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Electrochemical and Spectroscopic Studies of Pyridazine Derivatives

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Abstract

This work reports on cyclic voltammetry and spectroscopic UV-Vis investigations of some pyridazine derivatives *1-8* in dimethylformamide. In the electrochemical study, monochlorinated pyridazines *2-8* exhibit two reductions but in the case of dichlorinated derivative *1* an additional wave is seen for the reduction of the second carbon-chloride bond. The electronic absorption spectra display an intramolecular charge transfer band π-π* in the UV region of which depend substantially on the nature of both donor and acceptor moieties. These results indicate the π-electron delocalization in the conjugated system.

***Keywords*:** pyridazines; electrochemistry; electronic spectra; donor-π-bridge-acceptor systems.

Introduction

Several functionalized pyridazines exhibit important biological activity such as: antibacterial, antibiotic, antitumour, antiviral and antidiabetes [1]. The

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derivatives of pyridazines could also find application as ligands in supramolecular chemistry and in metallic complexes which exhibit catalytic properties [2-3]. These compounds could also be used as semi-conductor materials and as materials with non-linear optical properties [4].

Dipolar push-pull chromophores likely constitute the widest class of compounds investigated for their nonlinear optical (NLO) properties [5-6]. These push-pull NLO-phores are basically constituted by an electron-donor and an electron-acceptor as groups which interact through a π-conjugated spacer. It is already well-known that the hyperpolarizability (β), which characterizes the molecular NLO efficiency, depends on the strength of the donor and acceptor groups, on the extent of the π-conjugated path and, for conjugating spacers based on aromatic units, on the resonance stabilization energy of the aromatic system [7]. Studies demonstrate that heteroaromatic rings play a subtle role in influencing the NLO response properties of donor-acceptor compounds. While the aromaticity of heteroaromatics affects electronic transmissions between donor and acceptor substituents, the electron-excessive or electron-deficient nature of the heterocyclic ring systems also plays a major role in determining the overall electron-donating and accepting ability of the substituents: electron-excessive heterocycles act as auxiliary donors and electron-deficient heterocycles act as auxiliary acceptors [4-5]. Thus, attaching a strong acceptor to an electron-deficient heteroaromatic, such as pyridazines, will yield chromophores with significantly enhanced NLO responses [5].

In this paper we describe the effect of different groups R (donating or acceptor) in the electrochemical and spectroscopic studies of 3,6-disubstituted pyridazine derivatives. Mechanistic aspects of the reduction of these compounds are discussed on the basis of cyclic voltammetric data.

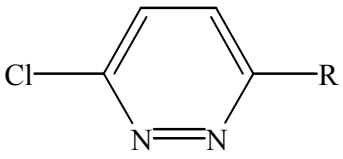
Experimental

Voltammetric measurements were performed using a potentiostat/galvanostat AUTOLAB /PSTAT 12 with the low current module ECD from ECO-CHEMIE and the data analysis processed by the General Purpose Electrochemical System

software package also from ECO-CHEMIE. Three electrode-two compartment cells equipped with vitreous carbon-disc working electrodes, a platinum-wire secondary electrode and a silver-wire pseudo-reference electrode were employed for cyclic voltammetric measurements. The concentrations of the compounds were typically 1-2 mmol dm^{-3} and 0.2 mol dm^{-3} $[NBu_4][BF_4]$ was used as the supporting electrolyte in dimethylformamide (DMF).

UV-Vis absorption spectra were obtained using a Shimadzu UV/2501PC spectrophotometer.

The chemical structures and the numbers of the pyridazine derivatives studied in this article are depicted in Fig. 1.



1-8

Compound	R
1	Cl
2	OMe
3	OEt
4	NH_2
5	NEt_2
6	piperidyl
7	4-cyanophenylamino
8	4-nitrophenylamino

Figure 1. Chemical structure of the 3,6-disubstituted pyridazines studied in this work.

The 3,6-dichloropyridazine *1* were purchased from Aldrich and used as received. The synthesis of 3,6-disubstituted pyridazine derivatives *2-8* has been described elsewhere [8]. These compounds were synthesized from 3,6-dichloropyridazine *1* through a nucleophilic aromatic substitution.

Results and Discussion

Electrochemistry

Table 1 provides cyclic voltammetric data obtained with a carbon electrode in DMF containing $[NBu_4][BF_4]$.

Table 1. Electrochemical data for pyridazine derivatives *1-8*.

	Reduction[a]			Oxidation[a]
Compound	$-^1E_p$/V	$-^2E_p$/V	Δ^2E_p/mV	E_p
1	1.99	2.24	-	**-**
2	2.28	2.64	-	**-**
3	2.28	2.64	-	**-**
4	2.47	2.80	-	**-**
5	2.46	2.80	-	**-**
6	2.45	2.79	-	**0.90**
7	2.15	2.26	75	**0.93**
8	**1.64**	**2.03**	**70**	**0.93**

[a] Measurements made in DMF containing 0.1-0.2 mol dm^{-3} $[NBu_4][BF_4]$ as base electrolyte at a carbon working electrode with a scan rate of 100 mV s^{-1}. Ferrocene was added as an internal standard at the end of each measurement, and all E_p values are quoted in volts *vs*. the ferrocene-ferrocenium couple.

Fig. 2 shows cyclic voltammograms for the reduction of pyridazine derivatives *1, 4* and *8*, at a carbon electrode in DMF containing 0.2 mol dm^{-3} [N Bu_4][BF_4] recorded at a scan rate of 100 mV s^{-1}. The reduction of 3,6-dichloropyridazine *1* (Fig. 2a) shows three well defined cathodic peaks; the first two reduction waves are due to the sequential cleavage of the two carbon-chlorine bonds, and the third wave arises from the reduction of pyridazine [9]. The cyclic voltammogram for the reduction of 3-amino-6-chloropyridazine *4* (Fig. 2b) gives two cathodic peaks and an anodic peak: the first cathodic wave is assignable to reductive cleavage of carbon-chlorine bond and the second cathodic peak is indeed due to the reduction of 3-aminopyridazine. Under the same experimental conditions, the cyclic voltametric behaviour of 3-chloro-6-(4´-nitroanilino)pyridazine *8* depicted in Fig. 2c is similar to that of 3-amino-6-chloropyridazine *4* but the third peak attributed of 3-(4´-nitroanilino)pyridazine is reversible.

Mechanistic of the reduction of chlorinated pyridazines

There is considerable similarity between the values obtained for the reductions of the mono- and dichloro pyridazines and those seen in the reductions of 2-

bromothiazol [10] and of mono- and dihalopyrimidines [11]. According, it is reasonable to propose a mechanistic scheme for the reductive cleavage of chlorinated pyridazines that resembles the processes invoked to explain the behaviour of those compounds previously studied.

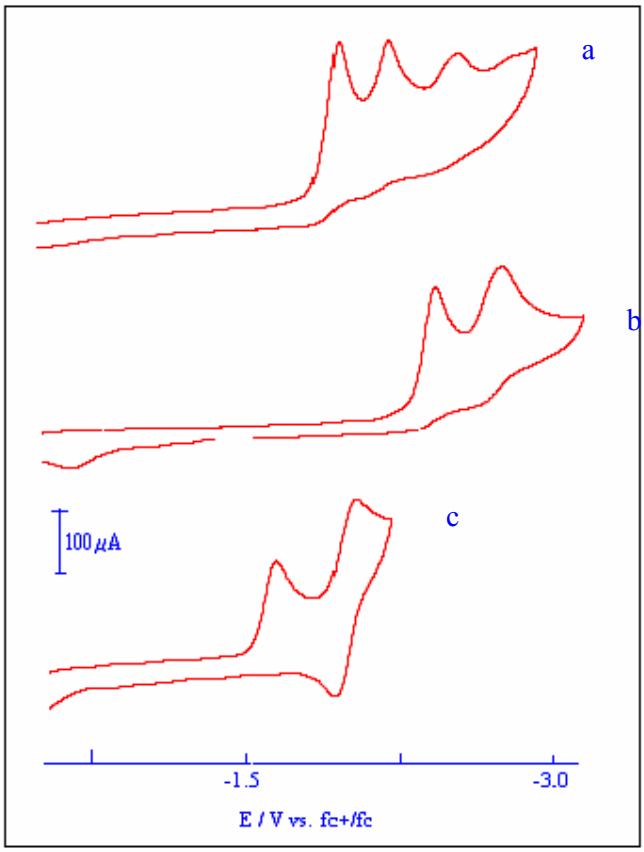
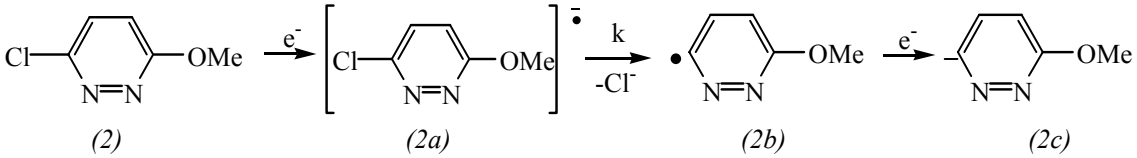


Figure 2. Cyclic voltammograms of 3,6-dichloropyridazine *1* (a), 3-amino-6-chloropyridazine *4* (b) and 3-chloro-6-(4′-nitroanilino)pyridazine *8* (c). Recorded in DMF – 0.2 mol dm^{-3} $[NBu_4][BF_4]$ at a vitreous carbon electrode, scan rate 100 mV s^{-1}, potential in V *vs.* fc^+/fc.

In the reduction of 3-chloro-6-methoxypyridazine *2* at a carbon electrode in DMF, we have the addition of one electron to yield a short-lived radical-anion *2a*, from which the chloride ion is expelled to give the 3-methoxypyridazinyl radical *2b* (Scheme 1).

This radical *2b* can be reduced to the 6-methoxypyridazenyl ion *2c* directly at the cathode (ECE process) or homogeneously by *2a* (DISP process): *2a* + *2b* ↔ *2*

+ *2c* after which *2c* can be protonated by the medium (supporting electrolyte or solvent) to yield 3-methoxypyridazine.



Scheme 1. Reduction of 3-chloro-6-methoxypyridazine at a carbon electrode in DMF.

UV-visible study

The UV-Vis absorption spectra were obtained for pyridazine derivatives in acetonitrile (Table 2).

Table 2. Electronic spectral data for pyridazine derivatives *1-8*.

Compound	λ_{max}/nm[a]	ε/dm^{3}mol^{-1}cm^{-1}	hν_{ICT}/eV
1	273.0	10425	4.54
2	278.5	19820	4.45
3	279.5	19050	4.44
4	239.0	16018	5.19
5	259.5	16695	4.78
6	260.0	18713	4.77
7	298.0	29412	4.16
8	363.5	24974	3.41

[a] Measured in acetonitrile.

The influence of the degree of conjugation between the substituted end groups along the conjugated bridge is demonstrated in Fig. 3 by comparison of the absorption maxima for 3,6-dichloropyridazine *1* (λ_{max} = 273.0 nm), 3-chloro-6-methoxypyridazine *2* (λ_{max} = 278.5 nm), and 3-(4′-nitroanilino)-6-chloropyridazine *8* (λ_{max} = 363,5 nm). The intramolecular charge transfer (ICT)

and absortivity coefficient (ε) depend substantially on the nature of the acceptor moieties.

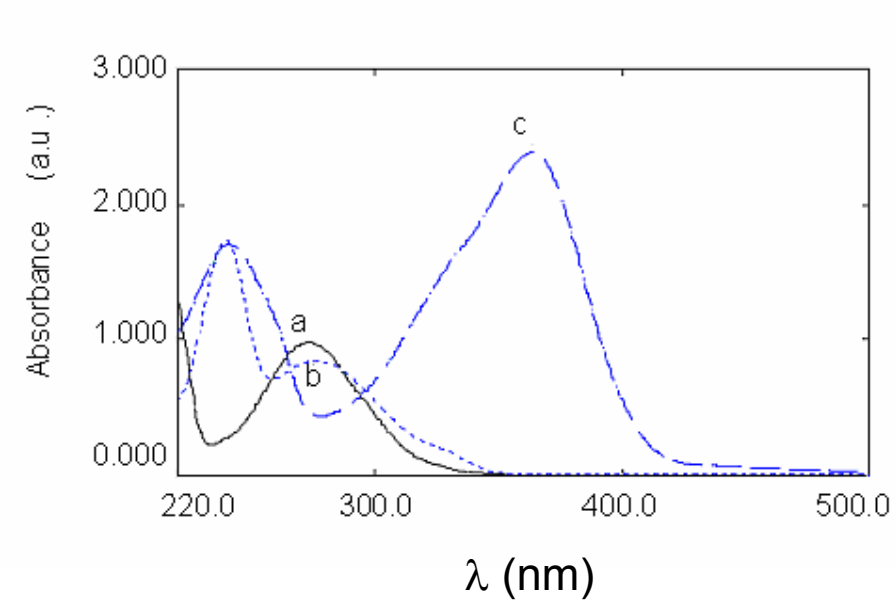


Figure 3. UV-Vis spectra of 3,6-dichloropyridazine *1* (a), 3-chloro-6-methoxypyridazine *2* (b) and 3-chloro-6-(4′-nitroanilino)pyridazine (c), recorded in acetonitrile, demonstrating the electron-withdrawing effect of the acceptor end group on absorption maxima.

Final Comments

In this work we report the electrochemical and the spectroscopic UV-Vis properties of a series of 3,6-disubstituted pyridazine derivatives.

Cyclic voltammogram for 3,6-dichloropyridazine exhibits three cathodic waves, whereas that for 3-chloro-6-substituted pyridazine shows two cathodic waves, arising from sequential cleavage of carbon-chloride bonds as well as the reduction of pyridazine.

The trends observed for the redox potentials and λ_{max} of the 3,6-disubstituted pyridazine derivatives are dependent on the donor/acceptor groups. The comparison of data for the 4′-cyano and 4′-nitroanilino derivatives, *7-8*, with the other compounds *1-6*, reveals that the last ones provide a more efficient delocalization.

Acknowledgements

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