Tetrahedron Vol 24, pp 2697 to 2700 Pergamon Press 1968 Printed in Great Britain

CHEMICAL CONSTITUTION AND ACTIVITY OF BIPYRIDYLIUM HERBICIDES—I

DIQUATERNARY SALTS OF 2,2'-DIPYRIDYL SULPHIDE

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(*Received in the UK* 26 *September* 1967; *accepted for publication* 5 *October* 1967)

Abstract Diquaternary salts of 2,2'-dipyridyl sulphide including the new cyclic structures 6,7-dihydrodipyrido-[2.1-*b*:1'.2'-*f*]-1,3,6-thiadiazepinium dibromide and 6*H*-dipyrido[2.1-*b*:1'.2'-*e*]-1,3,5-thiadiazinium dibromide have been prepared. They are reduced by a relatively slow one electron transfer to radical cations which are much less stable than those obtained from herbicidal bipyridylium diquaternary salts. The relative instability of the radical cations may account for the lack of herbicidal activity shown by the dipyridyl sulphide diquaternary salts

DIQUAT (I), paraquat (II) and related diquaternary salts of 2,2'- and 4,4'-bipyridyls have attracted much attention as herbicides.[1] Their mode of action is thought[2,3] to be connected with their ability to be rapidly reduced to stable radical cations at a potential (E_0) of about −0·35 to −0·45 volts 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. The influence 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 not so far been investigated. This paper describes the preparation and some of the properties of diquaternary salts of 2,2'-dipyridyl sulphide. Parts of the work have been reported in preliminary[4,5] and short[6] communications.

2,2'-Dipyridyl sulphide reacted readily with methyl iodide and ethyl bromide to afford the appropriate diquaternary salts (IX) which were usually accompanied by substantial amounts of the mono-quaternary salts. The formation of diquaternary salts of 2,2'-dipyridyl sulphide contrasts with the behaviour of di-(2-pyridyl)amine which gives compound III instead of the diquaternary salt on reaction with methyl iodide.[7] Di-(2-pyridyl)-methane[8] and 1,2-di-(4-pyridyl)-ethylene and -ethane,[9] however, form diquaternary salts with methyl iodide. 2,2'-Dipyridyl sulphide reacted easily too with ethylene dibromide to give the cyclic salt, 6,7-dihydrodipyrido-[2.1-*b*:1'.2'-*f*]-1,3,6-thiadiazepinium dibromide (IV), the structure of which was confirmed by elemental analyses (all bromine ionic) and by the NMR spectrum. With dibromomethane 2,2'-dipyridyl sulphide afforded 6*H*-dipyrido[2.1-*b*:1'.2'-*e*]-1,3,5-thiadiazinium dibromide (V). This structure represents the first authenticated example of a polycyclic system containing a methylene group flanked by two quaternary pyridine nitrogen atoms (cf. Refs 8, 13) although the related structure VI has been reported.[10] The formation of V contrasts with unsuccessful attempts to prepare the corresponding diquaternary salt from 2,2'-bipyridyl which gives instead the oxadiazepin di-cation (VII) with methylene sulphate[11,12] and the aromatic salt

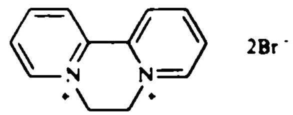
(VIII), *inter alia*, with methylene iodide.[13] The structure V was confirmed by elemental analyses (all bromine ionic) and by the NMR spectrum in water. In deuterium oxide at room temperature the signal due to the methylene protons, which appears as a singlet at $\delta = 7{\cdot}3$ ppm, decreased considerably in intensity due to the exchange of the hydrogen atoms with deuterium.

The diquaternary salts of 2,2'-dipyridyl sulphide were stable although some of them were deliquescent. The UV spectra in water of compounds IX (R = Me, X = I) and IX (R = Et, X = Br) were unchanged after one week. The cyclic salts IV and V were rather less stable in solution, small changes in their UV spectra appearing after 4–5 days. All the diquaternary salts were more prone to deterioration when exposed to sunlight and, as expected, they were rapidly decomposed by base. Hot hydroxylic solvents used in crystallisation also caused some breakdown especially with compounds IV and V.

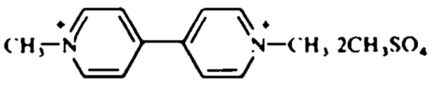
Aqueous solutions of the diquaternary salts of 2,2'-dipyridyl sulphide on treatment with zinc dust developed a yellow-green coloration after about one minute, especially in regions close to the surface of the zinc. On standing for several minutes the solutions became amber in colour. The yellow-green coloration is attributed, at least in part, to the appropriate radical cation. Structure X, for example is one canonical form of the radical cation from compound IV. The amber colour is considered to be due to products obtained by the decay of the free radicals.

Results obtained from polarography were consistent with the uptake of one electron by the diquaternary salts. At concentrations of 0·001M and 0·0015M in the pH range 6–8 the dipyridyl sulphide diquaternary salts gave typical symmetrical one electron reduction waves with half-wave potentials (E_0) between $-0{\cdot}38$ and $-0{\cdot}49$ volts independent of pH and concentration (see Ref. 6). Diquat dibromide (I) was included in the polarograph experiments for comparison. In substantial agreement with a recent report[14] it showed, *inter alia*, a symmetrical one electron reduction step with a half-wave potential of $-0{\cdot}36$ volts independent of pH, due to the formation of the corresponding radical cation. The formation of paramagnetic species on reduction of the dipyridyl sulphide salts was confirmed by the observation that an aqueous solution of IV after treatment with zinc dust gave an ESR signal consisting of about 40 lines with a total width of about 33 gauss. No signal was obtained before treatment with zinc powder. The NMR spectrum of IV in aqueous solution, however, taken ten minutes after the addition of zinc dust, showed no evidence of the presence of a high concentration of a free radical species (cf. Refs 15, 16, 17). The appearance of broad signals at $\delta = 6{\cdot}6$–$7{\cdot}6$ ppm, which are absent in the NMR spectrum of IV, indicated that about 20% of IV had been converted to reaction products. Moreover, when an aqueous solution (0·0001M) of IV was shaken with zinc powder, the UV spectrum, λ_{max} 242, 293 and 323 mμ, disappeared and a new spectrum, λ_{max} 282, 305 and 403 mμ, was obtained. The latter spectrum remained unchanged for several weeks when the reducing agent was removed thus confirming that the final products of the reduction are stable and are not reversibly oxidized by air. On exposure to sunlight an aqueous solution of IV showed similar changes in the UV spectrum. The other diquaternary salts of 2,2'-dipyridyl sulphide behaved likewise. These results clearly indicate that the radical species formed on reduction of the dipyridyl sulphide salts decay fairly rapidly to give products whose structures have not so far been determined.

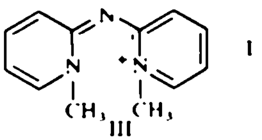
It is apparent that diquaternary salts of 2,2'-dipyridyl sulphide are reduced in



I



II



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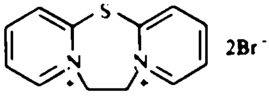

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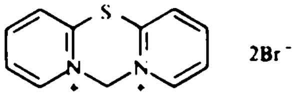
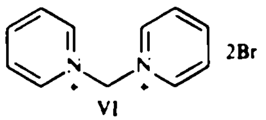
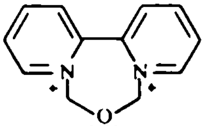


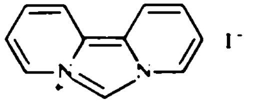
V



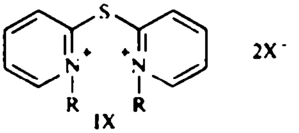
VI



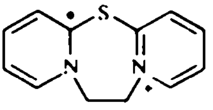
VII



VIII



IX



X

aqueous solution by a one electron transfer at about the same potential as diquat and paraquat. The uptake of the one electron, however, is a relatively slow process compared with the instantaneous and essentially quantitative conversion of the herbicidal diquaternary salts of 2,2'- and 4,4'-bipyridyls to their radical cations. The radical cations formed from the dipyridyl sulphide salts are apparently much less stable than those obtained from the bipyridylium compounds.

The diquaternary salts of 2,2'-dipyridyl sulphide showed no significant activity in post-emergent herbicidal tests on six plant species[6] at a rate equivalent to 7 lbs/acre. The reasons for the absence of activity in the diquaternary salts of 2,2'-dipyridyl sulphide are not clear but the strong evidence[2, 3] implicating radicals in the mode of action of bipyridylium herbicides indicates that the slow rate of formation of radical cations from dipyridyl sulphide salts and their relative instability once formed may well be responsible. These results are consistent with the theory[1 3] that for herbicidal activity of the type associated with bipyridylium salts, the compounds, *inter alia*, must be capable of being reduced at appropriate potentials to radical cations which are stable in aqueous solution and which are reversibly oxidized by air.

EXPERIMENTAL

UV absorption spectra were taken with 0·0001M solns in water. Extinction coefficients reported previously[4–6] were approximate. NMR spectra were determined by Mr. V. A. Pickles of the University of New South Wales at 60 Mc/s using sodium 3-trimethylsilyl-1-propanesulphonate as internal standard. The ESR spectrum was taken by Professor R. O. C. Norman and Mr. B. C. Gilbert of the University of York on a Varian V-4502 instrument with 12-in magnet and 100 kc modulation. The concentration of the salt was 5×10^{-3}M. Polarograph experiments were carried out on 0·001M and 0·0015M aqueous solutions at 20° in 0·067M Sorensen phosphate buffers at pH 5·9, 6·8 and 8·04 using a standard calomel electrode. The half-wave potentials are assumed to be E_0 values and were calculated by adding 0·25 volts to the $E_{\frac{1}{2}}$ values. Experimental error is ±0·02 volts. Microanalyses were by the Australian Microanalytical Service.

Dimethiodide of 2,2'-dipyridyl sulphide (IX; R = Me, X = I) was prepared by reacting 2,2'-dipyridyl sulphide with boiling MeI for 6 hr. The solid which precipitated during the reaction consisted of a mixture of the dimethiodide and the mono-methiodide salts. When the solid was treated with cold EtOH the mono-methiodide salt dissolved. The almost pure *dimethiodide of 2,2'-dipyridyl sulphide*, which remained undissolved, crystallized from aqueous EtOH as yellow crystals, m.p. 212° (with dec), yield = 50%. UV spectrum λ_{max} 269 sh (log ε 3·75), 304 mμ (4·06) Reduction potential E_0 −0·42 volts. (Found: C, 30·65; H, 3·2; N, 5·6; S, 6·9; I (ionic), 53·2. $C_{12}H_{14}I_2N_2S$ requires. C, 30·9; H, 3·0; N, 5·9; S, 6·8; I (ionic), 53·8%.)

N,N'-*Diethyl dibromide of 2,2'-dipyridyl sulphide* (IX; R = Et; X = Br) was obtained similarly from EtBr. It crystallized from EtOH as white crystals, m.p. 211°. Yield = 15%. UV spectrum λ_{max} 269 sh (log ε 3·72), 308 mμ (4·02). Reduction potential E_0 −0·42 volts. (Found: C, 40·9; H, 4·3; N, 6·7; S, 7·9; Br (ionic), 39·3. $C_{14}H_{18}Br_2N_2S$ requires: C, 41·4; H, 4·4; N, 6·9; S, 7·9; Br (ionic) 39·4%.)

6,7-*Dihydrodipyrido*[2,1-*b*. 1'.2'-*f*] 1,3,6-*thiadiazepinium dibromide* (IV) was prepared by treating 2,2'-dipyridyl sulphide with boiling ethylene dibromide for 1 hr. The grey ppt which was obtained was crystallized from aqueous EtOH to give the product as the monohydrate, m.p. 232°, yield = 65%; UV spectrum λ_{max} 242 (log ε 3·70), 293 (3·90), 323 mμ (4·08); NMR spectrum (D_2O) δ 5·7 (4H, s, methylene), 8·1 9·2 ppm (8H, m, aromatic). Reduction potential E_0 −0·38 volts. (Found: C, 36·5; H, 3·3; N, 6·7; S, 8·4; Br (ionic), 41·0. $C_{12}H_{12}Br_2N_2S.\ H_2O$ requires. C, 36·5; H, 3·6; N, 7·1; S, 8·1; Br (ionic) 40·6%.)

6H-*Dipyrido*[2,1-*b*:1'.2'-*e*] 1,3,5-*thiadiazinium dibromide* (V) was prepared similarly using dibromomethane (3 hr). It crystallized from aqueous EtOH as white crystals, m.p. 298° (with dec); yield = 50%; UV spectrum λ_{max} 235 (log ε 3·74), 290 (4·00), 313 mμ (3·99); NMR spectrum (H_2O) δ 7·3 (2H, s, methylene), 8·2–9·5 ppm (8H, ms, aromatic). Reduction potential E_0 −0·49 volts. (Found: C, 36·0; H, 3·0; N, 7·3; S, 8·7; Br (ionic) 43·9. $C_{11}H_{10}Br_2N_2S$ requires: C, 36·5; H, 2·8; N, 7·7; S, 8·8; Br (ionic) 44·2%

Acknowledgements—I thank Professor R. O. C. Norman and Mr. B. C. Gilbert of the University of York for the ESR spectrum and Mr. V. A. Pickles of the University of New South Wales for the NMR spectra. The herbicide tests were kindly arranged by Drs. J. E. Falk and J. N. Phillips of the Division of Plant Industry, C.S.I.R.O., Canberra. Dr. J. T. Braunholtz of Plant Protection, Ltd. kindly supplied a sample of diquat.

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