STUDIA UBB CHEMIA, LXVIII, 1, 2023 (p. 7-17)
(RECOMMENDED CITATION)
DOI:10.24193/subbchem.2023.1.01

GRAPHITE PASTE ELECTRODE MODIFIED WITH ZEOLITIC IMIDAZOLATE FRAMEWORK (ZIF-67) FOR THE DETERMINATION OF ACETAMINOPHEN

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ABSTRACT. A zeolitic imidazolate framework ZIF-67 was synthesized by an eco-friendly solvothermal method, using ethanol as solvent at room temperature. The morphology and structure of obtained ZIF-67 were characterized by X-ray diffraction, scanning electron microscopy (SEM), nitrogen adsorption/desorption isotherm, energy dispersive spectroscopy (EDS), and Fourier-transform infrared spectroscopy (FTIR). The ZIF-67 modified graphite paste electrode (ZIF-67-GPE) was prepared and used for the electrochemical detection of acetaminophen (AC). Cyclic voltammetry (CV) and square wave voltammetry (SWV) were employed to investigate the electrochemical behavior of AC at ZIF-67-GPE modified electrode. At the optimal working conditions, the limit of detection was 0.2 µM (S/N = 3) in the linear range of 2 - 10 µM AC. The good analytical parameters indicated its applicability for AC determination in real samples.

Keywords: *Zeolitic imidazolate framework, graphite paste modified electrode, acetaminophen*

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INTRODUCTION

Zeolitic imidazolate frameworks (ZIFs) are a class of metal-organic frameworks (MOFs) that have gained widespread interest for their applications in catalysis [1-3], gas storage, chemical separation [4, 5], sensing [6,7], and drug delivery because of their porous structure, tunable pore size, and high surface area.

The cobalt-based metal–organic zeolitic imidazolate frameworks (ZIF-67) belonging to the zeolitic imidazolate frameworks (ZIFs) class of substances, consists of a transition metal ion (Co^{2+}) and organic ligands (2-methylimidazole). ZIF-67 is topologically isomorphic with zeolites, with a metal-imidazole metal angle of ~145°, relatively similar to the Si-O-Si angle in zeolite [8-10]. The typical synthesis methods of ZIF-67 are solvothermal and hydrothermal methods which use large amounts of organic solvents, such as N,N-dimethyl formamide (DMF), N-methyl pyrrolidine, N,N-diethyl formamide, and methanol, etc. Nevertheless, these methods lead to disadvantages due to cost and environmental problems, because the used toxic organic solvents are found in the waste solutions. Therefore, the simple and environmentally friendly method is highly expected. In recent years, the synthesis of ZIF-67 by using either a friendly solvent, such as ethanol, or water, or a non-solvent synthesis route has been of interest [11, 12].

Acetaminophen (N-acetyl-p-aminophenol; paracetamol, AC) is a broadly recommended drug because it is used as a painkiller and antipyretic. However, in the case of an overdose, it would cause health problems to the liver or kidney. Therefore, AC detection has become an interesting research topic. Among the many techniques described in the literature for AC detection in the pharmaceutical formulation, the (i) optical methods (*i.e.*, UV/Vis spectrophotometric in the version of flow-injection, IR spectrophotometric (NIR or FTIR), spectrofluorimetric [1], (ii) electroanalytical methods (*i.e.*, titrimetry, amperometry, voltammetry, and immunoassays); (iii) chromatographic methods (*i.e.*, high-performance liquid chromatography (HPLC)), and (iv) capillary electrophoresis methods [2] are the most performant. In recent years, electrochemical techniques have been selected for AC determination due to their high sensitivity, simple technique, rapid response, and low expenses.

In this work, ZIF-67 was synthesized by an eco-friendly solvothermal method, using ethanol as solvent at room temperature and characterized by several techniques, such as X-ray diffraction (XRD), scanning electron microscopy (SEM), nitrogen adsorption/desorption isotherm, energy dispersive spectroscopy (EDS), Fourier-transform infrared spectroscopy (FTIR). The applicability of ZIF-67 material as a modifier for the development of a chemically modified electrode for AC electrochemical determination has been investigated by electrochemical methods (cyclic voltammetry, CV and square wave voltammetry, SWV) either in synthetic or in real sample solutions.

RESULTS AND DISCUSSION

Morpho-structural characterization of ZIF-67 material

The results obtained from different morpho-structural characterization techniques are described below.

Figure 1A shows the XRD pattern of the synthesized sample. Thus, the XRD pattern exhibited diffraction peaks at 2θ values of 7.4°, 10.4°, 12.7°, 14.8°, 16.5°, 18.0°, 22.1°, 24.5°, 25.5°, 26.7°, 29.5°, 30.6°, 31.6°and 32.5°, which correspond to (011), (002), (112), (022), (013), (222), (114), (233), (224), (134), (044), (334), (244) and (235) planes. These results are in good accordance with the already published pattern of ZIF-67 crystal [13].

The FT-IR spectrum of ZIF-67 is shown in Figure 1B. The peak observed at about 430 cm^{-1} was attributed to the stretching of the metal Co–N bond in 2-methylimidazolate [14–16]. The peak at about 997, 1140, and 1514 cm^{-1} are the stretching vibration of the C-N bond and C=N in 2-methylimidazolate, respectively [16, 17]. The stretching of the aromatic ring in 2-methylimidazolate and the C-H bond in the aliphatic hydrocarbon chain was revealed by the peaks at 2916 cm^{-1} and 3113 cm^{-1} [15-18].

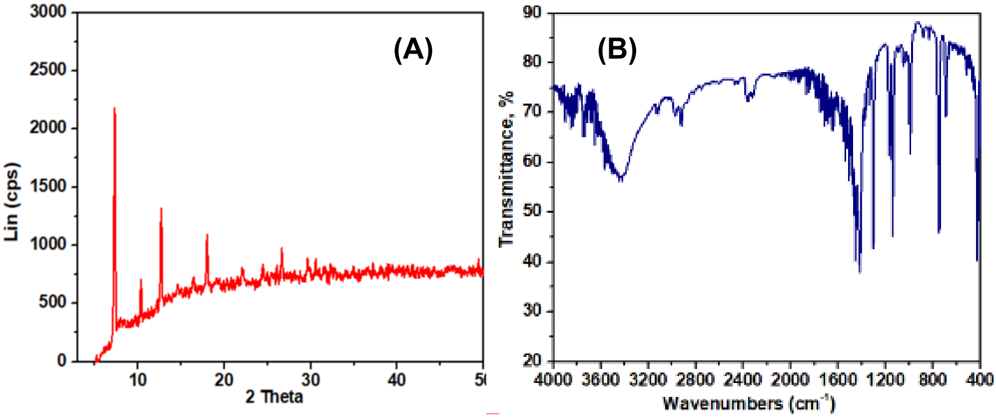
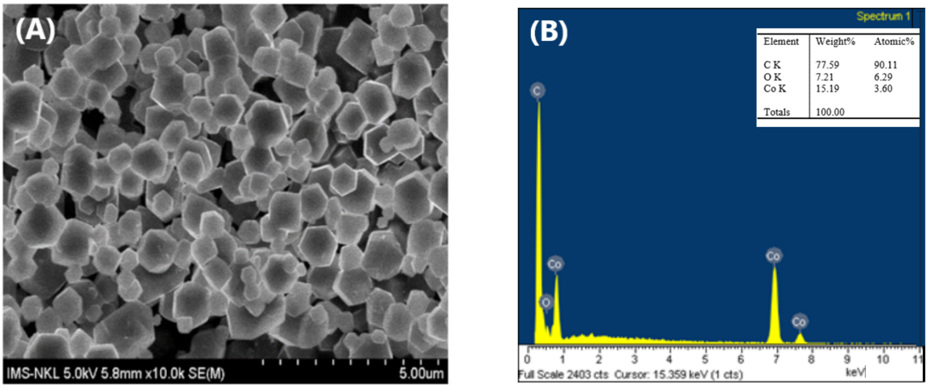


Figure 1. XRD pattern (A) and FTIR spectrum (B) of ZIF-67.

SEM images of the obtained ZIF-67 (Figure 2A) revealed the basic structure of the rhombohedral dodecahedron and smooth surfaces of ZIF-67 crystals with a particle size of about 500 - 1000 nm. Also, the results of the EDS analysis (Figure 2B) confirmed the presence of C, O, and Co elements on the surface of ZIF-67.

Figure 3 shows the nitrogen adsorption–desorption isotherm and the pore size distributions of ZIF-67 material. Thus, the N_2 adsorption-desorption isotherms (Figure 3A) used for the textural study of ZIF-67, displayed a typical reversible type I isotherm, according to the IUPAC classification, that is a characteristic of the microporous material because the adsorption of the sample ended at a low pressure (P/Po = 0.01) [19]. Also, the results showed the BET surface area of 1112 m^2/g and the micropore size mainly distributed at around 1.1 nm.



Element	Weight%	Atomic%
C K	77.59	90.11
O K	7.21	6.29
Co K	15.19	3.60
Totals	100.00	

Figure 2. SEM images of ZIF-67 (A) and EDS spectra of ZIF-67 (B).

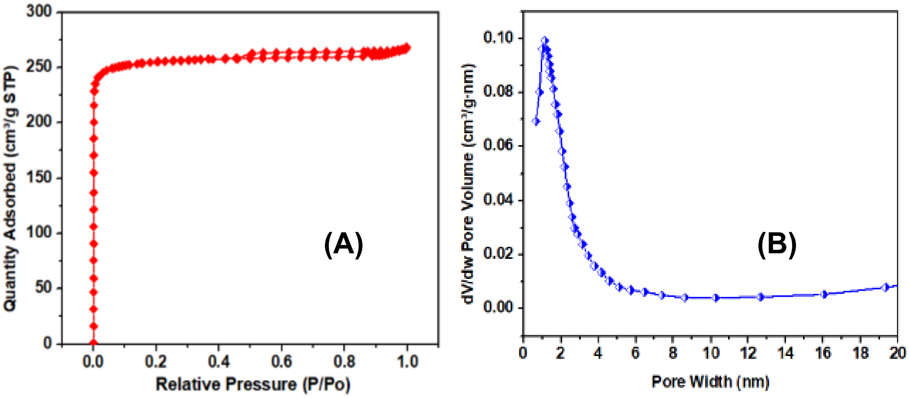


Figure 3. Nitrogen adsorption-desorption isotherms (A)
and pore size distribution of ZIF-67 (B).

The morpho-structural characterization of the ZIF-67 material, by XRD, SEM-EDS, BET, and FTIR confirmed the successful synthesis of this microporous crystalline material.

Electrochemical behavior of ZIF-67-GPE modified electrode

Cyclic voltammograms were recorded to compare the electrochemical behavior of AC at unmodified GCE and ZIF67-GCE-modified electrodes (Figure 4).

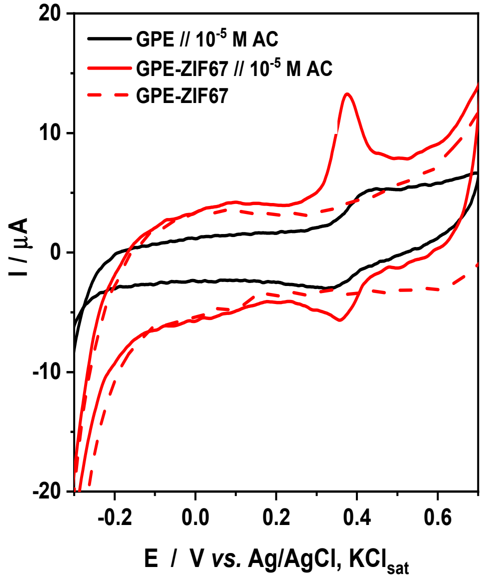


Figure 4. Cyclic voltammograms at GPE (black solid line) and ZIF-67-GPE (red solid line) modified electrode in the presence of 10^{-5} M AC and in the absence of AC (red dot line). Experimental conditions: electrolyte, 0.1 M phosphate buffer solution (PBS), pH = 7; scan rate, 50 mV s^{-1}; starting potential, -0.25 V *vs*. Ag/AgCl, KCl_{sat}.

The oxidation and reduction peaks were attributed to the redox behaviour of the acetaminophen and are placed at the following values of anodic/cathodic potentials (E_{pa}/E_{pc}) of +0.35 V/+0.33 V *vs.* Ag/AgCl, KCl_{sat} for ZIF-67-GPE and + 0.41 V/+0.32 V *vs.* Ag/AgCl, KCl_{sat} for GPE, respectively. Because the peak separation (calculated as $\Delta E = E_{pa} - E_{pc}$) is increasing from 0.02 V for ZIF-67-GPE modified electrode to 0.09 V in the case of GPE, it can be concluded that the presence of ZIF67 in the electrode matrix leads to a more reversible behaviour of the redox process. Also, the oxidation process is facilitated in the presence of ZIF-67 in the electrode matrix, because the anodic peak potential value is shifted towards a more negative potential value with 0.06 V. Moreover, the ratio of the peak current intensities (I_{pa}/I_{pc}) is 1 and 2.3 in the case of GPE and ZIF-67-GPE modified electrodes, respectively, the anodic redox process is visibly enhanced in the presence of ZIF-67.

Effect of pH

Square wave voltametry (SWV) was used to investigate the effect of pH on the AC oxidation at ZIF-67-GPE electrode (Figure 5A) in the range of 5.5 - 7.5.

As shown in figure 5B the oxidation peak current increased in the pH range of 5.5 - 6.5, reached a maximum at pH 6.5, and then decreased. Therefore, a pH value of 6.5 for the buffer solution was chosen for further experiments. The dependence of the oxidation peak potentials (E_{pa}) on pH in the same domain showed that the E_{pa} shifted linearly towards negative potential with the increase of the pH values.

This behavior indicated the involvement of protons in the redox reaction of AC.

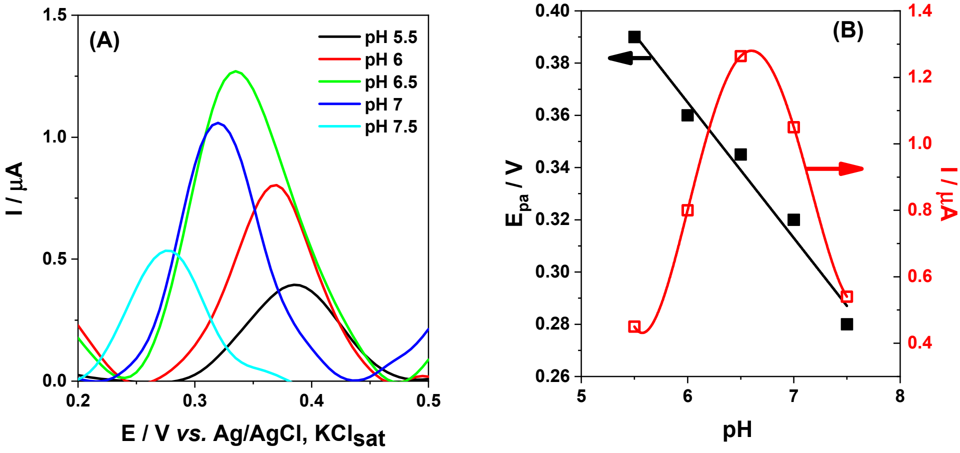
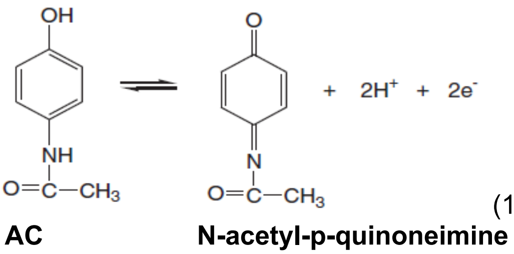


Figure 5. Square wave voltammograms at ZIF-67-GPE for 10^{-5} M AC in 0.1 M PBS at various pH value, see (A). Influence of pH on the formal potential Eo' and anodic peak current I_{pa} (B). Experimental conditions: electrolyte, 0.1 M phosphate buffer solution (PBS); starting potential -0.25 V *vs.* Ag/AgCl, KCl_{sat}; frequency, 20 Hz; step potential, 0.005 V; accumulation time, 150 s; deposition potential, 0 V.

The linear regression equation was expressed as follows: E_{pa}/V = -0.052 pH + 0.677 (R = 0.9884, 5 points). The slope of 0.052 V/pH, close to the theoretical Nernstian value of 0.059 V/pH, corresponds to a ratio of protons and electrons involved in the oxidation reaction of 1:1. According with the obtained electrochemical parameters the AC oxidation mechanism is presented in the following reaction (1).



(1)

Analytical parameters of ZIF-67-GPE modified electrode

Square wave voltammograms recorded at the ZIF-67-GPE modified electrode in the presence of different concentrations of AC in the range of 10^{-6} M to 10^{-5} M (Figure 6A) lead to plotting the corresponding calibration curve (Figure 6B). The dependence I - AC concentration was linear in the range of concentrations 2 - 10 μM. The linear regression equation was I_{pa}/μA = (-1.61 ± 0.10) + (1.49 ± 0.02) [AC]/μM, (R = 0.9996, 9 points). The estimated detection limit of AC was 0.20 μM (for a signal/noise ratio of 3) at ZIF-67-GPE. This result was lower than those obtained at several electrodes reported in the literature, *e.g.*, 1.1 μM at CPE-CNT-poly(3-aminophenol) [20]; 1.39 μM at PEDOT/SPE [21]; 6 μM at graphene oxide-GCE [21]; 1.45 μM at Pt/B(Al)SBA-15-GPE [23]; 1.4 μM at ZIF-67/GCE [24].

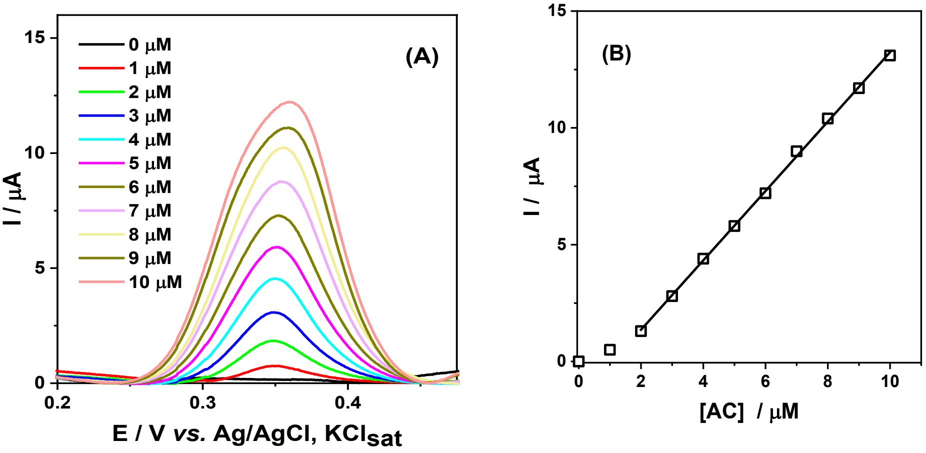


Figure 6. Square wave voltammograms recorded at ZIF-67-GPE increasing concentration of AC (A) and the corresponding calibration curve (B). Experimental conditions: electrolyte, 0.1 phosphate buffer solution (PBS), pH 6.5; starting potential -0.20 V *vs*. Ag/AgCl, KCl_{sat}; frequency, 20 Hz; step potential, 0.005 V; accumulation time, 150 s; deposition potential, 0 V.

Inteferences

In order to evaluate the interference effect of ascorbic acid (AA) on the detection of AC, 0.1 mM AA was added to a solution containing 5 μM AC. The obtained square wave voltammograms (Figure 7) illustrate that the oxidation reaction of AA and AC are placed at completely different peak potentials, thus at the investigated electrode surface the AC oxidation was not affected by the presence of AA. Moreover, the oxidation peak potentials placed at 0.014 V *vs.* Ag/AgCl, KCl_{sat} and +0.33 V *vs.* Ag/AgCl, KCl_{sat} for AA and AC, respectively, shifted with 20 mV towards more positive values, when both AA and AC are present in solution.

Real sample analysis

The ZIF-67-GPE modified electrode was used to determine the acetaminophen content in the commercial pharmaceutical tablet, as Panadol Extra (from Sanofi VietNam), using the standard addition method. The results are summarized in Table 1.

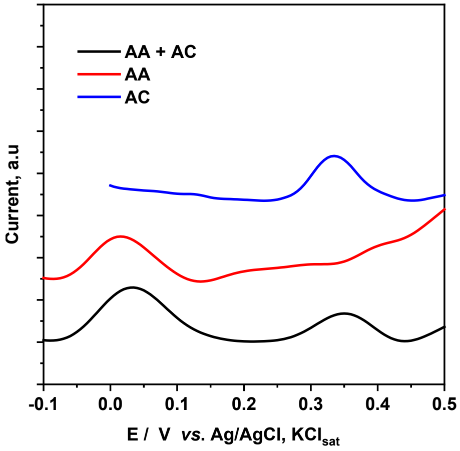


Figure 7. Square wave voltammograms recorded at ZIF-67-GPE modified electrode in the presence of 5 μM AC and 0.1 mM AA. Experimental conditions: electrolyte, 0.1 phosphate buffer solution (PBS), pH 6.5; starting potential -0.1 V *vs.* Ag/AgCl, KCl_{sat}; frequency, 20 Hz; step potential, 0.005 V; accumulation time, 150 s; deposition potential, 0 V.

Table 1. Results of real sample analysis

Sample	Added/μM	Found/μM	Recovery%	RSD%
AC (500 mg/tablet)	4	3.96 ± 0.04	99.0 ± 1.09	1.1

From these results, it may be concluded that the ZIF-67-GPE electrode have good efficiency for the AC analysis in real sample. The mean value of the AC concentration obtained by the calibration curve corresponds well to the value declared by the producer. The recovery of AC were in the range of 98.01% - 100.09%, and the relative standard deviation was lower than 2%, indicating the applicability of ZIF-67-GPE modified electrode in real sample analysis.

CONCLUSIONS

The rhombic dodecahedron ZIF-67 crystals were synthesized by an eco-friendly solvothermal method, using ethanol as solvent at room temperature. The material was used for preparing a ZIF-67 graphite paste-modified electrode which was characterized for AC redox behavior, by cyclic voltammetry and square-wave voltammetry. The estimated electroanalytical and analytical parameters demonstrated good expected electrochemical behavior, adequate sensitivity, and low detection limit for AC detection. Thus, the Co metal-containing porous structure of ZIF-67 provided a promising platform for the detection of AC from the synthetic sample and commercial pharmaceutical.

EXPERIMENTAL SECTION

Chemicals

$CH_3C_3H_2N_2H$, Hmim), and acetaminophen ($C_8H_9NO_2$), graphite powder, and paraffin oil were received from Sigma - Aldrich. Cobalt nitrate hexahydrate ($Co(NO_3)_2$ $6H_2O$) were purchased from Macklin (China), absolute ethanol (C_2H_5OH), methanol (CH_3OH), KH_2PO_4, K_2HPO_4 were purchased from Guangdong - Guanghua Sci-Tech Co. Ltd (China). Acetaminophen tablet (Panadol, 500 mg AC, from Sanofi VietNam) was purchased from a local pharmacy.

Preparation of ZIF-67 material

1.455 g of $Co(NO_3)_2{\cdot}6H_2O$ was dissolved in 50 mL of ethanol and 1,64 g of 2-methylimidazole (Hmim) was dissolved in 50mL of ethanol. Mole ratio of Co^{2+}: Hmim was 1 : 4. The Hmim solution was poured slowly into $Co(NO_3)_2{\cdot}6H_2O$ solution under stirring condition for 30 min at room temperature.

The obtained solution was kept at room temperature for 6 hours without stirring. The colloidal dispersion was observed, and the product was collected by centrifugation (4000 rpm, 30 min) and washed with ethanol three times, then dried at 80 ^{o}C, 12 hours.

Preparation of ZIF-67-GPE modified electrode

The ZIF-67-GPE modified electrode was prepared by thoroughly mixing 40 mg of graphite powder and 10 mg ZIF-67 powder with 15 µl of paraffin oil. The obtained paste was put into the cavity of a Teflon holder. The obtained electrode surface was smoothed using paper. When necessary, a new electrode surface was obtained by removing 2 mm of the outer paste layer and adding freshly modified paste.

Electrochemical measurements

Electrochemical measurements (cyclic voltammetry and square wave voltammetry) were performed by a custom-made multifunctional potentiogalvanostat MPGS - HH10 manufactured in the Institute of Chemistry, Vietnam Academy of Science and Technology, Hanoi, Vietnam. A conventional three-electrodes cell equipped with a working electrode (ZIF-67-GPE modified electrode or GPE unmodified electrode, with a geometrical area of 0.07 cm^2), a counter electrode (Pt wire), and a reference electrode (Ag/AgCl, KCl$_{sat}$) was used. The experimental conditions are presented in the capture of each figure.

ACKNOWLEDGMENTS

This research is conducted within the framework of Science and Technology Projects at institutional level of Quy Nhon University under the project code T2022.748.04

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