Electroreduction of 4-(2-Thienyl)quinazoline in Acetonitrile

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The electroreduction of 4-(2-thienyl)quinazoline (4-TQ) in acetonitrile solutions gave a single two-electron well-defined polarographic wave. The well-defined wave was found to be diffusion-controlled and irreversible on the basis of the usual criteria. Based on the controlled-potential electrolysis and cyclic voltammetric experiments, a disproportionation reaction mechanism is suggested for 4-TQ reduction in acetonitrile.

4-(2-Thienyl)quinazoline (4-TQ) possesses some biologically-active properties. It is found to be an analgesic, antiinflammatory, and antipyretic.[1,2] During our detailed electrochemical investigations on the reduction of this compound in amphiprotic[3] (methanol–water mixtures) and dipolar aprotic (*N*,*N*-dimethylformamide)[4,5] media, very interesting results have been obtained. In continuation of this work, we present here the results obtained on the electrochemical behaviour of 4-TQ in acetonitrile.

Experimental

4-(2-Thienyl)quinazoline was prepared according to the literature procedure and its purity tested by mp (65 °C), TLC, IR, and mass spectrometry.[6,7] AR(BDH) tetrabutylammonium iodide (TBAI) was used as supporting electrolyte without further purification. Acetonitrile (S. Merck) was dried by keeping it over heated anhydrous sodium sulfate for a day with intermittent shaking and the clear supernatant liquid was then distilled using all glass assembly in the presence of silver nitrate.[8] The middle fraction boiling at 82 °C was collected and stored in glass vessel painted black.[9] The purified sample had a water content of 0.04% (Karl Fischer titration). The measured specific conductance of the purified acetonitrile sample ($6.0\times10^{-8}\,\Omega^{-1}$ at 25 °C) was found to be in agreement with the reported value.[10] In the present investigation, the purification method outlined above was found to be satisfactory as shown by the absence of polarographic reduction waves in the region of potentials studied. However, in certain cases where the supporting electrolyte polarograms showed appreciable residual currents, a pre-electrolysis[11] of the distilled sample was necessary and it was carried out at a potential which is slightly positive to the decomposition potential of the supporting electrolyte.

The polarographic measurements using a three electrode system were similar to those described previously.[3] The dropping mercury electrode (d.m.e.) used in acetonitrile solution containing 0.1 M TBAI ($1\ \mathrm{M}=1\ \mathrm{mol\,dm^{-3}}$) supporting electrolyte at 55 cm height of the mercury column (height uncorrected for back pressure) had the following capillary characteristics under open circuit conditions: '*m*'= 0.6885 mg s^{-1}; '*t*'=7.1 s. The details of the cyclic voltammetric (CVM) experiments for 4-TQ reduction using hanging mercury drop electrode (HMDE) and the analysis of cyclic voltammograms for obtaining the kinetic parameters of the electrode process have been described previously.[4] All the measurements were carried out at 25 °C.

Results and Discussion

The d.c. and a.c. polarograms of 4-TQ (1.0×10^{-3} M) obtained in acetonitrile solution containing 0.1 M TBAI supporting electrolyte are shown in Fig. 1 and the corresponding polarographic data are presented in Table 1. It is seen from Fig. 1 that 4-TQ gives a single well-defined d.c. wave and the a.c. polarogram shows a single peak corresponding to the d.c. step. The well-defined wave was found to be diffusion-controlled as indicated by the linearity in the plots passing through the origin of (i) limiting currents *versus* concentration of 4-TQ and (ii) limiting

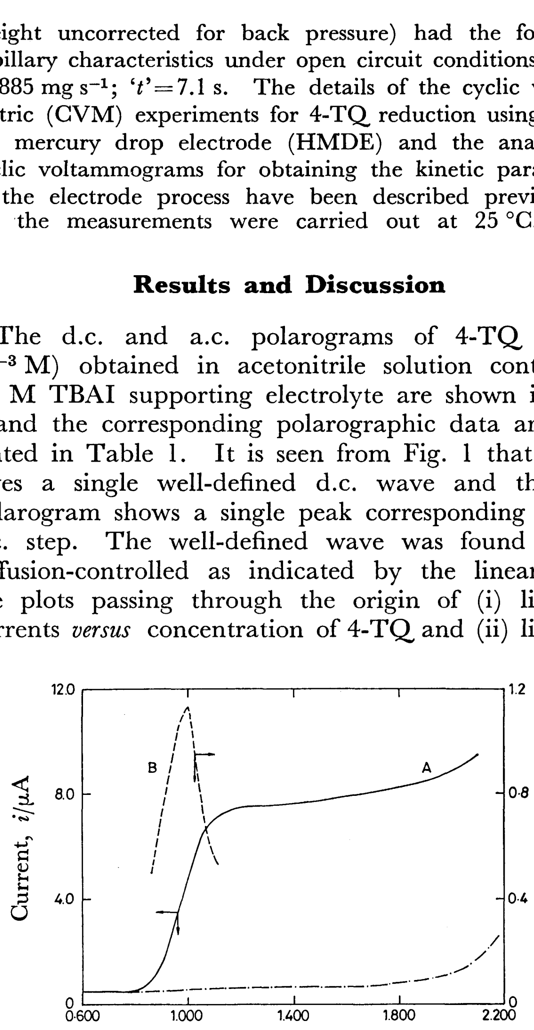

Fig. 1. D.c. Polarogram (A) and a.c. polarogram (B) of 4-TQ (1×10^{-3} M) in acetonitrile containing 0.1 M TBAI.

TABLE 1. POLAROGRAPHIC DATA FOR 4-TQ REDUCTION IN ACETONITRILE SOLUTIONS

Concentration of 4-TQ $\times10^{-3}$ / M	Limiting current i_l/μA$^{a)}$	Half-wave potential, ($-E_{1/2}$ *vs.* silver wire electrode)/V	$-(E_{3/4}-E_{1/4})$/V	Summit potential, ($-E_s$ *vs.* silver wire electrode)/V	Diffusion current constant, $I_d$$^{b)}$	$-\mathrm{d}E/\mathrm{d}\log\frac{(i_d-i)}{i}$
0.2	1.47	0.960	0.120	0.980	7.24	0.120
0.4	2.95	0.960	0.100	0.980	7.26	0.105
0.6	4.11	0.955	0.100	0.970	6.74	0.108
0.8	5.70	0.945	0.100	0.960	7.01	0.110
1.0	7.14	0.940	0.110	0.960	7.03	0.108

a) Average current. b) Corrected for the change in drop time of the d.m.e. with applied potential.

currents *versus* square root of the height of the mercury column. A slope of 0.50 in the (log i_l—log h) linear plot further confirmed the diffusion-controlled nature of the wave in acetonitrile solutions. The larger values of ($E_{3/4}-E_{1/4}$) and the slopes of the logarithmic plots[$-E$ *vs.* log $(i_d-i)/i$] for different concentrations of 4-TQ indicate irreversible nature of the wave (Table 1). This is further supported by the dependence of half-wave potential on the concentration of 4-TQ. The product of the average corrected diffusion current constant (I_d) and square root of the viscosity of acetonitrile ('η'=0.350 cP), $I_d\eta^{1/2}$ for 4-TQ reduction was calculated to be 4.17. This value is in good agreement with 4.20 reported by Wasa and Elving[12] for a two-electron reduction in acetonitrile.

The total number of electrons (n_{app}) involved in 4-TQ reduction in acetonitrile at the limiting region of the polarographic wave (−1.300 V *vs.* silver wire electrode) was calculated from microscale controlled-potential electrolysis (CPE) experiments[3] and found to be 1.97, 2.03, and 2.00 (accuracy ±0.04), respectively, for three separate experiments. Macroscale CPE experiments were not carried out due to volatility of acetonitrile.

Cyclic voltammograms of 4-TQ obtained at different sweep rates in acetonitrile solutions in the presence of 0.1 M TBAI supporting electrolyte are shown in Fig. 2. The CVM data are presented in Table 2. The cyclic voltammograms show two cathodic peaks in the forward scan and one anodic peak during the reverse scan. The first cathodic peak potential corresponds to the d.c. polarographic step and the anodic peak corresponds to the first cathodic peak. At lower sweep rates (less than 0.05 V s^{-1}, for example, at 0.008 V s^{-1}), the second cathodic and the first anodic peaks are absent and these peaks once again appear with increase in sweep rate (Fig. 2). Although a single well-defined two-electron wave is obtained in acetonitrile a *small* EPR signal observed[13] when 4-TQ in acetonitrile solution was electrolysed at the limiting region of the wave (−1.300 V *vs.* silver wire electrode) indicates single electron addition in the first step. The neutral radical of 4-TQ formed during the reduction undergoes a *fast* disproportionation (secondary) reaction[4] and the average disproportionation rate constant (k_d) in acetonitrile solution was calculated to be (2.14±0.38)×10^{-2} M^{-1} s^{-1} (Table 3). The presence of a fast second-order reaction following the first charge-transfer step is expected

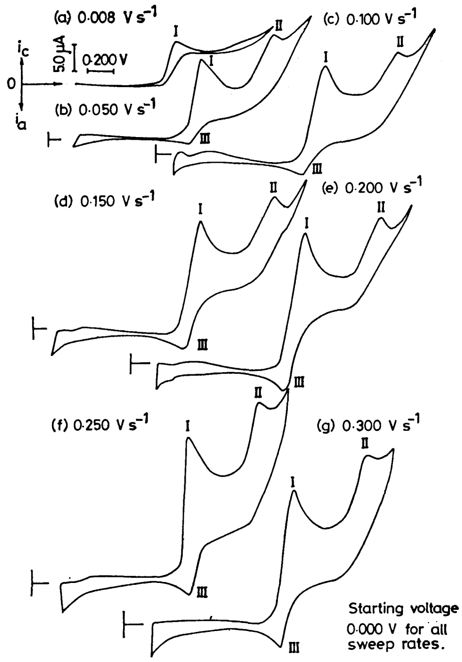

Fig. 2. Cyclic voltammograms for 4-TQ (1.0×10^{-3} M) reduction in acetonitrile containing 0.1 M TBAI at different sweep rates.

TABLE 2. CYCLIC VOLTAMMETRIC DATA FOR 4-TQ (1.0×10^{-3} M) REDUCTION IN ACETONITRILE SOLUTIONS

Sweep rate, v/V s^{-1}	Peak	i_p/μA[a)]	Peak potential, ($-E_p$ *vs.* silver wire electrode)/V	$i_p v^{-1/2} C_{ox}^{-1}$ [b)]	$(E_{p/2}-E_p)$/V
0.050	I	13.75	0.995	61.49	0.065
	II	7.50	1.490	—	—
	III	10.00	0.895	—	—
0.100	I	17.50	1.000	55.34	0.065
	II	8.50	1.495	—	—
	III	14.50	0.900	—	—
0.150	I	20.00	1.000	53.64	0.070
	II	10.25	1.150	—	—
	III	17.25	0.900	—	—
0.200	I	23.75	1.000	53.11	0.070
	II	11.75	1.500	—	—
	III	20.75	0.900	—	—
0.250	I	25.00	1.000	50.00	0.070
	II	12.25	1.510	—	—
	III	22.25	0.905	—	—
0.300	I	25.75	1.005	47.00	0.075
	II	12.75	1.520	—	—
	III	21.25	0.985	—	—

a) Cathodic peak current. b) Current function.

TABLE 3. HETEROGENEOUS CHARGE-TRANSFER AND HOMOGENEOUS DISPROPORTIONATION RATE CONSTANTS (k_s AND k_d, RESPECTIVELY) FROM CYCLIC VOLTAMMETRY

Sweep rate, v/V s^{-1}	E_p[a)]	$k_s \times 10^2$[b)] / cm s^{-1}	i_p^a/i_p^c	$\tau=(E_\lambda$[c)]$-E_{1/2})/v$	$-\log k_f C_{ox}\tau$	$k_d \times 10^2$[d)] / M^{-1} s^{-1}
0.050	0.100	0.44	0.727	14.80	0.75	1.60
0.100	0.100	0.63	0.829	7.40	1.01	1.75
0.150	0.100	0.77	0.863	4.93	1.14	2.00
0.200	0.100	0.89	0.874	3.70	1.18	2.40
0.250	0.095	1.02	0.890	2.96	1.25	2.50
0.300	0.120	0.69	0.903	2.47	1.32	2.60
		Average: 0.74±0.18				Average: 2.14±0.38

a) Difference between the anodic and cathodic peak potentials. b) $k_s=\Psi v^{1/2}/28.8$ cm s^{-1}.[18)] c) E_λ is switching potential. d) $k_d=k_f C_{ox}\tau/C_{ox}\tau$ M^{-1} s^{-1}.[19)]

to cause a shift in $E_{1/2}$ to positive values with increase in concentration of 4-TQ[14)] (Table 1). A comparison of disproportionation rate constants in DMF[4)] and acetonitrile solutions shows that in acetonitrile, the disproportionation reaction is about forty times faster than in DMF solutions. The observation of a single two-electron wave obtained under polarographic conditions is thus clear on the basis of a fast disproportionation reaction[15)] in acetonitrile.

Mechanism for 4-TQ Reduction (CEC-type) in Acetonitrile. Based on the polarographic and CPE experiments, the following mechanism is suggested for 4-TQ reduction in acetonitrile solution:

$$\text{4-TQ} + \text{H}^+ \rightleftharpoons [\text{4-TQH}]^+ \text{ (fast)},$$

$$[\text{4-TQH}]^+ + e \rightleftharpoons [\text{4-TQH}]^\cdot \text{ (first electron-transfer)},$$

$$2[\text{4-TQH}]^\cdot \longrightarrow \text{4-TQH}_2 + \text{4-TQ} \text{ ("fast" homogeneous disproportionation)}.$$

However, it may be pointed out that 4-TQ obtained in the fast homogeneous disproportionation step may undergo again single-electron reduction to give the final dihydro-4-TQ product *via* the free radical formation step. It is quite likely that the formation of the dihydro-4-TQ from 4-TQ radical also takes place through the uptake of a proton and an electron. The pre-protonation of 4-TQ in the suggested mechanism (prior to electron-transfer step) is brought out by the trace amount of water (proton donor) present in acetonitrile[16)] and this has been further evidenced by the correlation of EPR results with theoretical Hückel molecular orbital (HMO) calculations.[5)] It is also known that acetonitrile solvent itself could donate protons[17)] according to the equilibrium, $H_3C-C\equiv N \rightleftharpoons H_2C^{(-)}-C\equiv N+H^{(+)}$, since the conjugate base of acetonitrile is a resonance stabilised species. Mann also refers to the abstraction of protons from tetraalkylammonium ions.[16)]

It may be mentioned here that the mechanism suggested for 4-TQ reduction in acetonitrile solutions is similar that encountered in DMF solutions.[4)]

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