Asian Journal of Chemistry Vol. 19, No. 4 (2007), 3221-3227

Electrochemical Behaviour of 5-(Furan-2-yl)-4-(*p*-tolyl)-2,4-dihydro-1,2,4-triazole-3-thione by Using Glassy Carbon Electrode

YUSUF DILGIN*, AHMET CANSIZ†, AHMET ÇETIN†, PELIN KUTULAY†,
AYHAN ORAL and SELAHATTIN YILMAZ
Department of Chemistry, Faculty of Science & Art
Çanakkale Onsekiz Mart University, 17100 Canakkale, Turkey
Fax: (90)(286)2180533; Tel.: (90)(286)2180018/1812
E-mail: ydilgin@comu.edu.tr; ydilgin@yahoo.com

The electrochemical study of a thiotriazole compound, 5-(furan-2-yl)-4-(*p*-tolyl)-2,4-dihydro-1,2,4-triazole-3-thione (TTA) was performed by cyclic voltammetry (CV) and differential pulse voltammetry (DPV) using glassy carbon electrode (GCE) as working electrode and an Ag/AgCl reference electrode. The dependence of the current on pH and scan rate was investigated in the Britton Robinson Buffer. The best results for electrooxidation of TTA were obtained in basic media (pH 11.0 containing 5 % DMSO). This compound display one irreversible oxidation peak, which is attributed to a dimerization process involving the formation disulphide derivative.

Key Words: Thiotriazole, Electrochemical behaviour, Glassy carbon electrode, Voltammetry.

INTRODUCTION

Thiotriazoles and their derivatives enhanced considerable attention for the past few decades due to their chemotherapeutical values[1]. Many triazole compounds are known to exhibit antimicrobial, analgesic, antiinflammatory, local anesthetic, anticonvulsant, antineoplastic, antimalarial, antifungal activity, antiviral agents, antidepressant activities, antiploriferative and anticancer activity[1-11]. Among the pharmacological profiles of 1,2,4-triazoles, their antimicrobial, anticonvulsant and antidepressant properties seem to be the best documented. Therefore, recently many different triazole compounds have been synthesized and characterized by using spectroscopic methods such as FTIR, UV and NMR[12-15].

---

†Department of Chemistry, Faculty of Arts and Sciences, Firat University, 23119, Elazig, Turkey.

Recently, an important number of publications about these compounds have been appeared on their electrochemical investigation[16]. Some studies about electrochemical investigation of thiotriazoles[17,18], thiadiazoles[19,20] and triazines[21-23] have been reported. In this paper, the electrooxidation of a triazole compound, 5-(furan-2-yl)-4-(*p*-tolyl)-2,4-dihydro-1,2,4-triazole-3-thione (TTA) was investigated. Cyclic and differential pulse voltammograms of TTA were recorded at the different pH media by using Britton-Robinson (BR) buffer at glassy carbon electrode (GCE). The oxidation mechanism and pK_a value are also reported.

EXPERIMENTAL

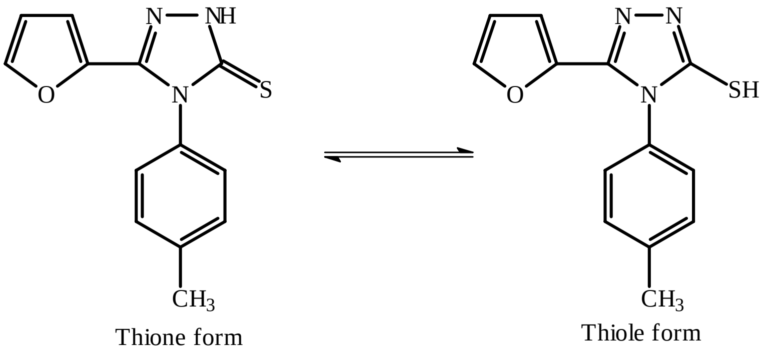
All reagents were of analytical grade. 5-(Furan-2-yl)-4-(*p*-tolyl)-2,4-dihydro-1,2,4-triazole-3-thione (TTA) was synthesized as the reference; its structure was characterized by FTIR, NMR and elemental analysis[13]. The stock solution of TTA (10^{-2} M) was prepared in dimethylsulphoxide (DMSO). BR buffer was used for varying pH. DMSO, CH_3COOH, H_3PO_4, H_3BO_3, NaOH and H_2SO_4 and were obtained from Merck.

The differential pulse voltammetry (DPV) and cyclic voltammetry (CV) were performed with a Metrohm Model 757 VA computrance with conventional three-electrode cell, GCE as the working electrode, an Ag/AgCl as the reference and Pt wire as counter electrode. All voltammetric measurements were conducted at room temperature in argon atmosphere. Before use, the working electrode was sequentially polished with graded alumina powder 10 µm (Merck) and rinsed with doubly distilled water. The pH values were measured with pH meter Metrohm Model 744. The supporting electrolytes used in all experiments contain 5 % (v/v) DMSO.

RESULTS AND DISCUSSION

The structure of TTA, which was synthesized by Dege *et al.*[13] is given in **Scheme-I**. Koparir *et al.*[15] reported that the crystal structure of thiol compounds corresponded to the thione form, but they showed thiol-thione tautomerism in solution. Due to the thiol-thione tautomerism of TTA (**Scheme-I**) it mostly appeared thiol form in solution because of containing oxidizable –SH group. Therefore, the electrochemical behavior of TTA was studied by using voltammetric techniques (DPV and CV) at GCE.

The pH dependence of the oxidation of TTA was studied in the pH range between 2 to 12 in BR buffer by DPV. As a way to quantify the pH effect on voltammetric behavior, the oxidation peak potential (Ep) and the peak current (Ip) of TTA were measured. The plot of the Ep as a function of pH was given in Fig. 1. It was observed that Ep was shifted to negative direction with increasing of the pH value of the buffer. That indicates participation of a proton transfer in the electrode process. In the curve, a linear



Scheme-I Thiol-thione tautomerism of TTA[13]

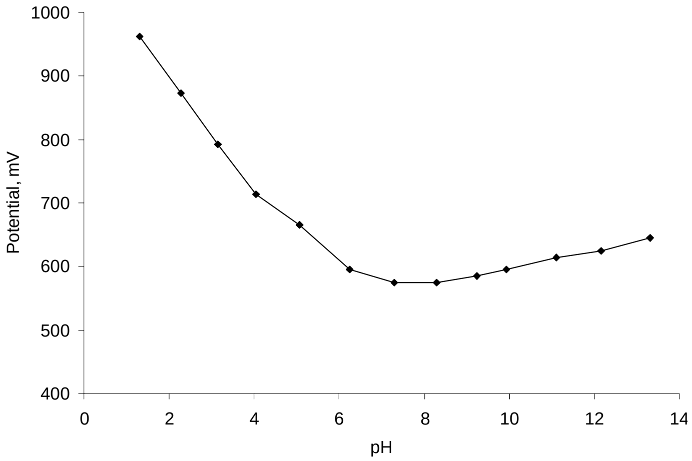


Fig. 1. Dependence of peak potential (Ep) of TTA *vs.* pH

decrease was obtained as 54 mV per pH between pH 4 and 6 and there was a horizontal line at about pH 7-8, this reflected that the voltammetric pK_a value of TTA is between 7 and 8. However, Ep was increased very slowly to positive direction after pH 8. This positive shifting can be neglected and it is concluded that Ep becomes independent on pH above 7. The pH-independent zone above pH 7 means that there are no proton transfer steps before the electron transfer rate-determining step. The voltammetric pK_a value of TTA was calculated as about 7.1 from Ep-pH curve (Fig. 1), which is in good agreement with pK_a values of some thiotriazoles[17,24]. It is reported that the oxidation peak potentials of thiol compounds vary linearly with pH by roughly 60 mV/pH when pH < pK_a (RSH) and are independent of pH at pH > pK_a[16]. It can be seen that this explanation harmonize with our results.

The slope of linear part of Ep-pH [y = -91.4x + 1081, r = 0.999] between pH 1.5 and 3.2 was found to be 91 mV. It can be concluded that the oxidation process take place through a mechanism that involves a $2H^+ : e^-$ ratio equal to two. This indicated that the thiol form of TTA can be converted to its protonated form (RSH_2^+). Thus, $2H^+$ is necessary in the oxidation of TTA in the acidic medium. The reports of Stoyanov and co-workers[25], the disulfides are immediately converted to the corresponding protonated thiones in acidic medium, can be supported our results. On the other hand, the slope of linear part of Ep-pH [y = -54.2x + 936, r = 0.998] between pH 4.1 and 6.2 is close to the Nernstain value of 59 mV, which reflects that the oxidation process take place through a mechanism that involves a $H^+:e^-$ ratio equal to one. Due to thiol compounds undergo an one electron oxidation process, one H^+ is transferred in the oxidation process forming thiyl radical form. This behaviour is exactly same for many thiol compounds[17].

The effect of pH on Ip is illustrated in Fig. 2. As shown in this figure, the Ip is pH dependent. Ip was increased by increasing pH from 2 to 11. It was observed that Ip decreased after pH 11. The reason of this decreasing after pH 11 can be depend on the forming of ionized thiol form (RS^-) in the strong basic medium. The current at pH 2 was about 4.5 times smaller that the value measured at pH 11. As it is seen (**Scheme-I**) the first step of oxidation process is the formation of thiyl radical. In this reaction, thiolic form is oxidized to radicalic form giving one H^+ and e^-. Thus, radicalic species was strongly formed in the basic media due to easily releasing of H^+. On the other hand, the solubilities of thione or thiol compounds in basic medium are higher than that in acidic medium. Due to the maximum

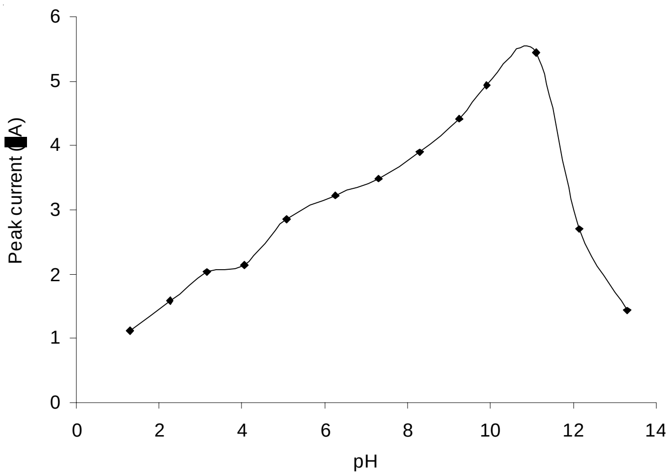


Fig. 2. Dependence of peak current (Ip) of TTA *vs.* pH

Ip was obtained for pH 11 BR buffer, this supporting electrolyte is used for further studies. Differential pulse voltammograms of 5.0×10^{-4} M TTA were also recorded at various DMSO content, which change between 5 and 25 %, at pH 11. It was observed that while the peak current of TTA was slowly decreased, the peak potential was not changed by increasing of content of DMSO at pH 11 BR buffer solution. In order to keep the ionic strength of the supporting electrolyte, buffers containing 5 % DMSO was used for all experiments.

Fig. 3 shows the DP voltammograms for various concentrations of TTA from 2.0×10^{-6} to 1.0×10^{-4} in pH 11 BR buffer. As illustrated, TTA was oxidized at one anodic peak, at about 650 mV. The peak current of TTA *vs.* its concentration at the surface of GCE was found to be linear up to 0.4 mM and is described by the equation $I(\mu A) = 72.9C_{TTA} + 0.4$, $r = 0.99$, where $I(\mu A)$ is the oxidation peak current, C_{TTA} is the analyte concentration (mM), r is the correlation coefficient. The linear dependence of peak current with concentration indicates that the oxidation of TTA is diffusion controlled.

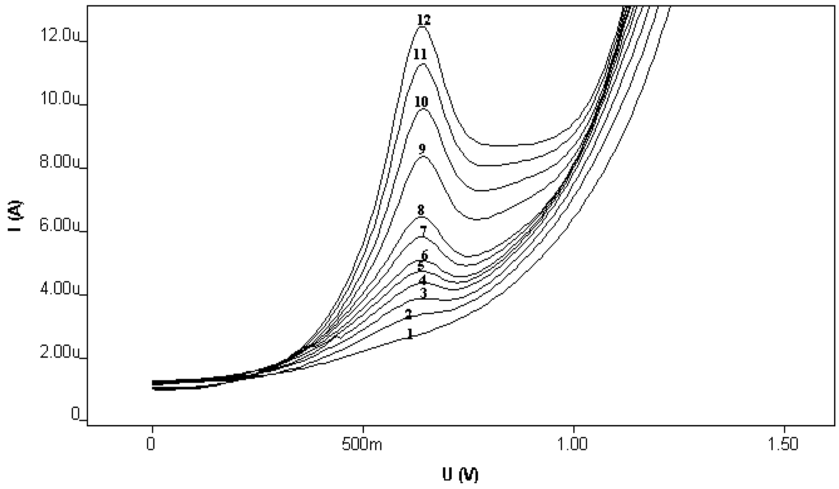
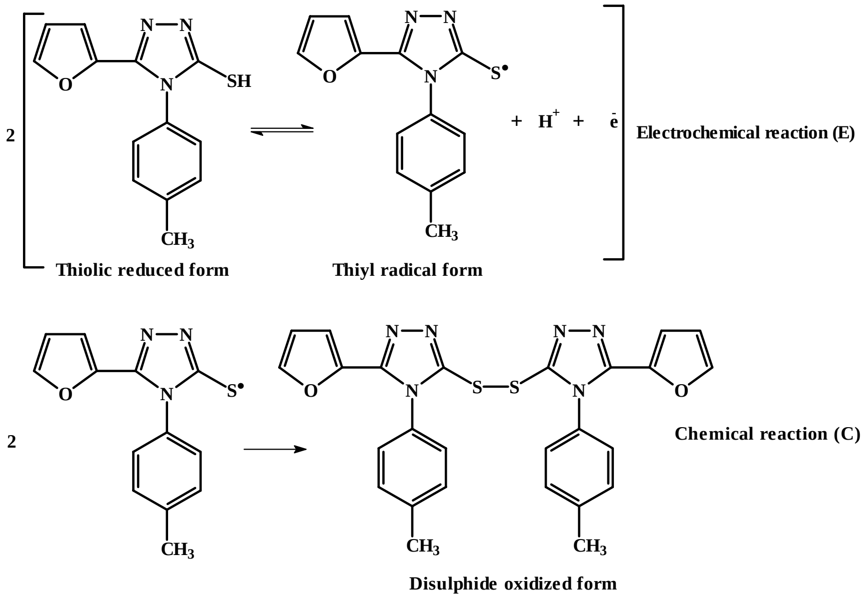


Fig. 3. Differential pulse voltammograms in pH 11 BR buffer solution at different concentration of TTA (1) blank (2) 2.0×10^{-6} (3) 4.0×10^{-6} (4) 6.0×10^{-6} (5) 8.0×10^{-6} (6) 1.0×10^{-5} (7) 1.5×10^{-5} (8) 2.0×10^{-5} (9) 4.0×10^{-5} (10) 6.0×10^{-5} (11) 8.0×10^{-5} (12) 1.0×10^{-4} M

A typical cyclic voltammogram of 0.5 mM of TTA at various scan rates is obtained on a GCE in pH 11 BR buffer. The positive scan shows a single irreversible oxidation peak at about 0.65 V, which is attributed to the oxidation of thiol due to the disulphide formation, at 100 mV/s scan rate (ν). No reduction peak corresponding to the oxidation was observed at the reverse scan. The linear increase in the oxidation peak current with the square root of the ν. ($I(\mu A) = 0.88\nu^{1/2} + 5.02$, r = 0.98) showed diffusion control process.

Electrochemical oxidation of TTA can be explained with electrochemical mechanism. Because the electrooxidation leads initially to the generation of radical species with simultaneous H^+ release followed by a dimerization step (**Scheme-II**). The curve of the current function ($i/\nu^{1/2}$) of the anodic peak *vs.* ν was also obtained. The current function decreases with increasing ν, which confirms the presence of coupled chemical reaction following the electron transfer process. A plot of log Ip *vs.* log ν gave a straight line with a slope of 0.35 ($\log I(\mu A) = 0.35 \log \nu + 0.44$, r = 0.99).



Scheme-II Electrooxidation mechanism of TTA in pH 11 BR buffer at GCE surface

As a result, it can be concluded that the TTA can be oxidized irreversibly at GCE. Its oxidation process includes one oxidation electron transfer followed by a dimerization chemical step which shows that the oxidation behavior of TTA follows the EC mechanism in RSH compounds. The pK_a value of TTA was found to be as 7.1 from the pH-peak potential curve, this is in good agreement with literature. The peak current was linearly related to the concentration of the TTA in concentration range of 10^{-4}-10^{-6} mol L^{-1}.

The stability of electrode was also investigated and it was observed that the electrode surface was inactivated by adsorption of the product (disulphide). Thus, the working electrode was used after polishing of electrode surface in the all experiments. The relative standard deviation (RSD) of the peak current to five determination of 6.0 × 10^{-5} M TTA was found to be 4.3 %. This indicated that GCE has a good reproducibility for electrochemical oxidation of TTA.

REFERENCES

1. B.S. Holla, M. Mahalinga, M.S. Karthikeyan, B. Poojary, P.M. Akberali and N.S. Kumari, *Eur. J. Med. Chem.*, **40**, 1073 (2005).
2. B.S. Holla, B. Veerendra, M.K. Shivananda and B. Poojary, *Eur. J. Med. Chem.*, **38**, 759 (2003)
3. A. Almasirad, S.A. Tabatabai, M. Faizi, A. Kebriaeezadeh, N. Mehrabi, A. Dalvandi and A. Shafiee, *Bioorg. Med. Chem. Lett.*, **14**, 6057 (2004).
4. N. Demirbas, S.A. Karaoglu, A. Demirbas and K. Sancak, *Eur. J. Med. Chem.*, **39**, 793 (2004).
5. Y.A. Al-Soud, N.A. Al-Masoudi and A.E.R.S. Ferwanah, *Bioorg. Med. Chem.*, **11**, 1701 (2003).
6. G. Turan-Zitouni, Z.A. Kaplancikli, K. Erol and F.S. Kiliç, *IL Farmaco*, **54**, 218 (1999).
7. P.A. Lambert, K.D. Somers, E.C. Kohn and R.R. Perry, *Surgery*, **122**, 372 (1997).
8. E.F. Rodriguez, J.L. Manzano and J.J. Benito, *J. Inorg. Biochem.*, **99**, 1558 (2005).
9. A. Baba, N. Kawamura, H. Makino, Y. Ohta, S. Taketomi and T. Sohda, *J. Med. Chem.*, **39**, 5176 (1996).
10. M.D. Mullican, M.W. Wilson, D.T. Connor, C.R. Kostlan, D.J. Schrier and R.D. Dyer, *J. Med. Chem.*, **36**, 1090 (1993).
11. Y.A. Al-Soud, M.N. Al-Dweri and N.A. Al-Masoudi, *IL Farmaco*, **59**, 775 (2004).
12. S.G. Bodige, M.M. Rojas and W.H. Watson, *J. Chem. Crystallogr.*, **29**, 931 (1999).
13. N. Dege, O. Andac, A. Cansiz, A. Çetin, M. Sekerci and M. Dinçer, *Acta Crystallogr. E*, **60**, o1405 (2000).
14. A. Cansiz, M. Koparir and A. Demirdag, *Molecules*, **9**, 204 (2004).
15. M. Koparir, A. Çetin and A. Cansiz, *Molecules*, **10**, 475 (2005).
16. H. Victler, J. Gruber and L.V. Pardini, in eds.: H.I. Und and O. Hammcrich, Organic Electrochemistry, Marcell Decker, New York, p. 622 (2001).
17. L. Fotouhi, F. Hajilari and M.M. Heravi, *Electroanalysis*, **14**, 1728 (2002).
18. L. Fotouhi and R. Sadeghi, *Polish J. Chem.*, **77**, 1313 (2003).
19. S. Mirel, R. Sandulescu, J-M. Kauffmann and L.J. Roman, *Pharm. Biomed. Anal.*, **18**, 535 (1998).
20. S. Picart and E. Genies, *J. Eectroanal. Chem.*, **408**, 53 (1996).
21. L. Fotouhi, N. Farzinnegad, M.M. Heravi and Sh. Khaleghi, *Bull. Korean Chem. Soc.*, **24**, 1751 (2003).
22. N. Farzinnejad, A.A.M. Beigi, L. Fotouhi, K. Torkestani and H.A. Ghadirian, *J. Electroanal. Chem.*, **580**, 245 (2005).
23. L.H. Madkour, *J. Chem. Res. (S)*, 514 (1998).
24. R.E. Notari and J.L. De Young, *J. Pharm. Sci.*, **64**, 1148 (1975).
25. S. Stoyanov, T. Stoyanova, L. Antonov, P. Karagiannidis and P. Akrivos, *Monatshefte für Chemie*, **127**, 495 (1996).

(*Received*: 13 December 2006; *Accepted*: 30 January 2007) AJC-5382