The Electrochemistry of 1-Substituted-1,4-diazaspiro[5.5]undecane-3,5-diones in Non-aqueous Media

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An investigation into the redox behaviour of a series of 1-substituted-1,4-diazaspiro[5.5]undecane-3,5-diones in non-aqueous media is reported. The main product of electrolytic oxidation is *N*-(1-aminocyclohexanecarbonyl)oxamic acid in 80% yield, while the main product of reduction is the alcohol, in 60% yield, with traces of the dimer (5%). The mechanisms of the processes are proposed and discussed.

1-Alkyl-1,4-diazaspiroalkane-3,5-dione derivatives are known to have analgesic and anticonvulsant properties[1] and structurally related compounds such as 1-ethyl-2,4-dimethyl-8-thioxo-7,9-diazaspiro[4.5]decane-6,10-diones, known medically as spirothiobarbitals, are used as hypnotics.[2]

From an electrochemical point of view these structures are interesting because they contain the sequence N–CH_2–CO–NH–CO, or a masked form of it. Furthermore, no electrochemical data has been detected in computer literature scanning. In this paper we report the redox data for a series of 1-alkyl-1,4-diazaspiroundecane-3,5-diones (**1a–e**), in non-aqueous media, in order to understand their behaviour at different solid electrodes, and to elucidate the relevant redox mechanisms.

Experimental

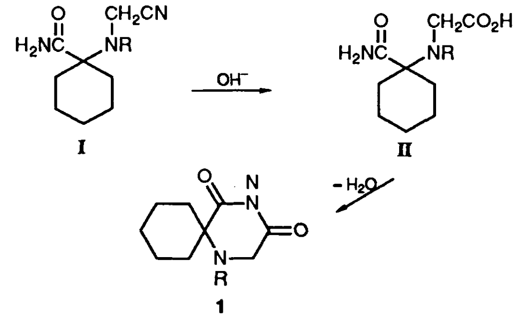
Reagents.—Benzonitrile and acetonitrile were purified by literature methods,[3,4] as were the supporting electrolytes $Bu_4N^+ClO_4^-$ (TBAP) and $LiClO_4$, which were purified by repeated recrystallization and dried before use.

Apparatus and Instruments.—Voltammetry. Voltammetric measurements were carried out with a type PCA 72C potentiostat with its potential source (scan generator VSG 72) (Bank-Electronic, Gottingen, W. Germany) together with an X-Y recorder (type Servogor XY, Metawatt, Nurnberg, Germany). A digital multimeter was used to check the applied potential (type T2201, Hartman and Braun, Germany). The working electrodes were of type 6.1204 mounted on a motor of the type 628-10 (Metrohm, Switzerland).

The electrode potential is expressed *versus* the saturated Ag/AgCl/Cl$^-$ benzonitrile electrode, which was periodically calibrated against the redox potential of the cobalticinium/cobaltocene system.[5] The standard potential of the Ag/AgCl/Cl$^-$ benzonitrile electrode against the normal hydrogen electrode (NHE) is −176 mV.[6]

Coulometry. The number of electrons transferred in the electrode processes were computed electronically with a type SS170 coulometer in conjunction with a potentioscan VSG 72 (Bank electronic, Gottingen, Germany). M.p.s are uncorrected. The IR spectra (potassium bromide) were recorded on a Pye Unicam SP-1100 spectrophotometer; ^1H NMR spectra were measured in $CDCl_3$ on a Varian EM-360 90 MHz spectrometer; chemical shifts are expressed in ppm; and elemental analyses were performed by the Microanalytical centre, Cairo University.

Organic Synthesis.—1-Alkyl-1,4-diazaspiro[5.5]undecane-3,5-diones. The general route illustrated in Scheme 1 for the synthesis of series **1a–e** begins with the alkaline hydrolysis of the 1-(*N*-alkyl-*N*-cyanomethyl)cyclohexanecarboxamide **I** to the corresponding acid **II**.



R
a Me
b Et
c $PhCH_2$
d 4-MeC_6H_4
e Ph

Scheme 1

The latter smoothly underwent cyclization, using 4 mol dm^{-3} HCl and ethylenediamine, to yield the desired products as described in the literature.[1] All compounds gave the correct C, H, N analyses and spectroscopic characteristics. M.p.s: **1a**, 115 °C (Pr^{i}OH); **1b**, 79 °C (hexane); **1c**, 130–132 °C (Pr^{i}OH); **1d**, 181–183 °C (MeOH) and **1e**, 160–163 °C (MeOH).

Controlled Potential Oxidation (CPO) of 1-(p-Tolyl)-1,4-diazaspiro[5.5]undecane-3,5-dione.—The title compound (80 mg) in CH_3CN (50 cm^3) together with $LiClO_4$ (0.1 mol dm^{-3}) was electrolysed at +1.4 V *vs.* Ag/AgCl/Cl$^-$ on a Pt gauze anode. The progress of electrolysis was followed by the periodic recording of DC-curves. The anode was periodically removed from the cell, sprayed with pure acetone, heated in a direct flame, cooled and replaced in the cell. The maximum recorded current was 1.5 mA, which dropped to 0.2 mA after the uptake of two electrons per molecule. At this stage the electrolysis was stopped and the cell was disconnected from the circuit. The mixture was removed and solvent was evaporated under reduced pressure. The residue was treated with $CHCl_3$, washed several times and filtered (to remove $LiClO_4$). The filtrate was dried *in vacuo*, and treated with CH_3CN when a brown precipitate formed. The solvent was decanted off, and the product dried. This substance, obtained in 80% yield, was identified as *N*-(*p*-tolylaminocyclohexanecarbonyl)oxamic acid, m.p. 65 °C; *m/z* 304 (M^+), 287 (M − 17), 259 (M − 45), 216, 187, 149 and 144; ν/cm^{-1} (KBr), 3420 (OH, CO_2H), 3230 (NH str), 3085 and 3020 (CH str, CH_2 cyclic), 2930 and 2860 (CH str, CH_3), 1725 (CO, CONHCO), 1700 (CO, CO_2H) and

Table 1 DC-Voltammetric data for compounds **1a–e** in benzonitrile

	Electrode type	Reduction $E_{\frac{1}{2}}$/mV	Reduction $E_{\frac{1}{4}} - E_{\frac{3}{4}}$/mV	Reduction S^{a}	Reduction αn	Oxidation $E_{\frac{1}{2}}$/mV	Oxidation $E_{\frac{3}{4}} - E_{\frac{1}{4}}$/mV	Oxidation S	Oxidation αn
1a	Pt	−1200	320	240	1.231×10^{-4}	1460	190	205	1.435×10^{-4}
	Au	−730	120	114	2.585×10^{-4}	1940	200	200	1.477×10^{-4}
	C	−1540	280	339	8.708×10^{-5}	1640	300	350	8.442×10^{-5}
1b	Pt	−600	140	187	1.576×10^{-4}	1220	290	193	1.527×10^{-4}
	Au	−740	180	222	1.329×10^{-4}	1820	200	214	1.378×10^{-4}
	C	−920	262	593	4.985×10^{-5}	1840	180	266	1.108×10^{-4}
1c	Pt	−1360	380	174	1.699×10^{-4}	1640	230	197	1.500×10^{-4}
	Au	−700	260	249	1.188×10^{-4}	1910	200	196	1.504×10^{-4}
	C	−1350	340	335	8.820×10^{-5}	1840	330	300	9.850×10^{-5}
1d	Pt	−700	200	222	1.329×10^{-4}	680	240	240	1.231×10^{-4}
	Au	−760	230	240	1.231×10^{-4}	1450	240	285	1.034×10^{-4}
	C	−1000	330	343	8.616×10^{-5}	1780	210	212	1.390×10^{-4}
1e	Pt	−780	220	250	1.182×10^{-4}	1570	200	222	1.329×10^{-4}
	Au	−880	200	250	1.182×10^{-4}	1600	210	266	1.108×10^{-4}
	C	−1040	340	240	1.229×10^{-4}	1570	140	153	1.921×10^{-4}

^{a} $S = d\log(i_l - i)/i$.

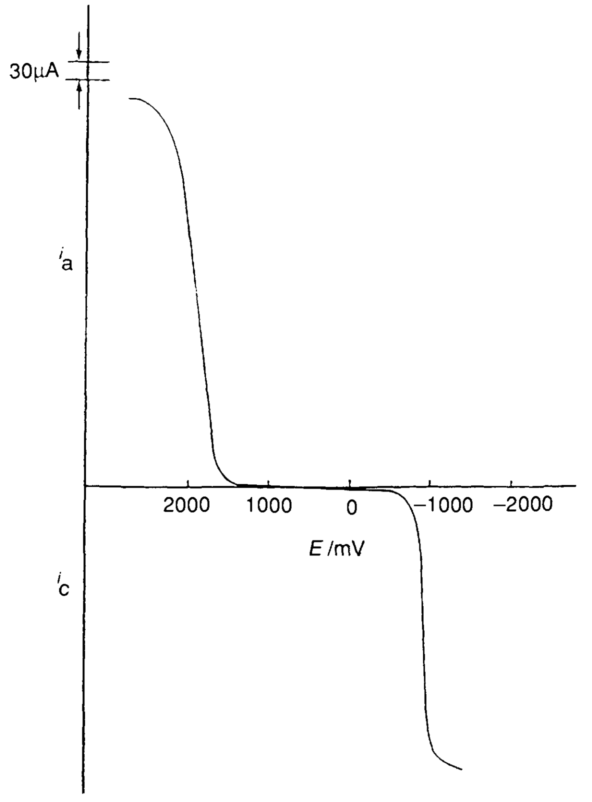


Fig. 1 DC-voltammogram of **1a** (0.1 mol dm^{-3}) in benzonitrile containing 1 mol dm^{-3} Bu_4NClO_4 at Pt-electrode

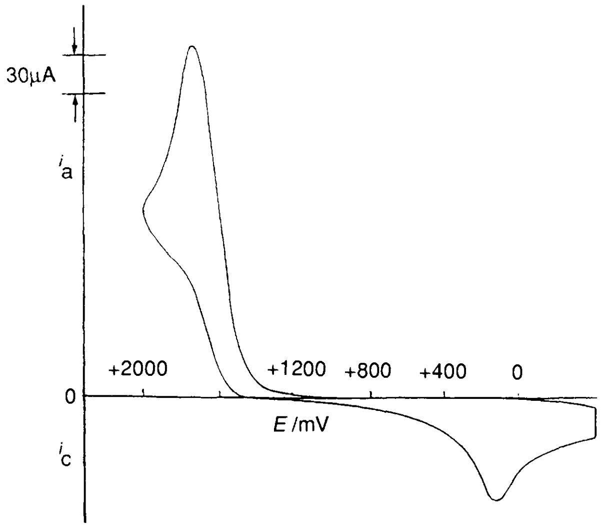


Fig. 2 Oxidation CV of **1a** (0.1 mol dm^{-3}) in benzonitrile containing 1 mol dm^{-3} Bu_4NClO_4 at Pt-electrode (scan rate 100 mV s^{-1})

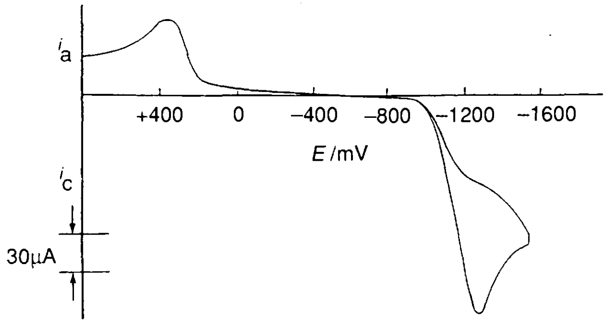


Fig. 3 Reduction CV of **1a** (0.1 mol dm^{-3}) in benzonitrile containing 1 mol dm^{-3} Bu_4NClO_4 at Pt-electrode (scan rate 100 mV s^{-1})

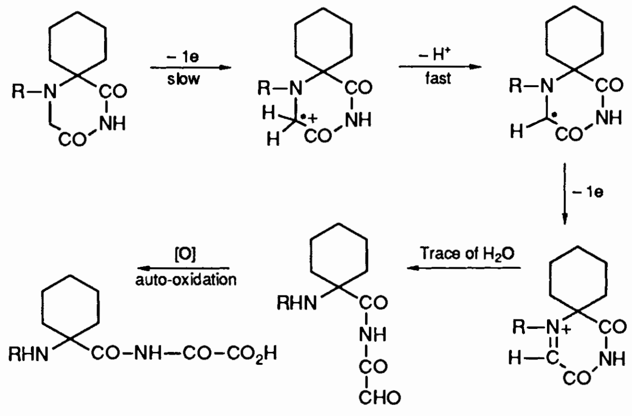
1520 (NH def); $\delta_H(CDCl_3)$ 8.2 (br, 1 H, CONHCO), 6.9–7.4 (m, 4 H, C_6H_4), 2.4 (s, 3 H, CH_3) and 1–2 (m, 10 H, $5CH_2$).

Controlled Potential Reduction (*CPR*) *of* 1-*Phenyl*-1,4-*diazaspiro*[5.5]*undecane*-3,5-*dione*.—The title compound (350 mg) in CH_3CN (50 cm^3), together with $LiClO_4$ (0.1 mol dm^{-3}) was electrolysed at −1.6 V *vs.* Ag/AgCl/Cl$^-$ on a Pt gauze cathode. The progress of electrolysis was followed coulometrically. The current dropped from its maximum value (1.3 mA) to 0.2 mA after the passage of two electrons per molecule. A white precipitate appeared in the cell. The cell was then disconnected from the circuit and the precipitate was removed by filtration, dried and chromatographed by TLC ($CHCl_3$–EtOH, 99:1). The band at R_f 0.107 (under UV light) was removed and the compound was extracted into EtOH and identified as the dimer (yield 5%), m.p. 195 °C; IR, same pattern as starting material, with a broad OH band at 3422 cm^{-1}; *m/z* 518 (M^+) and 259 (M − 259). The remaining solvent was removed under reduced pressure and the residue was treated with $CHCl_3$ and filtered off. Solvent was removed under reduced pressure and the final residue was treated with light petroleum (b.p. 40–60 °C) and white, yellowish crystals were isolated, m.p. 105–108 °C (yield *ca.* 70%). This compound was identified as either 1-phenyl-5-hydroxy-1,4-diazabicyclo[5.5.0]undecane-3-one, or 1-phenyl-3-hydroxy-1,4-diazabicyclo[5.5.0]undecane-3-one, since the spectral data obtained did not help in deciding which of the carbonyl groups in positions 3 and 5 was transformed to an alcohol; ν/cm^{-1} (KBr), 3450 (OH str), 2976 and 2886 (CH str), and 1640 (CN); δ_H 7–7.6 (m, 5 H, C_6H_5) and 1–2 (m, 10 H, $5CH_2$); *m/z* 260 M$^+$, 243 (M − 17) and 183 (M − 77).

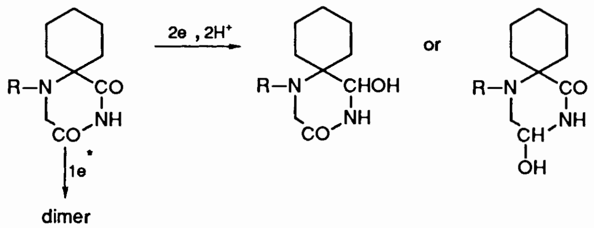
Results and Discussion

The redox characteristics of compounds **1a–e** in benzonitrile containing 0.1 mol dm^{-3} $LiClO_4$ at different solid electrodes, namely Pt, Au and glassy C, were extensively studied. DC-voltammetric data are compiled in Table 1. Fig. 1 illustrates the typical representative *i–E* curve, while Figs. 2 and 3 show the corresponding cyclic voltammograms for both oxidation and reduction processes, respectively. It is clear from the data in Table 1 that these compounds are oxidized and reduced *via* a single, irreversible two-electron wave. The irreversibility of the electrode process is clearly observed from the shape of the cyclic voltammograms.[7] For further confirmation of the irreversible nature, logarithmic analysis[8] and $E_{\frac{3}{4}} - E_{\frac{1}{4}}$ calculations[9] were undertaken. The values obtained, given in Table 1, indicate that the process is completely irreversible. As is obvious from the data obtained the redox behaviour of this series of compounds on different solid electrodes is very similar, as no drastic change in characteristic values is observed. On the other hand, it is important to mention that CPE experiments in benzonitrile were subject to several experimental problems, and it was impossible to identify or separate any electrolysis product from either redox experiment, since the controlled value of the potential was very high, and affected benzonitrile itself. For this reason, in large scale preparative electrolysis, we used acetonitrile containing $LiClO_4$, and the working electrode was platinum gauze. This is because, on working with a graphite electrode, adsorption of the starting compound on the surface of the graphite blocked the electrode, causing high resistance and a simultaneous drop in current efficiency. From the data we have collected and from the isolation and identification of the electrolysis products, Schemes 2 and 3 have been suggested for the redox mechanism.

The electrooxidation process follows the ECEC pattern as illustrated in Scheme 2. That only a single two-electron wave is observed can be explained by the fact that the individual energies of the single-electron uptakes are very close to each other, and amalgamate to form one wave. The appearance of a small peak in the reverse cycle of oxidation at very low positive potential is characteristic of the reduction of protons which are lost during the oxidation process. This peak vanishes on addition of solid sodium carbonate.[10] The acid, and not the aldehyde, is the separated product of large scale electrolysis, because the aldehyde is air-oxidized during the separation techniques.



Scheme 2



Scheme 3

On the other hand, the separated product of CPR in good yield (*ca.* 60%) is the alcohol, while the dimer could be considered to arise from a side reaction due to its very low yield (*ca.* 5%). This can be explained by the fact that the dianion formed during the two-electron uptake would be a strong enough base to abstract protons from the solvent to give the corresponding alcohol,[11,12] or, in other words, the consecutive electron uptake is fast enough for only a very small amount of the first-electron uptake to form a dimer (Scheme 3). Finally, the abstraction of protons in both Schemes 2 and 3 is from moisture present in acetonitrile and not from disproportionation reactions, since CV-curves did not indicate such reactions.[7]

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References

1 M. Nabil Aboul-Enein and A. A. El-Azzouny, *Acta Pharm. Suec.*, 1986, **23**, 107.
2 *The Merck Index*, Merck and Co. Inc., USA, 10th edn., 1983, p. 8607, no. 8611.
3 G. Abou-Elenien, N. Ismail, J. Reser and K. Wallenfels, *Liebigs Ann. Chem.*, 1981, 1598.
4 W. Summermann, Ph.D. Thesis, Freiburg, Germany, 1970, p. 10.
5 H. M. Koeppm, H. Wendt and H. Strehlow, *Z. Electrochem.*, 1960, **64**, 483.
6 G. Wilkinson, *J. Am. Chem. Soc.*, 1952, **74**, 6148.
7 J. Heinze, *Angew. Chem., Int. Ed. Engl.*, 1984, **23 11**, 831.
8 J. Heyrovsky and J. Kuta, *Principles of Polarography*, The Czechoslovak Academy, 1965, p. 129.
9 J. Tomes, *Collect. Czech Chem. Commun.*, 1935, **7**, 198.
10 G. Cauquis, H. M. Fahmy, G. Pierre and M. H. Elnagdi, *Electrochem. Acta*, 1979, **24**, 391.
11 J. L. Sadler and A. J. Bard, *J. Am. Chem. Soc.*, 1968, **90**, 1979.
12 K. G. Boto and F. G. Thomas, *Aust. J. Chem.*, 1973, **26**, 125.
13 A. J. Fry, *Synthetic Organic Electrochemistry*, Hayer, New York, 1972, p. 88.

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