Biochimica et Biophysica Acta, 765 (1984) 236–238
Elsevier

BBA Report

BBA 40034

DIOXATHIADIAZA-HETEROPENTALENES

NEW PHOTOSYSTEM-I ELECTRON ACCEPTORS

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(Received January 20th, 1984)

Key words: Heteropentalene; Photosystem I; Redox potential; Pulse radiolysis; Cyclic voltammetry

The redox properties of some dioxathiadiaza-heteropentalenes have been studied by pulse radiolysis and cyclic voltammetry. The midpoint potential at pH 7 for reduction of this class of compounds to the corresponding anion radical is comparable with the first reduction potential of the bipyridinium herbicides. The heteropentalenes act as Photosystem-I electron acceptors at concentrations of the order of $1 \cdot 10^{-6}$ M. The herbicidal properties of the heteropentalenes are similar to those of the bipyridinium herbicides.

It is now well established [1] that the herbicidal action of the bipyridinium herbicides, in particular paraquat (MV^{2+}) and diquat, is primarily associated with the reduction potential of the dication. This latter species is claimed to intercept the photosynthetic electron-transport process by competing with a natural substrate, such as ferredoxin for electrons emanating from P-700, the primary electron donor of Photosystem I (PS I). The reduction of MV^{2+} leads to the formation of the cation radical MV^{+} which reacts very rapidly with oxygen [2] ($k = 7.7 \cdot 10^{8}\ M^{-1} \cdot s^{-1}$) to give superoxide, $O_2^{\overline{\cdot}}$ and to regenerate MV^{2+}. It is generally thought [3] that superoxide in the presence of hydrogen peroxide is the phytotoxic species in the biological action of the bipyridinium herbicides. In the course of a search for compounds with effects on plants similar to those shown by the bipyridinium herbicides, but with lower mammalian toxicity, a group of compounds, herein referred to as dioxathiadiaza-heteropentalenes [4], have been discovered.

The structures of the dioxathiadiaza-heteropentalenes that show the most promising biological activity are shown in Table I. These heterocyclic molecules are pale-yellow highly crystalline solids that are sparingly soluble in water. Using cyclic voltammetry, we have found that these compounds are reversibly reducible (Fig. 1). We have also carried out a pulse radiolysis study [5] of these compounds. This technique has made possible the determination of (i) the one-electron reduction potential (E_7^1) of these molecules (A) in an aqueous environment at pH 7, (ii) the rate constants of the reaction of the respective anion radicals ($A^{\overline{\cdot}}$) with oxygen, and (iii) the pK_a of the equilibrium, $AH^{\cdot} \rightleftharpoons A^{\overline{\cdot}} + H^{+}$. Results are presented in Table I. The reaction of the anion radicals with oxygen probably results in the formation of the superoxide anion radical, $O_2^{\overline{\cdot}}$, and regeneration of the substrate, A. The one-electron reduction potential E_7^1, is linearly related to the half-peak potentials,

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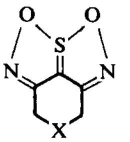
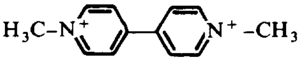
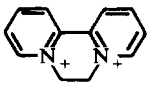
Abbreviations: PS, Photosystem; HEP, heteropentalene.

TABLE I

THE ELECTROCHEMICAL PROPERTIES OF SOME DIOXATHIADIAZA-HETEROPENTALENES, PARAQUAT AND DIQUAT

Compound	Structure 	E_7^1 (mV)	$E_{P/2}$ (MeOH/water 3:1 by volume) (mV)	pK_a $(AH^{\cdot}/A^{\cdot-})$	k^c $(O_2 + A^{\cdot-})$ $(M^{-1} \cdot s^{-1})$
HEP I	$X = CH_2$	−416	−470	5.9	$3.5 \cdot 10^{+8}$
HEP II	$X = S$	−375	−420	4.5	$4.5 \cdot 10^{+8}$
HEP III	$X = SO$	−277	−350	–	$1.2 \cdot 10^{+8}$
HEP IV	$X = SO_2$	−227	−300	–	$0.57 \cdot 10^{+8}$
Paraquat	 $2Cl^-$	−447	−455 [c]	2.9 [b]	$7.7 \cdot 10^{+8}$ [a]
Diquat	 $2Cl^-$	−350	−354 [c]	–	$4.7 \cdot 10^{+8}$ [a]

[a] Results from Ref. 2.

[b] Results from Ref. 8.

[c] Determination at pH 7 in phosphate buffer.

[d] Results from Ref. 9.

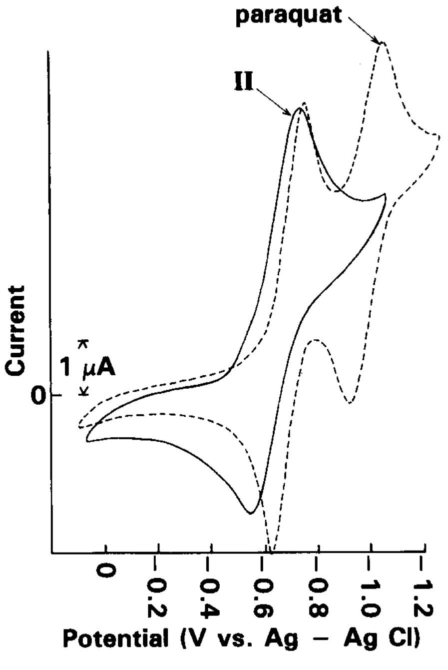


Fig. 1. A comparison of the cyclic voltammogram of HEP II (———) in MeOH/H_2O (3:1 by volume) and paraquat (- - - - -) in water at neutral pH.

$E_{P/2}$, determined by cyclic voltammetry in methanol/water (3:1 by volume). As predicted [6] by the Marcus treatment for electron-transfer processes, the natural logarithm of the rate constant of the reaction of oxygen with the anion radical, $A^{\cdot-}$, is to a good approximation linearly related to E_7^1 of the substrate, A.

The dioxathiadiaza-heteropentalenes in Table I have appropriate reduction potentials to intercept electron transport in the same way as the bipyridinium herbicides. Like paraquat, these compounds have been found to act as Photosystem-I electron acceptors in vitro at concentrations of the order of $1 \cdot 10^{-6}$ M. Superoxide radicals are generated by the reaction between oxygen and heteropentalene reduced by Photosystem I, as is the case for paraquat [7]. None of the compounds inhibit the Hill reaction at concentrations of up to $1 \cdot 10^{-4}$ M. In vivo, these new herbicides are absorbed both by the leaves and by the roots of susceptible plant species, unlike paraquat, which is only foliar active (Table II) and quickly inactivated by the soil. The effects of foliar application develop

TABLE II

DIOXATHIADIAZA-HETEROPENTALENES AND HERBICIDE SCREEN RESULTS [a]

Test compound	Dose (kg/ha)	Foliar spray [b]								Preemergence [b]							
		MA	RI	BG	OA	LI	MU	SB	SO	MA	RI	BG	OA	LI	MU	SB	SO
HEP I	5	5	5	8	6	9	9	9	8	3	7	9	3	4	5	5	2
	1	3	3	6	3	6	7	7	6	0	4	5	2	2	2	0	0
HEP II	5	8	9	9	8	9	9	9	9	8	–	9	7	7	9	9	8
	1	5	8	9	6	8	9	9	8	5	–	8	5	5	8	8	4
HEP III	5	8	9	9	8	9	9	9	9	8	–	9	7	6	8	8	0
	1	6	7	9	5	7	9	9	8	6	–	9	5	2	5	4	0
HEP IV	5	7	8	9	8	9	9	9	9	3	–	7	3	4	7	0	0
	1	4	6	8	6	8	9	5	7	3	–	5	2	0	3	0	0
Paraquat	5	9	9	9	9	9	9	9	9	0	0	0	0	0	0	0	0
	1	8	9	9	9	9	9	9	9	0	0	0	0	0	0	0	0

[a] The foliar spray and preemergence activity was assessed 10 days after treatment. Toxicity ratings are 0–9, with 0 indicating no effect, 9 indicating complete kill.

[b] Plant species mentioned: MA, maize (*Zea mays*); RI, rice (*Oryza sativa*); BG, barnyard grass (*Echinochloa crus-galli*); OA, oat (*Avena sativa*); LI, linseed (*Linum usitatissimum*); MU, mustard (*Sinapsis alba*); SB, sugar beet (*Beta vulgaris*); SO, soyabean (*Glycine max*).

rapidly (within 24 h) and the symptoms of activity are growth retardation, necrosis and chlorosis. The toxicity of the compounds in experimental animals appears to be lower than that of paraquat [10]. The acute oral LD_{50} of HEP II in rats lies in the range 250–1000 mg/kg, whilst that in mice is greater than 1000 mg/kg.

Field trials of HEP II in the U.K., Brazil and the West Indies have shown that this compound is of interest in controlling the growth of mono- and dicotyledonous weeds, mainly by post-emergence application. The practical value of HEP II has not been fully explored, but the control of the growth of weeds in tropical crops (e.g., sugar cane or coffee) seems to be possible.

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