

Voltammetric Behaviour of Oxa and Thiadiazole
Substituted 5-Nitroimidazole Compounds.

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Several authors demonstrated a high efficiency of Megazol (Fig.1) against *T.cruzi* (1,2). The exact nature of its pharmacological mode of action is unknown but there are strong evidences that the reduction of megazol is key in that mechanism. The single electron reduction of megazol by NADPH :cytochrome P-450 reductase, by rat liver as well as by trypanosome microsomes was confirmed by ESR experiments (3). Considering the similarity between the electrochemical reactions with the enzymatic ones, the knowledge of the mechanism of electroreduction could be a support on the mechanism of action. Only one previous work (4) related to the polarographic behavior of megazol have been informed. In this work we study the voltammetric behaviour of megazol and its oxadiazole substituted related compound GC-284 (Fig.1) with the aim to investigate how the change of O by S in the diazole moiety affects the reduction ability of the nitroimidazole group.

The electrochemical study of megazol and GC-284 was carried out in protic media (ethanol : Britton Robinson Buffer/30:70) and KCl as supporting electrolyte. Electrochemical experiments, differential pulse polarography (DPP), fast polarography (TP), cyclic voltammetry (CV), chronocoulometry and differential pulse voltammetry (DPV) were performed with a totally automated BAS CV-50W voltammetric analyzer. A dropping mercury electrode (DME) was used for polarographic experiments as working electrode. A glassy carbon electrode (GCE) was used for DPV and CV and a hanging mercury drop electrode was also used for CV. Chronocoulometric experiments were performed on GCE.

Both compounds were polarographically reducible on the mercury electrode producing two well-resolved peaks by DPP (Fig.2). The peak at -240 mV or -400 mV, at pH 6, for megazol and GC-284, respectively, corresponds to the four-electron reduction of the nitro group. The peaks appearing at higher cathodic potentials are due to the reduction of the thiadiazole or oxadiazole moieties in megazol and GC-284, respectively. The potential peak due to the nitro group reduction for both compounds was strongly dependent with the pH solution and megazol was more easily reduced than gC-284 in all the pH range. In strong alkaline media (pH>9) the nitro reduction was clearly different between both compounds (Fig. 3). In the case of GC-284 compound a couple due to the $\text{ArNO}_2 / \text{ArNO}_2^{\bullet-}$ redox pair was observed. By studying this couple in isolation we can observe that the current ratio change with the sweep rate according to an EC mechanism(Fig.4). Furthermore we have obtained a k_2 value of $1556.4 \text{ M}^{-1} \text{ s}^{-1}$ for the chemical step.

References

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Acknowledgements

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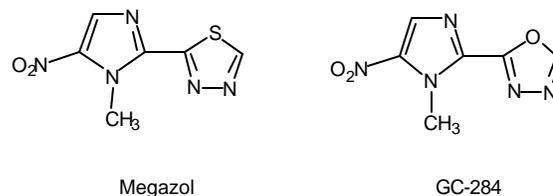


Fig. 1.- Molecular structures of 5-nitroimidazole compounds.

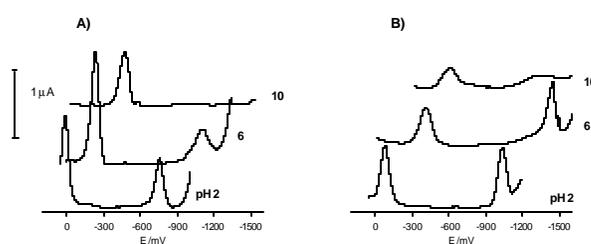


Fig. 2.- DP Polarograms of A) Megazol and B) GC-284 at different pHs in protic media

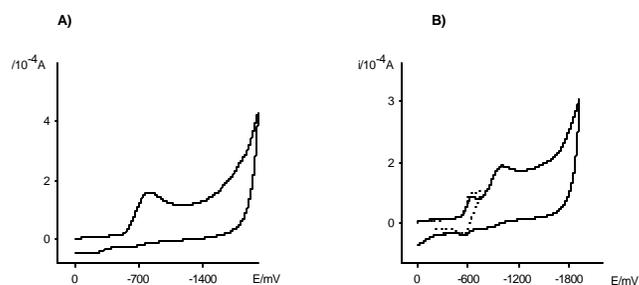


Fig. 3.- Cyclic voltammograms of A)Megazol and B) GC-284 on glassy carbon electrode at pH 12, V=1 V/s

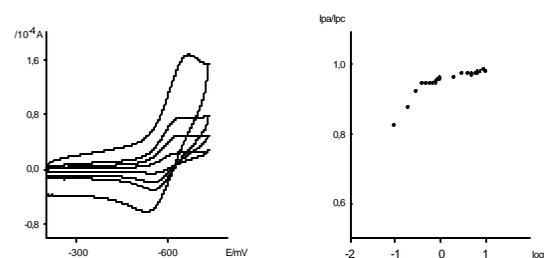


Fig. 4.- Cyclic voltammograms of GC-284 in protic media pH 12, at different sweep rates: 1.2, 1.5, 1 and 5 V/s