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Obtaining of Pyrazine-2,3-Dicarboxylic Acid through Electrochemical Quinoxaline Oxidation using Copper Alloys as Anodes

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Abstract: Previous studies have shown that quinoxaline (Q) oxidation with electrochemically regenerated $KMnO_4$, with the formation of pyrazine-2,3-dicarboxylic acid (PDCA), is possible using Pt, Ni, stainless steel and Cu electrodes. In order to improve current knowledge and to expand the variety of electrodes used for the pyrazine-2,3-dicarboxilic acid (PDCA) production process, we investigated the behavior of the copper alloy anodes – brass and bronze. A laboratory electrolyser for PDCA synthesis with copper alloy anode was manufactured. Depending on the anode – copper, brass and bronze - the effect of various parameters on the current and substance efficiencies was investigated. These parameters are: anodic current density, amount of electricity, temperature and initial concentration of quinoxaline. The best performances of this electrolyser are ~88% current efficiencies on the brass electrode and up to 80% substance efficiencies on the bronze electrode, at a current density of 3,5 A/dm^2. These performances are greater than those obtained on the copper anode.

Keywords: pyrazine-2,3-dicarboxylic acid, quinoxaline, copper alloy anodes, current efficiencies, substance efficiencies

1. Introduction

Tuberculosis (TB), caused by *Mycobacterium tuberculosis* (MTB), was responsible for the death of approximately one billion people in the last two centuries. MTB is an insidious pathogenic agent that latently infects approximately two billion people. This is almost 1/3 of the world's population [1]. Globally, 8 million new TB cases appear every year and death ensues in 2 million of those. TB cases are currently on the rise because of drug – resistant strains. The danger is amplified by HIV interference, which affects the immune system [2] and allows latent TB reactivation and increases reinfection susceptibility. Under these conditions TB becomes lethal. Because of these reasons the World Health Organization – WHO – declared in 1993 that TB is a global danger.

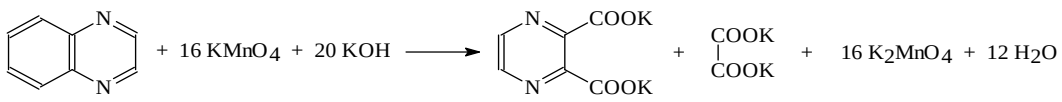
In this context, pyrazinamide (PZA) became one of the main agents used against MTB. Even though PZA is clinically used since 1950, only recently [3] an action mechanism was identified that inhibits MTB fatty acid synthetase I. The inhibition mechanism is similar to the one observed in eukaryotes. It is considered that PZA is a prodrug of pyrazinoic acid (POA), supposed to be the MBA active inhibitor [4]. The essential intermediary pyrazine-2,3-dicarboxylic acid (PDCA) is present in the PZA formation process. This process, as it is specified in the technical literature, consists in the chemical oxidation of quinoxaline with $KMnO_4$ in the presence of NaOH or KOH [5].

The resulting manganate immediately decomposes with the formation of MnO_2 that precipitates and exits the system (eventually the oxidant species is destroyed with methanol resulting MnO_2 and formic acid). This reaction is not competitive because it involves a very large consumption of potassium permanganate. The ratio Q : $KMnO_4$ = 1:16 M (1:14.6 mass).

The studies presented in this paper show how PDCA can be obtained through quinoxaline (Q) oxidation in an electrochemical system, in the presence of $KMnO_4$ and KOH in electrolysis cells with asymmetric current densities. The electrochemical reaction is similar to that observed in the chemical process, but the destruction of obtained permanganate was avoided by carefully controlling the reaction parameters. Furthermore the permanganate was transformed into potassium permanganate – reusable – which leads to a considerable decrease in permanganate consumption.

The K_2MnO_4 reduction to MnO_2 is a secondary reaction which takes place partially through disproportioning and partially through cathodic reduction. In order to confine cathodic reduction the electrode surfaces must be uneven. The advantages of using this electrochemical method are: a considerable decrease in permanganate consumption and subsequently a small resulting MnO_2 quantity.

Previous cyclic voltammetry studies have shown that PDCA formation through Q oxidation with electrochemically regenerated $KMnO_4$ is possible on the Pt [6], Ni [7], stainless-steel [8] and Cu [9] electrodes.



In order to improve current knowledge and to expand the variety of electrodes used for the pyrazine-2,3-dicarboxilic acid (PDCA) production process, the behavior of copper anode alloys – brass and bronze – has been investigated.

2. Experimental

Experimental studies were conducted using a 150 mL water-jacketed glass electrolysis cell. The cell was connected to the electronic assembly shown in figures 1 and 2. This includes: EC – electrolysis cell, mV – milivoltmeter, A – ampermeter, C – coulometer, Re – etalon resistance, Rv – variable resistance, S – power source.

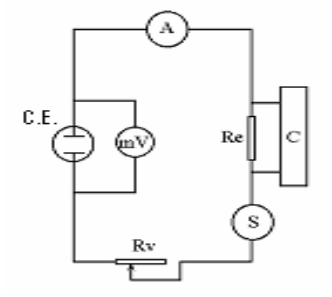


Figure 1. Electronic assembly used for studying Q oxidation through $KMnO_4$ regeneration

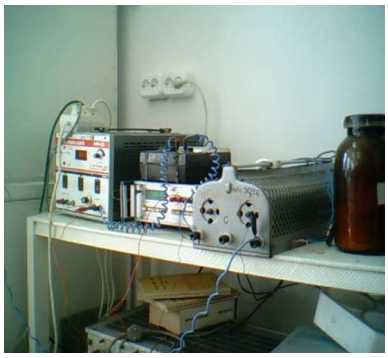


Figure 2. Electronic assembly used for powering the electrolysis cell

Using a thermostat bath the temperature inside the cell was maintained at 35 and 45ºC, respectively. A magnetic stirrer was used for electrolyte solution homogenization.

The electrodes were fixed in the electrolyzer cap. The cathode was manufactured from stainless steel and the anode from copper, bronze and brass, respectively – figures 3 – 5.

Figure 3 shows the copper anode used in the experiments. It was manufactured from a 0.5 mm thick perforated copper plate that ensured access to the solution on both sides of the electrode.

The surface of the anode was 56.5 cm^2 and that of the stainless-steel cathode was 3.4 cm^2. Under these conditions the surface ratio (Sa/Sc) is 16.6.

Copper – zinc (brass) and copper – tin (bronze) mesh electrodes were also used in order to ease the anode manufacturing process as well as to maximally improve solution access to the electrolyte on both sides of the electrode.

Figure 3. Copper anode

First the bronze mesh anode was manufactured (Cu–S alloy) with the following characteristics: 0.24 x 0.071 Φ 0.16 1600. The surface of the bronze anode was 56 cm^2, the surface of the cathode was 3.4 cm^2 and the Sa/Sc ratio was 16.5. Working conditions were the same as with the other electrodes. The anode was prepared through pickling in diluted HNO_3 solution and between syntheses the obtained MnO_2 was removed with a diluted sulfuric and oxalic acid solution. This phase was required because MnO_2 was present in the meshes. The cleaning process unfolded without any problems. The working electrode block is shown in figure 4.

Figure 4. Working electrode block housing the bronze anode and the stainless-steel cathode

Figure 5. Working electrode block housing the brass anode and the stainless-steel cathode

Next the behavior of the brass anode in the Mn(VII) regeneration process was studied. The brass mesh characteristics are: 0.4 Φ 0.16 1200. The working electrode block is shown in figure 5. The surface of the anode was the same (56 cm^2) while that of the cathode was 3.4 cm^2. Electrode preparation for reaction and between determinations was identical with that of the bronze electrode.

Before use, any oxides that could have been present on the surface of the anode were removed through pickling in diluted HNO_3 solution. Between syntheses, when necessary, any MnO_2 deposits were removed by dipping the electrode in a diluted sulfuric and oxalic acid solution. Initial KOH concentration in the electrolyte solution was 16.6% and the amount of potassium permanganate was 1g (1.4%). 2 g of quinoxaline were dissolved in H_2O (6.25% solution) and subsequently added to the reaction process in 3 mL doses (0.2 g Q) at every 10 minutes and a current density of 3.5 A/dm^2 – equivalent to a 2 A current. This was the ratio between the Q, KOH and amount of electricity used during the syntheses. By modifying one of the parameters the others are also modified accordingly, ensuring their appropriate correlation.

Essential for reaction success is to ensure a good correlation between the rate of the Mn(VII) electrochemical regeneration reaction and the rate of the quinoxaline chemical oxidation reaction for PDCA formation. This is the reason why Q is added in several stages – it is a known fact that the rate of a chemical reaction is proportional with the rate constant and with reagent concentrations. Mn(VII) concentration has to be constant – something that can be achieved by controlling the rate of its electrochemical regeneration reaction (anodic current density) – so that the chemical reaction can be controlled only through the Q concentration added in the reaction. If the Q concentration in the electrolyte solution is too high, the chemical reaction rate is also too high and there's the risk that all Mn(VII) will be consumed as well as the Mn(VI). This way the obtained MnO_2 cannot be reoxydated to a higher oxidation state, it precipitates and exits the system. As a result the reaction stops – which is exactly what mustn't happen. In order to avoid this the Q feeding rate in the electrolyte was correlated with the current density, thus ensuring that only the necessary Q quantity reacts with regenerated Mn(VII) and – most importantly – that Mn(VII) is not further reduced to Mn(VI) (with regenerable MnO_2 formation).

The reaction process can be followed visually through the color of the electrolyte – purple when Mn(VII) concentration is high, green when the Mn(VI) concentration is high and brown when MnO_2 formed.

After MnO_2 formation the reaction is either stopped [its continuation is pointless because the there is no oxidation agent, MnO_2 can no longer be oxidized to Mn(VII)] or more Mn(VII) is added and the regeneration cycle is resumed.

It seems that MnO_2 also has a catalytic effect on the advanced reduction of Mn(VII) as well as Mn(VI) because its presence in the electrolyte solution increases reaction stagnation probability. The possibility of electrolyte filtering for quick MnO_2 elimination should be taken into account.

After reaction completion the electrolyte solution is cooled down, unreacted Q is recovered through repeated extraction in ethylic ether, ethylic alcohol is added until complete decolorization [all traces of Mn(VII) and Mn(VI) are consumed], obtained MnO_2 is filtered and the clear and colorless solution is processed. The processing consisted in electrolyte solution analysis through conductometric titration, UV investigation and separation of obtained PDCA.

Working conditions effect was investigated – current density, temperature, initial Q and KOH concentrations, used electricity quantity – and the following working parameters were monitored: obtained PDCA potassium salt ($PDCAK_2$) quantity, unreacted Q quantity, current efficiency, substance efficiency and specific energy consumption for $PDCAK_2$ formation.

3. Results and Discussion

Results obtained on the Cu electrode are shown in table 1.

The values from table 1 show that Q oxidation with PDCA formation has taken place. Given a sufficient amount of energy, conversions up to 100% can be achieved.

During the electrochemical reaction, apart from the previously mentioned parameters, the color of the electrolyte solution was also investigated. Even though the initial potassium permanganate quantity was very small – 1 g compared to a necessary of 14.6 g/L g Q for a purely chemical process – the color of the electrolyte solution was purple [due to Mn(VII)] with slight shades of green [due to Mn(VI)] throughout the entire process and regardless of the Q amount. The persistence of the purple color is the best evidence that Mn(VII) electrochemical regeneration takes place on the Cu electrode and thus there is always reagent for Q chemical oxidation.

TABLE 1. Results obtained on the Cu electrode

Nr. crt.	I [A]	i [A/dm^2]	El. Q. [C]	U_{avr} [V]	t [ºC]	m_{Qi} [g]	m_{Qf} [g]	Conv [%]	m_{PDCAK2} [g]	η_s [%]	η_c [%]	En. C. kWh/kg
1.	2	3.5	32400	2.9	45	2	0.2	90	2.7	71.9	52.73	9.67
2.	4	7.1	55000	3.5	45	4	0	100	3.2	42.6	36.82	16.71
3.	1	1.7	30000	2.5	35	2	0.34	83	2	53.3	42.19	10.42
4.	2	3.5	15000	3.1	35	1	0.4	60	1.3	69.3	54.84	9.94
5.	1	1.7	15000	2.2	45	2	1	50	1.88	50.1	79.31	4.88
6.	1	1.7	26000	2.2	45	2	0	100	2.1	55.9	51.11	7.57

Current efficiencies (η_c) varied from 37 to 80% and substance efficiencies (η_s) from 43 to 72%. Under these conditions, specific energy consumptions (*En.C.*) varied between 4.8 and 17 kWh/kg PDCA. The highest current efficiency – of about 80% – was achieved at a current density (*i*) of 1.7 A/dm^2, at 45°C and an electricity quantity (*El. Q.*) of ~ 50% of that theoretically necessary for the complete consumption of Q added to the process. Under these conditions a 50% conversion rate (*Conv*) and a 50% current efficiency were achieved.

The best performances – current efficiencies of ~ 55% and substance efficiencies of up to 72% – were achieved at a current density of 3.5 A/dm^2, at conversions of maximum 90%. Doubling the current density leads to a significant decrease of the current efficiency – down to 37%. This behavior, favored by the high anodic potential, might be due to simultaneous oxygen release and Mn(VII) formation – which means there is current consumption for a by-product.

Temperature has no significant effect in the specified interval. Still the 45°C temperature was used because it is known that the rate of a chemical reaction increases with temperature. At temperatures higher than 50°C secondary reactions incidence also increases and thus 45ºC seems to be the best temperature choice.

In conclusion, Mn(VII) regeneration from Mn(VI), formed during the Q oxidation chemical process, takes place on the Cu electrode. The best performances – maximum current and substance efficiencies and minimum specific energy consumption – are achieved at a current density of 3.5 A/dm^2 in the 35 – 45ºC temperature interval. In order to obtain high current efficiencies studies have to take place at small Q conversions. This implies additional manual labor for unreacted Q separation. In order to achieve high conversion and substance efficiencies studies have to take place at small current efficiencies and this way Q extraction and separation are no longer necessary. The best solution can only be chosen after a serious economic analysis.

As previously specified, different types of electrodes were studied in order to determine their use in the Q oxidation process with electrochemically regenerated potassium permanganate. The results obtained on the bronze electrode are shown in table 2.

The results are as expected – Mn(VI) oxidation to Mn(VII) takes place – and performances obtained on the bronze anode are comparable with those obtained on the Cu electrode. Again, substance efficiencies of up to 80% and current efficiencies of 82% are achieved depending on working and conversion conditions. Conversion efficiency can be 100% given that the used electricity quantity is high enough.

Highest efficiencies were at a 3.5 A/dm^2 current density – substance and current efficiencies of 80% and 82%, respectively. Decreasing current density to 1.7 A/dm^2 leads to an approximately 15% efficiency decrease, but also to an approximately 30% energy consumption decrease, which is significant. When working at small current densities the danger of potassium manganate exhaustion – itself with good oxidative properties – during chemical reaction has to be taken into account. This way MnO_2 is formed, precipitates, cannot be reoxydated to Mn^{7+} and the reaction stops.

Increasing current density to 5.3 A/dm^2 leads mainly to a decrease in current efficiency for reasons already mentioned, but also to an energy consumption increase of ~ 50%.

In conclusion, Mn^{7+} regeneration also takes place on the mesh bronze electrode, with efficiencies and consumptions similar to those obtained on the Cu electrode. The bronze mesh is an achievable solution for manufacturing the electrolyzer anode used in Q oxidation process through potassium permanganate regeneration.

Table 3 shows the results obtained by working on the brass electrode in the same conditions as with the bronze one.

The data from table 3 shows that the brass anode behaves almost identically with the bronze one. The best performances – substance and current efficiencies – are achieved at a current density of 3.5 A/dm^2 and a 45ºC temperature. The smallest specific energy consumptions are obtained at a 1.7 A/dm^2 current density and by increasing this value to 5.3 A/dm^2 energy consumption increases with ~ 100%.

TABLE 2. Results obtained on the bronze anode

Nr. crt.	I [A]	i [A/dm^2]	El. Q. [C]	U_{avr} [V]	t [ºC]	m_{Qi} [g]	m_{Qf} [g]	Conv [%]	m_{PDCAK2} [g]	η_s [%]	η_c [%]	En. C. kWh/kg
1	1	1.7	10000	2.1	45	1	0.3	70	1.1	58.6	69.61	5.30
2	1	1.7	20000	2.1	45	1	0	100	1.3	69.3	41.13	8.97
3	2	3.5	10000	3.5	45	1	0.2	80	1.3	69.3	82.26	7.48
4	2	3.5	20000	3.5	45	1	0	100	1.5	79.9	47.46	12.96
5	3	5.3	20000	3.8	45	1	0	100	1.1	58.6	34.80	19.19

TABLE 3. Results obtained on the brass electrode

Nr. crt.	I [A]	i [A/dm^2]	El. Q. [C]	U_{avr} [V]	t [ºC]	m_{Qi} [g]	m_{Qf} [g]	Conv [%]	m_{PDCAK2} [g]	η_s [%]	η_c [%]	En. C. kWh/kg
1.	1	1.7	10000	2.1	45	1	0.3	70	1	53.3	63.28	5.83
2.	1	1.7	20000	2.1	45	1	0	100	1.35	71.9	42.71	8.64
3.	2	3.5	10000	3.5	45	1	0.2	80	1.4	74.6	88.59	6.94
4.	2	3.5	20000	3.5	45	1	0	100	1.5	79.9	47.46	12.96
5.	3	5.3	20000	3.8	45	1	0	100	0.9	48.0	28.48	23.46

The brass electrode can be successfully used for Mn(VII) regeneration which in turn is used at PDCA formation from Q. By comparing the results obtained on the three electrodes (tables 4 and 5) it can be noticed that the best results are those from the brass electrode at 45ºC and a current density of 3.5 A/dm^2.

TABLE 4. Variation of obtained results at 3.5 A/dm^2 and 45ºC, 80 – 90% conversion efficiency depending on anode type

Electrode	η_s [%]	η_c [%]	En. C. kWh/kg
Cu	71.9	52.73	9.67
Bronze	69.3	82.26	7.48
Brass	74.6	88.59	6.94

TABLE 5. Variation of obtained results at 1.7 A/dm^2 and 45ºC. 100% conversion efficiency depending on anode type and a much higher used energy quantity than theoretically necessary

Electrode	η_s [%]	η_c [%]	En. C. kWh/kg
Cu	55.9	51.11	7.57
Bronze	69.3	41.13	8.97
Brass	71.9	42.71	8.64

4. Conclusions

Results from preliminary syntheses show that Mn^{7+} regeneration from Mn(VI) achieved during the Q oxidation process with PDCA formation is possible and can be done using the studied anodes – copper, bronze and brass. Perforated and mesh anodes were used to ensure electrolyte access on both sides of the electrode.

In order to ensure reaction efficiency it is essential to obtain a good correlation between the Mn(VII) regeneration electrochemical reaction rate and the Q oxidation chemical reaction rate with PDCA formation. This is the reason why Q is added in several stages – to control chemical reaction rate. On the other hand Mn^{7+} concentration should be kept constant and this is ensured by controlling the electrochemical regeneration reaction rate (through anodic current density). If the Q concentration in the electrolyte solution is too high, the chemical reaction rate is also high and there's the risk that all Mn(VII) will be consumed as well as the Mn(VI). This way the obtained MnO_2 cannot be reoxydated to a higher oxidation state, it precipitates and exits the system. As a result the reaction stops – which is exactly what mustn't happen. In order to avoid this the Q feeding rate in the electrolyte was correlated with the current density, thus ensuring that only the necessary Q quantity reacts with regenerated Mn(VII) and – most importantly – that Mn(VII) is not further reduced to Mn(VI) (with regenerable MnO_2 formation).

The reaction process can be followed visually through the color of the electrolyte – purple when Mn(VII) concentration is high, green when the Mn(VI) concentration is high and brown when MnO_2 formed. After MnO_2 formation the reaction is either stopped [its continuation is pointless because there is no oxidation agent, MnO_2 can no longer be oxidized to Mn(VII)] or more Mn(VII) is added and the regeneration cycle is resumed.

It seems that MnO_2 also has a catalytic effect on the advanced reduction of Mn(VII) as well as Mn(VI) because its presence in the electrolyte solution increases reaction stagnation probability.

By analyzing the obtained experimental data, working conditions for Q oxidation with electrochemically regenerated potassium permanganate on copper and copper alloy anodes were established: temperatures of 35 and 45°C, a current density of 3.5 A/dm^2 and intense stirring. Under these conditions, depending on the amount of used electricity quantity, Q conversions of up to 100% efficiency, substance efficiencies between 60 and 85%, current efficiencies between 40 and 80% and specific energy consumptions between 5 and 9 kWh/kg can be obtained.

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