



Original Research Article

Electrochemical behaviour of 5-methoxy-5,6-bis(3-nitrophenyl-4,5-dihydro-1,2,4-triazine-3(2H))-thione in presence of salicylaldehyde on zinc cathode with surface morphology and biological activity

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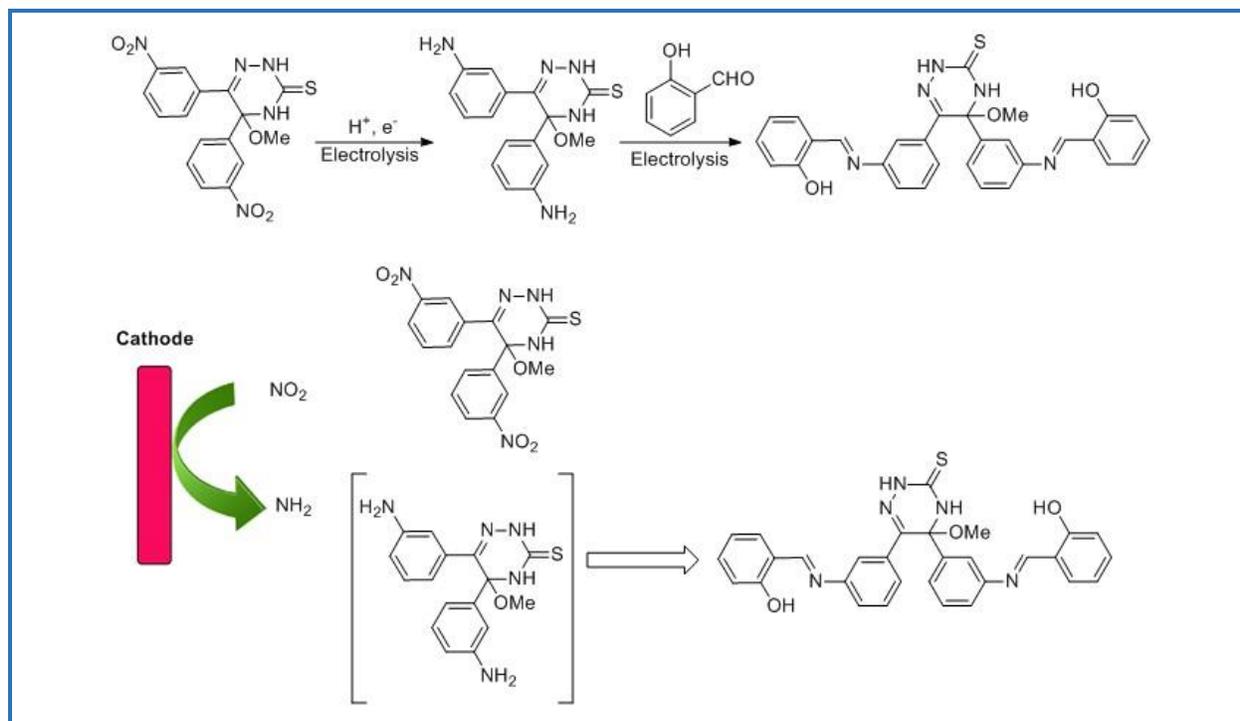
Cathode

ABSTRACT

This paper presents an innovative, green and organic electro synthesis in order to prepare Schiff base product by the reduction of 5-methoxy-5,6-bis(3-nitrophenyl-4,5-dihydro-1,2,4-triazine-3(2H))-thione followed by the condensation on zinc cathode in aqueous alkaline ethanol media in the presence of salicylaldehyde at room temperature. The main characteristic of this proposal is the electro-reduction and electro-condensation. The bulk electrolysis at constant potential was performed in a three-electrode undivided cell in order to prepare Schiff base. In this sense, good yields and easy purification were achieved. Results indicate that the reduction produced high current in the cell and succeeded a green chemistry process. Products were characterized by IR, NMR (^1H , ^{13}C), and SEM.

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Graphical Abstract



Introduction

During the last decades, chemists have shown their interest in the electrochemical reduction of organic compounds by bringing the organic compounds into contact to a cathode, wherein the cathode comprises a support made of an electrically conductive material and an electrically conductive, cathodically polarized layer formed thereon in situ by alleviation [1–5]. This analysis has to be guided by a series of factors such as physico-chemical parameters of the organic compound, chemical composition, particle size, structure and morphology or environment.

The electrochemical reduction of nitro organic compounds has been used for the cathodic dimerization of acrylonitrile. Because the current densities were inadequate in economic terms, which meant that space-time yields (STY) were too small, the current yields were too low, hydrogen was being formed, selectivities –with a view to a number of possible reduction steps –were too low, and the special catalytically active cathodes were not sufficiently available on a technical scale. Herein, more information is required on electrochemical behavior for the electrochemical reduction on cathodes to be utilized industrially [6–10].

It has been clarified that from publications on preparative organic electrochemistry, anodes and cathodes used in preparative electrochemistry must have special electrochemical characteristics. Such electrodes are often used for metal-organic frame works representing a class of hybrid

materials comprised of the ordered networks formed *via* combining metal ions with organic ligands. Metal-organic frame works have been used as efficient electrodes in fuel cell systems [11–15].

The electrodes and electrolytes are crucial in electro catalysis as different electrodes and electrolytes can induce different products. Modifying the surface of electrodes to provide some control over how the electrode interacts with its environment has been one of the most active areas of research interest in electrochemistry within the last 30 years [16–25].

The absorption of the drugs is especially affected by particle size because the bioavailability is, in most cases, dissolution-rate controlled. In the pharmaceutical industry, several conventional techniques have been utilized for particle size reduction, such as spray drying, freeze drying and liquid antisolvent precipitation [26–30].

A drawback of these established fabrication methods is that the electrodes, after inactivation of the catalytically active layer, often have to be removed from the electrolytic apparatus and subjected to external regeneration, the drawback is the laborious preparation of the catalytically active layer as such and the difficulties in achieving adequate bonding to the support electrode.

In view of the prior art set forth above, it is an object of the invention to provide a process for reducing organic compounds, which on the one hand gives high space time yields, and on the other, permits high selectivity in the case of multiple reducible compounds, avoiding the formation of hydrogen during the reduction which can be used on an industrial scale [31].

The mean particle size of the particles forming the above defined layer and the thickness of the layer are always chosen so as to ensure an optimum ratio of filter pressure drop and hydraulic through putting and enabling optimum mass transfer. The mean particle size is generally from about 1 to about 400 μm , preferably from about 30 to about 150 μm , and the thickness of the layer is generally from about 0.05 mm to about 20 mm, preferably from about 0.1 to about 5 mm.

After the reduction is complete or when the catalytically active layer is spent, it can be separated from the support by a simple switch of the flow direction, and, then, can be disposed of or regenerated independently of the reduction. After the spent layer has been completely removed from the system, it is then possible once more to recoat the support with the particles forming the layer. Afterwards, the particles have been completely alleviated in order to continue the reduction of the organic compound. Organic compounds, which are suitable for use in the mentioned process, comprise organic compounds containing reducible groups as starting materials. The products which can be obtained in the process include, depending on the total electric charge introduced, both partially reduced compounds and completely reduced compounds [32].

Experimental

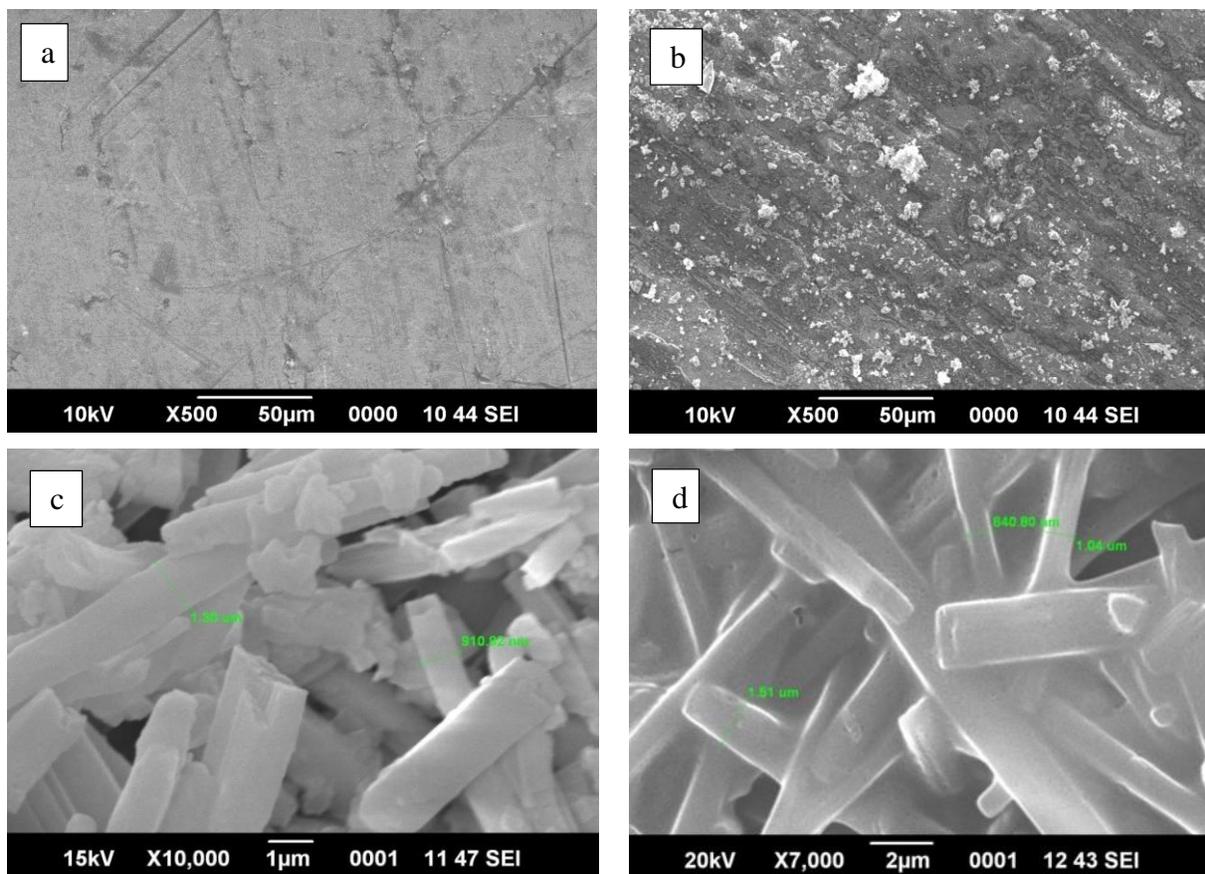


Figure 1. The SEM images of the morphologies of electrolysis product a

Materials and methods

All chemicals were analytical grade from Aldrich chemicals and solvents for electrochemical process were methanol and ethanol from Aldrich chemicals. The water was obtained from double distillation. The reported melting point was uncorrected and the purity of the compound was checked by TLC on glass plates coated with silica gel as absorbent, using acetone: methanol in 1:1 ratio. The IR spectra were taken in KBr beam splitter on a thermo nicolelet avatar 370. ^1H NMR was recorded on a Bruker Avance III, 400 MHz. Instrument using DMSO as solvent and TMS as internal standard. JSM-6390 scanning electron microscope at the accelerating voltage of 10-20 Kv was used for SEM analysis. All spectral analyses were carried out at the sophisticated analytical Instrumentation Facility, cochin university and technology, cochin, Kerala, India.

Procedure for electrolysis

The electrochemical reduction of 5-methoxy-5,6-bis(3-nitrophenyl)-4,5-dihydro-1,2,4-triazine **3** (2*H*)-thione was carried out in an undivided cell. (0.38 g, 1 mmol) 5-methoxy-5,6-bis(3-nitrophenyl)-

4,5-dihydro-1,2,4-triazine-3(2H)-thione was taken in an undivided cell along with 75 mL of ethanol and 25 mL of water. To this mixture, a 10% aqueous solution of sodium hydroxide (1 g) was added drop wise at room temperature. The undivided cell was equipped with a zinc cathode (0.014 cm²), platinum anode (Pt) and calomel electrode. The constant potential was supplied with DC power supply (9.5 V). The reaction was electrolysed with constant stirring using a magnetic stirrer for 20 minutes and, then, electrolysis was stopped. To this electrolysed solution, salicylaldehyde (0.122 g, 1 mmol) was added slowly with stirring, and, then, the whole electrolysed solution was immediately converted into pale yellow solid. Afterwards, the solid was washed with ethanol and water repeatedly and recrystallised from the mixture of solvent (DMSO and DMF) to get the pure product. The isolated yield was 98% (0.58 g) mp 225 °C.

Procedure for antibacterial and antifungal activity

The *in vitro* antibacterial activity was carried out by a well-diffusion method using nutrient agar as the medium, DMSO as the control and fluconazole as the standard fungicide. The newly synthesized compound was screened for antibacterial activity against *staphylococcus aureus*, *bacillus cereus*, *streptococcus sp*, *proteus mirabilis*, *staphylococcus epidermidis*, *enterobacter aerogenes*, *shigella flexneri*, *klebsiella pneumonia*, *vibrio cholerae* and species of fungi against *aspergillus flavus*, *aspergillus niger*, *cryptococcus neoformans*, *curvularia sp*, *trichosporon sp*, and *candida albicans* by well-in agar method. The synthesized compounds (1 mg/mL⁻¹) and the controlled drugs were dissolved in redistilled DMSO for determining both the antibacterial and antifungal activities. The zones of inhibition were determined at the end of an incubation period of 24 hours at 37 °C. During this period, the test solution was defused into the medium and the growth of inoculated microorganism was affected. The antifungal activities were determined at 26–28 °C for 48 hours.

Results and Discussion

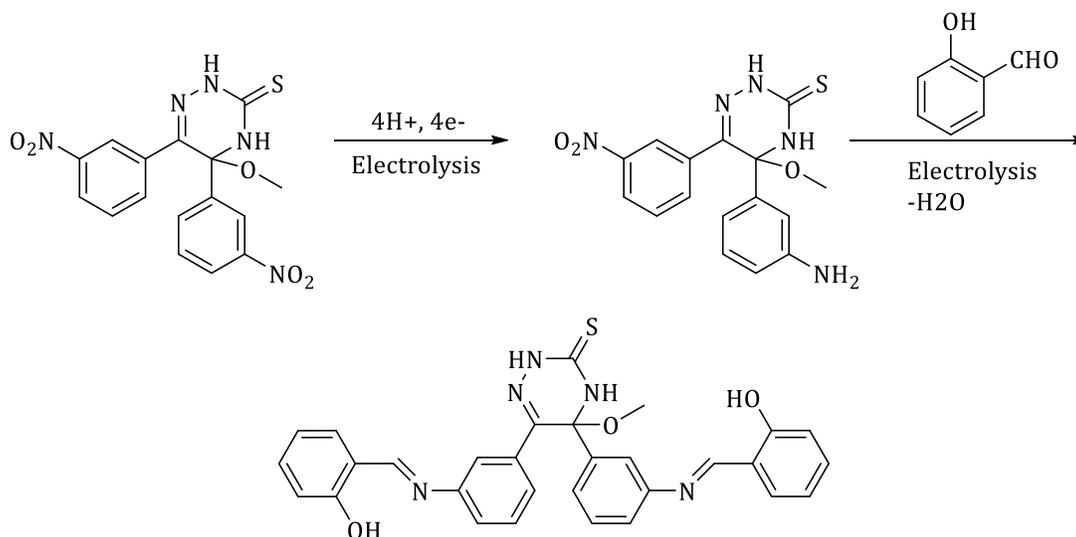
The preparative electrolysis of the dinitro compound in aqueous alkaline alcoholic media has been studied. The compound 5-methoxy-5,6-bis(3-nitrophenyl)-4,5-dihydro-1,2,4-triazine-3(2H)-thione has been reduced on a zinc cathode at a cathode potential of -2.3 V and produced a pale yellow solid a while stirring the solution with salicylaldehyde. The speed of the reaction between the reduction product and the aldehyde is very interesting because the same reaction takes more than two hours in conventional method.

The preparative electrolysis of the dinitrocompound in aqueous alkaline alcoholic media has been studied using DC suppliers operated at a standard output of 0.5 to 2.5 A/0–35 V. These were connected with ammeter and voltmeter in series. The electrode reactions have been successfully

performed in an undivided cell which is a simple beaker type apparatus. The solution was stirred using a magnetic stirrer. The calomel electrode was used as reference electrode to monitor the operating potential.

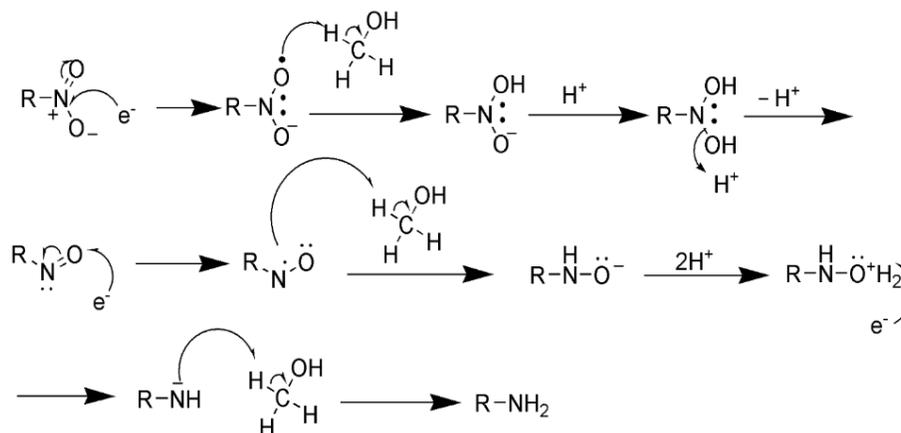
Mechanism

The reaction which proceeded through one electron-reduction of the nitro compounds to form the corresponding nitro-free radical anion was followed by protonation in which the nitro compound is reduced to amino compound which have been further condensed with salicylaldehyde producing schiff base ([Scheme 1](#)).



Scheme 1. Reaction for Electrochemical reduction and condensation

The one electron transfer from cathode to nitro compound followed by protonation occurred as shown below.



The one electron transfer from cathode to nitro compound followed by protonation occurred as shown below. Surface morphology of the electrode before and after electrolysis was studied. The surface morphology was analyzed by SEM analysis and it was observed that there is a difference in the morphology of the surface of zinc cathode which is due to the reduction of 5-methoxy-5,6-bis(3-nitrophenyl)-4,5-dihydro-1,2,4-triazine-3(2*H*)-thione on the surface of zinc cathode. The SEM image of a on the surface of zinc cathode is shown in [Figure 1c](#) and [d](#) (After electrolysis). The scanning electron microscope (SEM) images of surface of zinc cathode were shown in [Figure a](#) (Before electrolysis). The SEM image of 5-methoxy-5,6-bis(3-nitrophenyl)-4,5-dihydro-1,2,4-triazine-3(2*H*)-thione is shown in [Figure b](#) (Before electrolysis). In this sense, the product can be proved by spectroscopic study.

The average diameter of these particles is about 840 nm. The SEM micrographs show slab-like crystallites of average particle dimensions approximately at 840 nm. The technique is a new way of doing electron-diffraction with an SEM. In standard SEM-based electron diffraction, the researcher analyzes patterns that are formed by electrons that bounce back after striking atoms in the sample. If the sample is a crystalline material with a regular pattern to the arrangement of atoms, these diffracted electrons form a pattern of lines that reveal the particular crystal structure or "phase" and orientation of the material.

Scanning electron microscope (SEM) is the method of choice to investigate particle size shape and structure. According to the SEM images in [Figure 1c](#) and [d](#), the obtained structure has a uniform morphology. Scanning electron micrographs (SEMs) were used to study the morphology of the compounds and to observe the interfacial quality between the phases. Fractured surfaces of the samples from the notched impact tests were coated with a gold/palladium alloy and observed at a voltage of 20 kV. The surface morphology and cross sectional morphology of schiff base of the reduction product 5-methoxy-5,6-bis(3-nitrophenyl)-4,5-dihydro-1,2,4-triazine-3(2*H*)-thione A ([Figure 1c](#) and [d](#)) were characterized by SEM. The SEM images showed a microporous and fibrous structure. The expected interactions between the formation of imine linkage make the Schiff base derivatives stable with many hydrophilic sites at the surface. The cross sectional morphology of the same one showed the fine interaction with pores and micro voids. The pores are effective in increasing the functional surface in the Schiff bases which enabled the same one to be used promising material.

The Schiff bases of the reduction product 5-methoxy-5,6-bis(3-nitrophenyl)-4,5-dihydro-1,2,4-triazine-3(2*H*)-thione were evaluated for their anti-bacterial activity *in vitro* using zone inhibition technique against gram negative and gram positive bacteria such as *Pseudomonas aeruginosa* and *bacillus subtilis* at different concentration (10 µg, 50 µg, 100 µg, and 200 µg). The obtained results

were compared to that of the standard drug streptomycin as a standard bactericide and fluconazole as standard fungicide. The electrochemically produced Schiff base showed promising antibacterial and antifungal activities. The zone of inhibition is given in Table 1 and 2.

Table 1. Antibacterial activity (zone of inhibition in mm)

Sl. No.	Bacterial strains used	Zone of inhibition in mm
1	Staphylococcus aureus	30
2	Bacillus cereus	15
3	Streptococcus sp	45
4	Proteus mirabilis	15
5	Staphylococcus epidermidis	16
6	Enterobacter aerogenes	35
7	Shigella flexneri	37
8	Klebsiella pneumoniae	50
9	Vibrio cholerae	30

Standard streptomycin

Table 2. Antifungal activity (zone of inhibition in mm)

Sl. No.	Type of fungi	Zone of inhibition in mm
1	Aspergillus flavus	34
2	Aspergillus niger	14
3	Cryptococcus neoformans	54
4	Curvularia sp	16
5	Trichosporon sp	15
6	Candida albicans	37

Spectroscopic analysis

In the FT-IR spectrum of the electrochemical product, the stretching frequency for O-H, the broad peak appears at 3496 cm^{-1} , and the stretching frequency for N=CH appears at 1605 cm^{-1} . In the ^1H NMR spectrum, two OH protons appear at 10.5 ppm, one NH proton appears at 9 ppm, one imine proton appears at 8.3 ppm, three methoxy protons appear at 3.3 ppm. In the ^{13}C NMR spectrum, the carbon of imine appears at 169 ppm and the carbon of C=S appears at 190 ppm. The above results indicated that only nitro group of the 5-methoxy-5,6-bis(3-nitrophenyl)-4,5-dihydro-1,2,4-triazine-3(2H)-thione was electrochemically converted to imine in the presence of salicylaldehyde.

Conclusions

The study of the electrochemical reduction of 5-methoxy-5,6-bis(3-nitrophenyl)-4,5-dihydro-1,2,4-triazine-3(2H)-thione in the presence of salicylaldehyde was investigated in a basic, water/ethanol homogeneous medium. The main attention was first paid to the following key parameters, the cathode material, the cathode potential and water/methanol. For conventional electrolysis, the best experimental conditions for Schiff base of 5-methoxy-5,6-bis(3-nitrophenyl)-4,5-dihydro-1,2,4-triazine-3(2H)-thione are the use of a zinc cathode and the potential of -2.7 V/SCE. The bulk synthesis of Schiff base was achieved in single step in an undivided cell.

Disclosure Statement

No potential conflict of interest was reported by the authors.

Supporting Information

Additional supporting information related to this article can be found, in the online version, at DOI: [10.33945/SAMI/AJGC.2020.2.3](https://doi.org/10.33945/SAMI/AJGC.2020.2.3)

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