Preparation of some Quinoxaline Quinones, their Electrochemical Reduction, and EPR and Theoretical Studies on their Semiquinone Anions

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Novel 2,3-disubstituted quinoxaline quinones and a tricyclic quinone containing the quinoxaline nucleus are reported together with their one-electron reduction chemistry and the EPR spectra of the radical anions.

The 2,3-substituents on quinoxaline quinones have an effect on the stability of the compounds. This is indicated by the observation that the parent quinone **1** is not stable and is best prepared immediately before use whereas the 2,3-bis(ethylsulfanyl)- and 2,3-dimethoxy-quinoxaline-5,8-quinones, **2** and **3**, respectively are relatively stable in air and can be left in the solid state in the dark for a month or more without significant decomposition. Our investigations were undertaken in order to gain more understanding of the effects produced by substituents at the 2- and 3-positions of the quinoxaline quinone nucleus on the ease of reduction of the quinone (Q) and the properties of the radical anion $(Q^{\bullet -})$ (Fig. 1). The present study was carried out using DMF as the solvent since semiquinones are more stable in aprotic solvents than in water.[5] Good correlations exist between $E(Q/Q^{\bullet -})$ in water and in DMF.

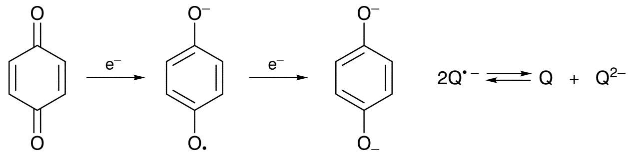
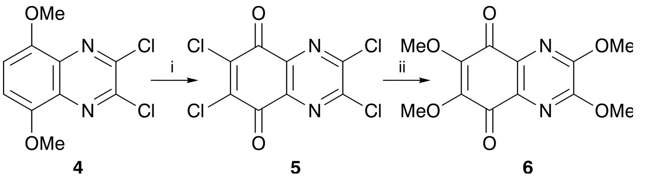
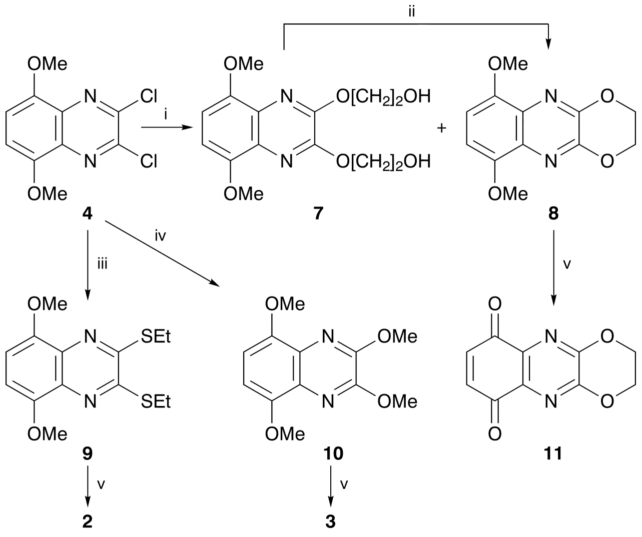


Fig. 1 Stepwise one-electron reduction of a *para*-quinone and the equilibrium between quinone, radical anion and dianion

The tetrachloroquinoxaline quinone **5** was obtained from 5,8-dimethoxyquinoxaline **4**[17] by oxidation with a mixture of concentrated nitric and hydrochloric acids, and the tetramethoxyquinoxaline quinone **6** was formed by the action of sodium methoxide in methanol on **5** (Scheme 1). Reaction of **4** with 2 equiv. of disodium ethylene glycolate gave both **7** and **8**, and **8** was also readily prepared from **7** by the action of sodium hydride in DMSO (Scheme 2).[6] The tetramethoxyquinoxaline **10** was available from **4**.



Scheme 1 *Reagents and conditions:* i, concentrated HCl, concentrated HNO_3, r.t., 1.5 h; ii, MeOH, NaOMe, r.t., 1 h



Scheme 2 *Reagents and conditions:* i, $HOCH_2CH_2OH$, Na, THF, reflux, 4 h; ii, DMSO, NaH, r.t., 4 h; iii, EtSNa, EtOH, reflux, 2 h; iv, MeOH, NaOMe, r.t., 1 h; v, CAN, MeOH, H_2O, ice-bath, 0.5 h

Oxidation of 5,8-dimethoxyquinoxalines **8**, **9** and **10** to the corresponding quinones **11**, **2** and **3** was achieved using ammonium cerium(IV) nitrate (CAN) (Scheme 2). The quinones showed a singlet between δ 6.90 and 6.95 in their ^1H NMR spectra due to the quinone ring hydrogens. This is at higher field than for the quinoxaline-5,8-diones **1**, **12** and **13** which have a singlet in their NMR spectra in the range δ 7.24 to 7.29. The upfield shift for **2**, **3** and **11** is probably due to strong electron release from the 2- and 3-substituents. Treatment of the quinone **3** with 1-acetoxybutadiene gave **14** in a process involving both loss of acetic acid and dehydrogenation.

The five compounds studied **2**, **5**, **6**, **11** and **14**, displayed two reversible reduction processes corresponding to the reduction of Q to $Q^{\bullet -}$ and of $Q^{\bullet -}$ to Q^{2-} respectively, where Q^{2-} is the quinol dianion, with $E(Q^{\bullet -}/Q^{2-}) - E(Q/Q^{\bullet -})$ values of between –540 and –700 mV (Table 1). Calculation of comproportion equilibrium constants $(K_{com} = \exp\{-(F/RT)[E(Q^{\bullet -}/Q^{2-}) - E(Q/Q^{\bullet -})]\})$ from these data indicate that the semiquinones are stable with respect to disproportionation (Fig. 1).

For comparison, the reduction potentials of 2,3-dichloro-1,4-naphthquinone under identical conditions were –0.472 and –1.480 V respectively and fall within the range of the values obtained for the quinoxaline quinones so indicating that the nitrogen atoms have little effect upon the reduction potentials.

Plots of return current against the square root of the scan rate for the first reduction processes gave straight lines even when the second reduction was cycled and thus also confirm the reversibility of the couples.

The EPR spectra of the radical anions revealed *g* values of ≈2.005, typical of organic radicals, and small hyperfine

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Table 1 Electrochemical data for compounds **2**, **5**, **6**, **11** and **14**[a]

	$E(Q/Q^{\bullet -})$		$E(Q^{\bullet -}/Q^{2-})$			
Compound	$E_{1/2}$/V	ΔE_p/mV	$E_{1/2}$/V	ΔE_p/mV	$E(Q/Q^{\bullet -}) - E(Q^{\bullet -}/Q^{2-})$/V	Comproportion equilibrium constants
2	−0.91	145	−1.58	675	−0.67	1.9×10^{11}
5	−0.49	85	−1.19	85	−0.70	6.0×10^{11}
6	−1.07	110	−1.61	335	−0.54	1.2×10^{9}
9	−0.96	75	−1.55	195	−0.59	8.4×10^{9}
14	−1.19	115	−1.77	465	−0.58	5.8×10^{9}

[a]Conditions are given in the Experimental section (full text).

splittings (<1 mT), showing that the hyperfine coupling constants of the active nuclei are small. Initial attempts to record the spectrum of compound **5** led to the observation of a weak spectrum without the application of a current due to chemical reduction by the mercury working electrode.

Semiempirical INDO calculations were carried out on the radical anions of the quinones as an aid to the assignment of the hyperfine coupling constants and in order to obtain their signs.

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Techniques used: IR, ^{1}H NMR, EPR, mass spectrometry, cyclic voltammetry, INDO calculations

References: 17

Schemes: 3

Fig. 2: Some resonance effects in 2,3-dimethoxyquinoxaline 5,8-quinone

Fig. 3: Cyclic voltammogram of compound **5** at scan rate 200 mV s^{-1}

Fig. 4: Cyclic voltammogram of compound **14** at scan rate 200 mV s^{-1}

Fig. 5: *g* Values and hyperfine coupling constants of the radical anions of compounds **2**, **5**, **6**, **11** and **14**. Calculated hyperfine coupling constants are given in parentheses

Fig. 6: Experimental and simulated EPR spectra of the radical anion of compound **2**, (a) whole spectrum, (b) expansion

Fig. 7: Experimental and simulated EPR spectra of the radical anion of compound **14**

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