3S_2$ requires C, 29.4; H, 2.0; N, 13.7%).

Sulphone derivative (**9**). 0.95 g (5 mmol) of (**7**) was dissolved in chloroform (10 ml). *m*-Chloroperbenzoic acid (2.2 g, 12 mmol) in chloroform (10 ml) was added with stirring. The solution was warmed up to 40 °C for 2 h; after cooling, it was washed three times with saturated sodium hydrogencarbonate solution and then dried (Na_2SO_4). Removal of solvent and recrystallisation of the residue from methanol gave pale orange needles (0.7 g, 64%), m.p. 167—168 °C; $\delta_H([^2H_6]DMSO)$ 5.45 (4 H, s) (Found: C, 27.3; H, 1.7; N, 12.6. $C_5H_4N_2O_2S_2$ requires C, 27.3; H, 1.8; N, 12.7%).

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