Electrochemical Reduction of Pyrazolo [5,1-c] Triazine

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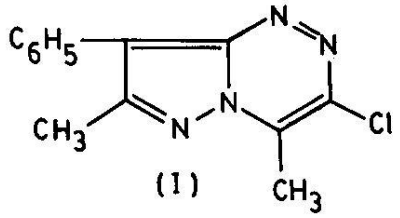
Summary: The pyrazolo [5,1-c] triazine derivative (1) is electochemically reduced via a two electron process to give the corresponding 3,4-dihydro derivative (2), CPE was carried out and the resulting product was identified.

Introduction

Interest in the chemistry of condensed pyrazoles has recently been revived. Several condensed pyrazoles have shown interesting activities as CAMP-phosphodiasterase inhibitors and as antipyritic drugs [1-4]. Recently, a comprehensive paper [5] on the electrochemical reduction of pyrazolo [1,5-a] pyrimidine- 7-amines in an acidic buffered hydroorganic solution (50 % CH_3CN, pH 1.15) has been reported. In the present work, we wish to report the electroreduction of 6-chloro-2,7-dimethyl-3- phenylpyrazolo [5,1-c] 1,2,4-triazine (I), in alcoholic aqueous media. This compound was synthesized from 5-amino-3-methyl-4-phenylprya zole according to a previously reported procedure (m.p. 112°C, yield 90% orange crystals) [6].



(I)

Experimental

i-E curves were recorded with a potentioscan Wenking (POS73) in conjunction with an X-Y recorded (PL 3) JJ instruments. The capillary characteristic in H_2O open circuit are:

$t = 2.7$ s drop^{-1}, m = 1.3 mg s^{-1} at h = 55 cm.

Cyclic voltammetry was carried out in 50% by volume alcoholic aqueous solutions with varying scan rates 50-800 mVs^{-1}. All experiments were carried out at 25 ± 2°C. A conventional three electrode system consisting of Pt (auxiliary), SCE (reference) and the DME or HDME (as working electrode) was used. The $E_{1/2}$ values were measured graphically with an accuracy of ± 0.005 V. The pH measurements were done with a digital pH-meter (Ministis type 5000. Tacussel). Details of polarographic measurements are as previously reported [7]. Britton-Robinson buffers [8] were used as supporting electrolyte.

Controlled Potential Electrolysis (CPE) and Identification of the Resulting Compounds

An H type cell was used. In the first compartment, a 250 ml mixture of 60-% EtOH and 40% 2N HCl were introduced. In the electrolysis compartment, 250 ml of the same mixture with 100 mg of compound was used. The potential was fixed at -0.5 V vs SCE. After complete electrolysis, the obtained colourless solution was neutralized and partially evaporated to half of its original volume. The precipitated product was filtered and washed with water several times. The obtained product (yield 25-30 %) has the following characteristic: mp 75°C. IR ν (cm^{-1}): 3400 (NH), 2960, 2920, (CH_3 and CH_2). MS (m/z) 271, 195, 149, 137 and 115.

Results and Discussion

The polarographic i-E curves of 2x10^{-4}M of 1 in 40% by volume ethanolic buffers revealed one well defined wave throughout the whole pH range. The varation of $E_{1/2}$ and i_l with increase of pH is illustrated in Fig. 1. As is clear this behaviour recalls the typical reduction pattern of an aromatic azo compound [9-11]. The shift of $E_{1/2}$ with increase of pH gives a straight line which can be

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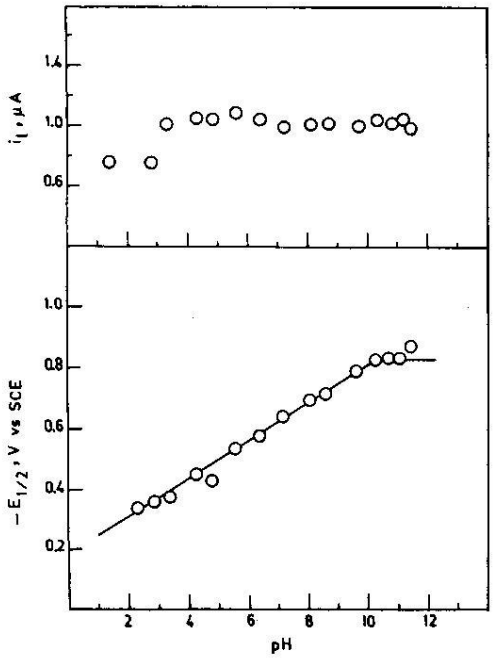


Fig.1: pH-Dependence of $E_{1/2}$ and i_l values for compound 1.

described by $E_{1/2}$ = -0.18-0.064 pH. It has to be mentioned out that the limiting current is pH independent and its value corresponds to a typical 2 electron reduction process. Logarithmic analysis at different pH values yielded slopes of 0.037 to 0.032 indicating that the process is reversible in nature. Also, the follow up electolysis experiments in a period of time of about 140 minutes showed the formation of the hydrazo compound which was a further confirmation of the reversibility of this process. For further confirmation, the cyclic voltammograms of $5x10^{-4}$M solutions of compound (1) in three different media (2N HCl, pH 8 and pH 11) using a HDME were run and inspected, as illustrated in Fig. 2, the process is reversible in nature for pH < 8. At pH 9 i.e. in highly alkaline media such as pH 11, the anodic peak is missing at low scan rate ca. 50 mV/sec and appears at high scan rate as illustrated in Fig. 2.

A relation between i_{pa}/i_{pc} versus scan rate is given in Fig. 3, the plots show that the electrochemical processes up till pH 8 are reversible in nature predicting mechanistic pattern of scheme I which is a reversible preprotonation of the molecule followed by a reversible uptake of two electrons [12] followed by a chemical reaction. On the other hand the relation at pH 11 indicates a reversible uptake of electrons followed by irreversible chemical reaction occurring on the hydrazo form

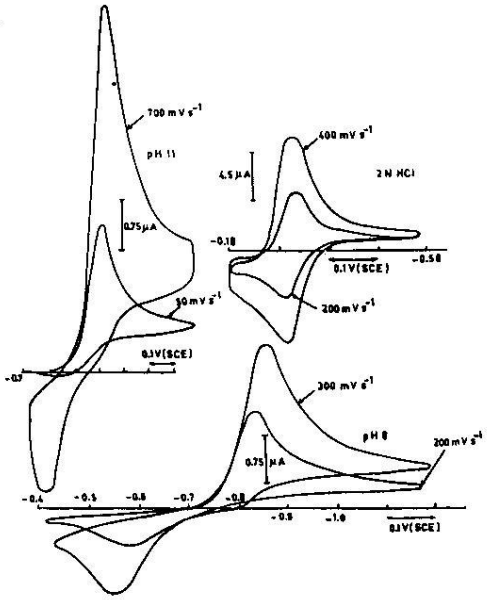


Fig.2: Typical cyclic voltammograms for compound 1. pH values, scales and scan rates are given on the plots.

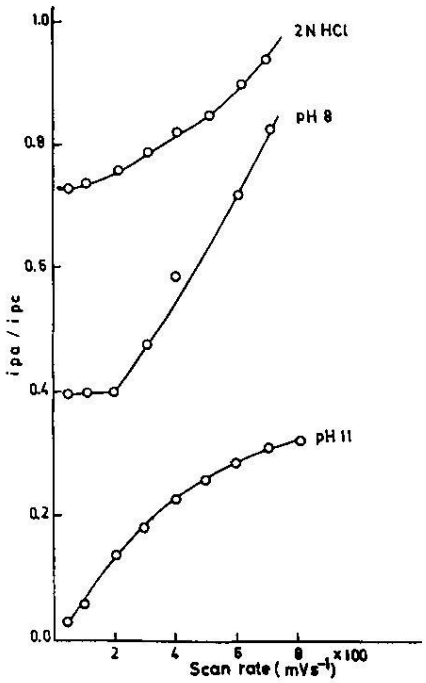
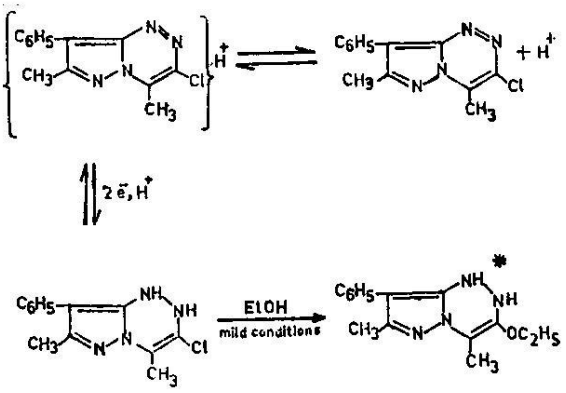


Fig. 3: Plots of the ratio of anodic to cathodic peak currents (ipa/ipc) as a function of scan rate.

such as a chemical rearrangement of the structure or alkaline hydrolysis etc. Finally, the separated product was 6-ethoxy-2,7-dimethyl-4,5- dihydro-3-phenylpyrazolo [5,1-c] 1,2,4-triazine (2). This compound could only be formed through ethoxylation during its chemical separation. The reaction of vinyl chlorocompound with ethanol in faint basic media is well known reaction.

Thus the two electron reduction could be formulated as follows:



Separated and Identified compound.

This mechanism is compatible with the obtained results which indicate that the compound is reduced in the mono-protonated form, since the slope 64 mV is an indication that one proton is involved according to Mairnovskii's equation [13], ($E_{1/2}$ -pH relation), also the mass spectra of the obtained product is in accordance with this scheme since the total mass was 271.

Finally it is important to mention that a smass of m/z 271 indicates that Cl substitution with OC_2H_5 group occurred during the process of electrochemical reaction, similar substitution is well known and documented in molecules containing the pyrazolo ring [14].

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