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CYCLIC VOLTAMMETRY OF SOME QUINOXALINE DI-*N*-OXIDES AND QUINOXALINES IN DIMETHYLFORMAMIDE

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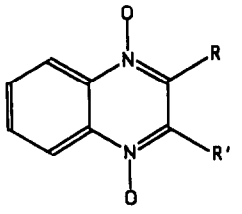
Abstract—The first cathodic reductions of two series of substituted quinoxaline di-*N*-oxides and quinoxalines in dimethylformamide were measured The effect of substituent on these reductions is reported and reversibility is discussed

Key words quinoxaline-*N*-oxides, quinoxalines, cyclic voltammetry, reversibility

INTRODUCTION

The electrochemical behavior of heteroaromatic amines and heteroaromatic amine-*N*-oxides, including quinoxaline di-*N*-oxides, has been studied in aqueous solutions[1–4] However, the studies of quinoxaline-1,4-dioxides in nonaqueous solvents are limited[5–9] Some of the investigations have examined alkyl or aryl substituents in the 2- and the 2,3-positions We now expand the results of the prior work by surveying materials that contain a variety of substituents attached adjacent to the nitrone functionalities



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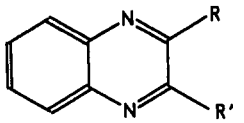

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EXPERIMENTAL

Cyclic voltammetric (*cv*) measurements were made using a Princeton Applied Research Corporation (PARC) model 264A Polarographic Analyser connected to a PARC model 303A SMDE, and a Yokogawa model 3022 A4 *X–Y* recorder The reference electrode was a saturated calomel electrode (*sce*), separated from the working solution by a salt bridge filled with electrolyte, connected to the back panel reference electrode test point The internal silver wire in the electrode block was isolated from the test solution by covering it with an empty reference electrode jacket Scan rates employed ranged from 20 to 200 mV s^{-1}, reported values are for a scan rate of 100 mV s^{-1} Solutions were 0 5 mM in chromatographic grade dimethylformamide (Aldrich Chemical Co), containing 0 1 M tetraethylammonium perchlorate (TEAP, G F Smith Chemical Co) as the supporting electrolyte

Quinoxaline-1,4-dioxides (1) and quinoxalines (2) (Tables 1 and 2) were prepared and characterized (^{1}H-NMR, *uv*–vis, and m p) by literature procedures[10–20] with occasional modifications

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RESULTS AND DISCUSSION

Representative cyclic voltammograms are given in Figs 1 and 2 The following methods were applied to analyze the *cv* curves The Nicholson expression was used to calculate the ratio i_{pa}/i_{pc}[21] The value of the half-wave potential was determined by the equation $E_{1/2} = (E_{pc} + E_{pa})/2$, which is in principle applicable to a reversible redox system[22] This equation gave $E_{1/2}$ values, for the first reduction wave, essentially independent of the sweep rate Cyclic voltammetry is also a measure of the reversibility of the electrode reaction[1, 23]

Crawford and co-workers reported a value of −1 21 V for quinoxaline-1,4-dioxide 1a[6], which will be used as the standard Incorporation of a 2-methyl group into the parent resulted in a more negative reduction potential, *cf* compounds 1a and 1b (Table 1) Addition of a second methyl group at position 3 makes the reduction more difficult by 70 mV From the results in Table 1 it appears that each methyl group makes $E_{1/2}$ more negative by about 0 1 V The effect of an acyclic ring, fused at positions 2 and 3, can be determined by comparing compounds 1c, 1d, and 1e Neither the presence of a ring nor its size appears to have a substantial consequence on the reduction peak Barqawi and Atfah found similar results in acetonitrile[8]

Alcohol 1f underwent a reversible one-electron reduction with $E_{1/2} = -1\,27$ V The radical anion, stable only at high scan rates, is less stable than that

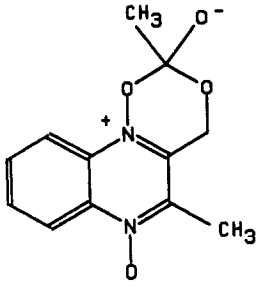
Table 1 Structures and cyclic voltammetry data of quinoxaline-1,4-dioxides

Quinoxaline di-*N*-oxide	R	R′	$E_{1/2}$/V	ΔE_p/mV*	Reference for preparation
1a	H	H	−1 21†	70	—
1b	H	CH_3	−1 32†	—	—
1c	CH_3	CH_3	−1 39	80	[10]
1d	-$CH_2CH_2CH_2$-		−1 35	75	[11]
1e	-$CH_2CH_2CH_2CH_2$-		−1 36	70	[11]
1f	CH_3	CH_2OH	−1 27	80	[12]
1g	CH_2OH	CH_2OH	−1 06‡	—	—
1h	CH_3	CH_2OCOCH_3	−1 16§	70¶	[12]
1i	H	Ph	−1 19	70	[13]
1j	Ph	Ph	−1 24	70	[14]
1k	Ph	CH_2Ph	−1 23	80	[14]
1m	H	CF_3	−0 93	65	[15]
1n	CH_3	$COCH_3$	−1 07	70	[13]
1o	CH_3	CO_2CH_3	−1 11	75	[14]
1p	Ph	COPh	−1 09	70	[13]
1q	CH_3	COPh	−1 08	75	[16]

*$\Delta E_p = |E_{pa} - E_{pc}|$
†Ref [6]
‡Ref [5]
§Irreversible wave, E_p, 100 mV s^{-1}
¶$E_{pp/2}$ value

of the dimethyl The inductive effect of the hydroxyl and hydrogen bonding with *N*-oxide can be used to rationalize the greater ease of reduction for 1f *vs* 1c Hydrogen bonding enhances the positive nature of the nitrogen, thus increasing electron attracting ability and stabilizing the oxyanions formed during charge transfer, the first reduction is due to the reduction of the *N*-oxide functionality, to form the radical anion The diol 1g reduced at −1 06 V[5] Evidently the addition of the second alcohol functionality influences the reduction more than the first

Acetate 1h had an E_p which was 0 19 V more positive than 1c, and gave an irreversible wave The greater ease of electron uptake follows from the presence of the electronegative acetate group The correspondence with alcohol is evident Ryan *et al* [5] suggested the effect of the ester moiety might be further enhanced by the interaction with nitrone as in structure 3 Earlier workers associated the ease of reduction of acetate substituted quinoxaline *N*-oxides with the liability of the methylene protons[9]



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The effect of an aromatic substituent can be determined by comparing compounds 1a, 1i and 1j 2-Phenylquinoxaline-1,4-dioxide produced $E_{1/2}$ of −1 19 V As a first approximation, it may be expected that incorporation of a second phenyl substituent would facilitate reduction as evidenced in prior studies[24] However, compound 1j generated an $E_{1/2}$ of −1 24 V, in agreement with Crawford *et al* [6] The results may be rationalized by steric

Table 2 Structures and cyclic voltammetry data of quinoxalines

Quinoxaline	R	R′	$E_{1/2}$/V	ΔE_p/mV*	Reference for preparation
2a	H	H	−1 80†	—	—
2b	H	CH_3	−1 71†	—	—
2c	CH_3	CH_3	−1 87‡	70§	commercial
2d	-$CH_2CH_2CH_2CH_2$-		−1 54	80	[17]
2e	H	Ph	−1 54	80	[18]
2f	Ph	Ph	−1 55	85	[19]
2g	Ph	CH_2Ph	−1 60‡	65§	[17]
2h	CH_3	$COCH_3$	−1 28	75	[20]
2i	Ph	COPh	−1 28	75	[13]

*$\Delta E_p = |E_{pa} - E_{pc}|$
†Ref [6]
‡Quasireversible wave, E_p, 100 mV s^{-1}
§$E_{pp/2}$ value

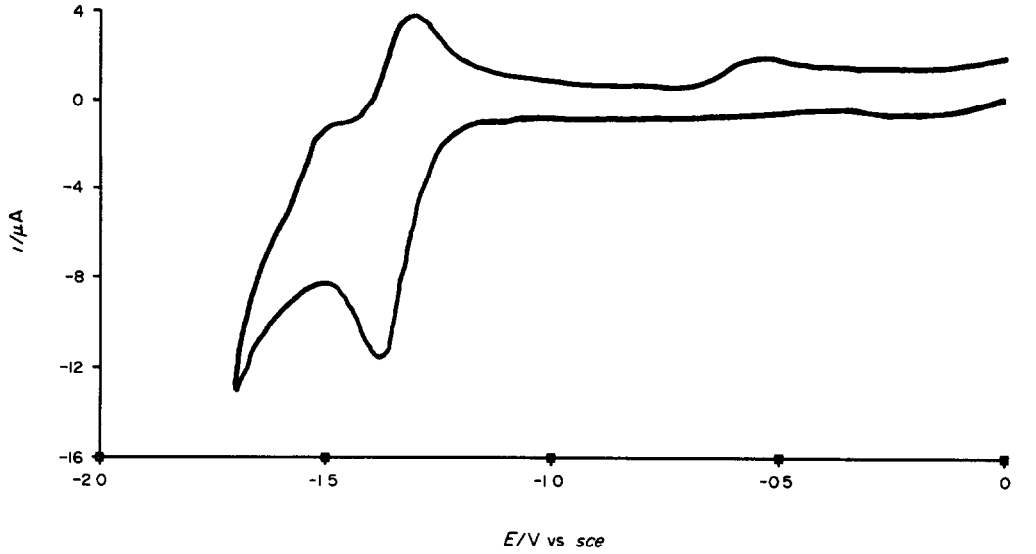

Fig 1 Cyclic voltammogram of 1d in dimethylformamide containing 0 1 M TEAP supporting electrolyte, 0 1 Vs^{-1}

effects The potential exists for sufficient orbital overlap between nucleus and phenyl ring in 1i such that the anion radical generated after electron uptake may be stabilized by delocalization Thus, reduction occurs at a slightly more positive potential than in compound 1a Apparently, this effect is lessened for the 2,3-diphenyl material due to the added steric interference resulting from crowding by the two aromatic groups[25] Hayashi and co-workers have stated that the conjugation between the phenyl group and the quinoxaline ring is lessened by the presence of bulky substituents on the adjacent carbon[26] Estimates from molecular mechanics calculations (made by using the programs PC model and MMX, available from Serena Software, Bloomington, Indiana) for the dihedral angle between the diazine nucleus and the phenyl ring indicate that the value is about 10° larger in the diphenyl material, *ie* 10° farther from coplanarity Both compounds reduce at potentials more positive than their methyl analogs Thus, the phenyl substituent acts as an electron-withdrawing group Zuman has suggested that differences observed with phenyl and other substituents are predominantly due to a polar effect[27] There is little change in reduction potential when a methylene group is inserted between the heteroaromatic and phenyl rings as in compound 1k Therefore, sterics do appear to affect reduction

Examination of quinoxaline dioxides with other electron withdrawing substituents attached in the 2- and the 2,3-positions resulted in more positive reduction potentials than the alkyl substituted materials For example, 2-trifluoromethylquinoxaline-1,4-dioxide reduced at a potential about 400 mV more positive than compound 1b Fieser and Fieser have reported a positive shift in reduction potential upon substitution of halogen for hydrogen[28]

The replacement of a methyl group with an acetyl group as in compound 1n caused about a 0 3 V increase in the reduction value The result for the

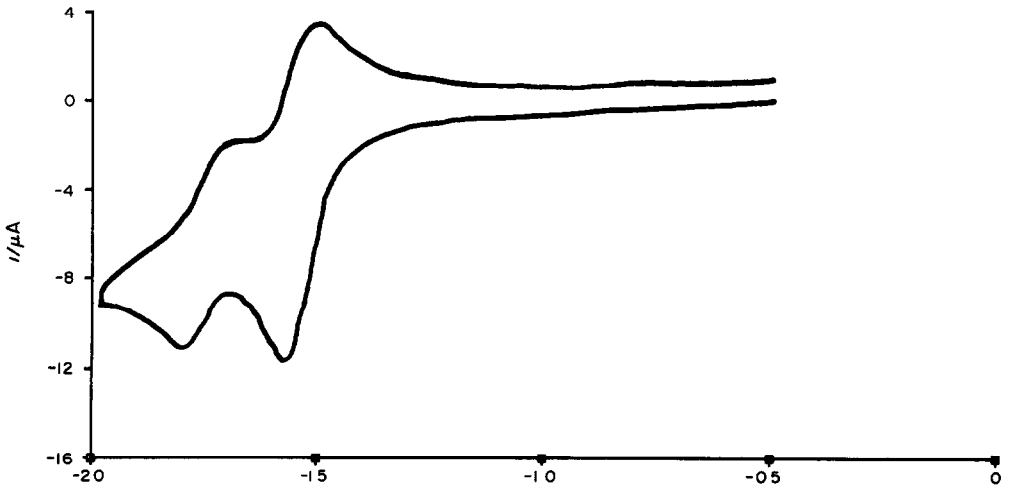

Fig 2 Cyclic voltammogram of 2d in dimethylformamide containing 0 1 M TEAP supporting electrolyte, 0 1 Vs^{-1}

ester 1o is only slightly more negative than ketone Ester and ketone functionalities have approximately the same electron-withdrawing ability[29] A similar situation exists for phenyl and benzoyl, *cf* 1j and 1p, although the difference in potentials is only about 150 mV Perhaps steric interactions do not allow for conjugation between carbonyl or phenyl and heterocyclic ring as proposed for the diphenyl compound (*vide supra*) Further support comes from 2-benzoyl-3-methylquinoxaline-1,4-dioxide, 1g which reduced at an $E_{1/2}$ of -1 08 V The methyl group is apparently large enough to reduce orbital overlap

The reduction in the quinoxaline series (Table 2) is due to the formation of a radical anion It is clear that the reduction is more difficult than in the di-*N*-oxides This is likely to be due to the coordinated oxygen atoms in the nitrones, which make the quinoxaline ring more electrophilic and provide increased resonance stabilization of the radical anion[30] Electron uptake depends on the electrophilicity of the material being reduced and the stability of the radical produced[31]

A similar trend in reduction potentials for the diazines as the dioxides can be observed in Table 2 Electron releasing groups yield more negative values than electron withdrawing substituents, *ie* compounds 2h and 2i reduced approximately 300 mV more positive than the others Data for compound 2d is somewhat surprising since the value is more positive than compound 2c and close to those for the phenyl substituted materials This was not observed with the dioxides, the reasons for this are unknown to us

The reversibility of the reductions may be discussed using the ΔE_p and i_{pa}/i_{pc} values The difference between peak potentials for 1m was close to theoretical for a one-electron reversible process, whereas the others were somewhat higher, ranging from 70 to 85 mV, and independent of the scan rate The calculated i_{pa}/i_{pc} values for all dioxides except 1f were close to unity, deviating only slightly at slower scan rates, indicating the formation of a relatively stable reduction product Evidently a slow irreversible reaction takes place after electron uptake with 1f The voltammograms for compound 1h had an $|E_p - E_{p/2}|$ value of 70 mV, thus implying electron transfer accompanied by fast follow-up chemistry A prior investigation of several of the current samples in acetonitrile noted a dependence of the reversibility of the first wave on the switching potential and the scan rate[8] Results from the unoxidized compounds were somewhat different Although the separation between forward and reverse scans was about 80 mV, the current ratio for compounds 2d–f deviated significantly from one, generally ranging from 0 6 to 0 8 Apparently, kinetic or other complications occur in the electrode process Compounds 2h and 2i produced values greater than 0 95

In summary, groups which lower the reduction potential of the parent are generally those which facilitate substitution in an aromatic ring, *eg* benzene, and those which increase the reduction potential have the opposite effect and retard aromatic substitution

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