

ELECTROCHEMICAL HALOGENATION OF FLUORESCEIN IN BATCH AND FLOW REACTORS

D VASUDEVAN AND C A BASHA

Central Electrochemical Research Institute, Karaikudi 630 006. INDIA

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Electrochemical halogenation of fluorescein has been carried out in a batch and a flow reactor with batch recirculation, to yield eosin and erythrosin, in continuation of the earlier work. The effect of halogenating agent on the product yield, advantages of the electrochemical method and advantages of the flow reactor with batch recirculation over that of a batch reactor are discussed. The probable mechanism of electrochemical halogenation is discussed.

Keywords: Electrochemical halogenation, Eosin, Erythrosin, Batch and flow reactors, Mechanism

INTRODUCTION

Eosin and erythrosin, the disodium salts of tetrabromo and tetraiodofluorescein, find extensive industrial applications [1-4]. For their synthesis, electrochemical halogenation was sought for, in view of a mixture of halogenated products obtained upon chemical halogenation [2,3-5]. Accordingly, in previous studies [6-8], a detailed investigation on the electrochemical halogenation of fluorescein was made in a batch reactor and the conditions for obtaining pure eosin and erythrosin optimised to obtain best yield of the product and are as follows:

Anode-DSA; Cathode-Stainless steel; Separator-nylon; Electrolyte- NaHCO_3 (for eosin) and Na_2CO_3 (for erythrosin); Halogenating agent- KBr (for eosin) and I_2 (for erythrosin)

In continuation to the earlier studies, the present work has been extended to the use of different halogenating agents for the bromination and iodination of fluorescein, under electrochemical conditions. Chemical synthesis has also been made and the chemical and electrochemical synthetic products have been compared. The electrochemical halogenation has been carried out both in a batch reactor and in a flow reactor with batch recirculation and the results compared and the advantages of the flow reactor for this

reaction have been highlighted. Attempts to understand the mechanism of halogenation have been made.

EXPERIMENTAL

Galvanostatic electrolysis was carried out using a DC power supply (Aplab 7711), in a 100 ml beaker (batch reactor) with 2 stainless steel cathodes covered with nylon as separator (2 rounds) and a dimensionally stable anode (DSA or $\text{Ti/TiO}_2/\text{RuO}_2$ of area 0.013 dm^2 , Titanium Tantalum products, Madras) with inter-electrode distance of 1 cm. The electrolyte solution consisted of 1 g fluorescein, 2.2 g NaBr (or 2.53 g of KBr or 3.1 ml Br_2) and 5 g NaHCO_3 dissolved in 50 ml water. The solution was stirred using a magnetic stirrer and a pellet. A current of 0.65 A was passed. At the end of electrolysis, the current was switched off and the solution was neutralised with HCl to precipitate tetrabromo/tetraiodofluorescein.

For the flow reactor with batch recirculation, a one litre beaker served as the reservoir. The electrolyte constituents were 10 g fluorescein, 21 g NaBr and 50 g NaHCO_3 in 500 ml water. Expanded DSA (0.4 cm^2) and 2 stainless steel sheets with 2 rounds of nylon wound around served as the electrodes. Flow of the electrolyte into the reactor was initiated through a magnetic pump (Syp. Engineering

Corporation, Bombay, Model MD 30R). The power source was then switched on and a current of 2 A passed.

During the progress of electrolysis in a batch/flow reactor, the parameters-cell voltage, pH and temperature were monitored. UV visible spectra were recorded at regular time intervals during the progress of electrolysis. The absorptivity of the disodium salts in 1 gm cm^{-1} of fluorescein, mono, di, tri and tetra halofluorescein are reported in literature [6,7]. Paper chromatograms were developed with Whatman No. 1 as adsorbent and a solvent mixture consisting of EtCOMe: NH_3 : MeCOMe in the ratio 4:1:1 as the eluant in the case of iodination [6].

Chemical synthesis of eosin and erythrosin in glacial acetic acid was made, as per the literature method [2,5] and the products analysed by UV-visible spectra recorded at regular time intervals. Also chemical synthesis was attempted with conditions as used under electrochemical conditions.

RESULTS AND DISCUSSION

Bromination in a batch reactor/flow reactor with batch recirculation

The results of the effect of brominating agent on the yield and absorption maxima (λ_{max}) of the product are given in Table I. It can be concluded from Table I that bromination of fluorescein is complete (yielding eosin, λ_{max} 518 nm), only under electrochemical conditions (with $\text{Br}_2/\text{NaBr}/\text{KBr}$ as brominating agent). The pH and voltage changes during the course of the electrochemical bromination were found to be similar (8.4-9.0 for all three cases and 5.0-5.5 V, 4.5-5.0 and 4.5-5.0 V) in the three cases. Chemical bromination to eosin (conditions similar to that under electrochemical conditions) is ruled out as the product

TABLE I: Effect of brominating agent on the yield and λ_{max} of the product in a batch reactor under electrochemical (current density 5 A/dm^2) and chemical bromination

Brominating agent	Yield (%)	λ_{max} (nm)
KBr	94	518
NaBr	93	518
Br_2	91	518
Br_2^{a}	*	500
Br_2^{b}	*	515

a Chemical bromination (with electrolytes as used under electrochemical conditions); b Conventional chemical method

TABLE II: Effect of current density (CD) on the λ_{max} of the bromination product of fluorescein in a flow reactor with batch recirculation

CD (A/dm^2)	Yield (%)	λ_{max} (nm)
2.5	*	514
5.0	93	518
7.5	*	515

* Yield not determined as the product eosin is contaminated with di and tribromofluorescein

corresponds only to dibromofluorescein (λ_{max} 500 nm) when the reaction was carried out without passing current. Chemical bromination in acetic acid medium [2] resulted in a mixture of tri and tetrabromofluorescein (λ_{max} 515 nm) under our lab conditions.

The effect of current density on the yield and λ_{max} of the product for the bromination of fluorescein in a flow reactor with batch recirculation is shown in Table II. It can be seen that at a current density of 2.5 A/dm^2 , the λ_{max} of the product is only 514 nm, indicating that the current density (electrode potential) is too low for the reaction to proceed to completion. At a current density of 7.5 A/dm^2 , the λ_{max} of the product is only 515 nm, indicating incomplete bromination, possibly due to oxygen evolution being facilitated at higher current densities. 5.0 A/dm^2 is the optimum current density for the reaction.

Iodination in a batch reactor/flow reactor with batch recirculation

The paper chromatograms developed during the progress of electrolysis showed well separated bands with retention factors of 0.05, 0.11, 0.41, 0.61 and 0.91 corresponding to fluorescein, mono, di, tri and tetraiodofluorescein, respectively. The colours of the bands varied from deep

TABLE III: Effect of varying the stoichiometric ratio f:KI on the λ_{max} of the product and yield of erythrosin

f:KI	Yield (%)	λ_{max} (nm)
1:1	*	500
1:4	*	510
1:6	*	515
1:8	90.2	525

* Yield not determined as the product erythrosin is contaminated with di and tri-iodo-fluorescein

TABLE IV: Effect of iodinating agent on the λ_{\max} and yield of erythrosin in a batch reactor under electrochemical (CD = 5 A/dm²) and chemical iodination

Iodinating agent	Yield (%)	λ_{\max} (nm)
KI	90.2	525
I ₂	*	515
I ₂ ^a	*	500
I ₂ ^b	*	510

* Yield not determined as the product erythrosin is contaminated with di and triiodofluorescein

a Chemical iodination (with electrolytes as used under electrochemical conditions)

b Conventional chemical method

orange to orange, orange rose, light rose and rose, respectively.

The effect of varying the stoichiometric ratio of fluorescein:KI(f:KI) for the reaction in a batch reactor on the λ_{\max} of the product and the yield of erythrosin can be seen in Table III. With f:KI stoichiometric ratio of 1:8, the reaction goes to completion (to erythrosin, yield 90% with λ_{\max} of 525 nm, which is very close to that for erythrosin) and at other stoichiometric ratios, only mono, di or triiodofluorescein is formed, as can be seen from much lower values of λ_{\max} observed.)

Table IV compares the effect of iodinating agents on the λ_{\max} and yield of erythrosin for reaction in a batch reactor. It is seen from Table IV from the λ_{\max} values of the product that better electrochemical conversion to tetraiodo product is

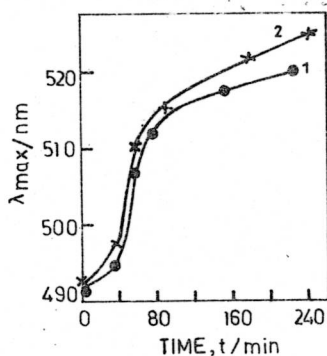


Fig. 1: Plot of λ_{\max} versus electrolysis time for the electrochemical iodination of fluorescein in a batch reactor with I₂ (1) and KI (2) as the iodinating agents (f: I₂ in 1:8 stoichiometry)

achieved with KI rather than with I₂. Lower solubility of iodine and/loss of iodine by sublimation may be responsible for lower conversion. Chemical iodination results only in the mono or diiodo fluorescein. Typical plot of λ_{\max} versus time of electrolysis for the electrochemical iodination of fluorescein in a batch reactor with I₂ and KI is shown in Fig. 1 (F: I₂/KI in 1:8 stoichiometry).

The effect of current density on the yield and λ_{\max} of the product for the iodination of fluorescein in a flow reactor with batch recirculation is shown in Table V. It can be seen that at a current density of 2.5 A/dm², the λ_{\max} of the product is only 516 nm indicating incomplete iodination. At a current density of 7.5 A/dm², the λ_{\max} of the product is only 515 nm, again indicating incomplete iodination, possibly due to oxygen evolution being facilitated at higher current densities. 5.0 A/dm² is the optimum current density for the reaction.

Discussion and mechanism of halogenation

Electrochemical halogenation of fluorescein (under optimised conditions) yielded purer products as compared to chemical halogenation. Use of hazardous Br₂ can be avoided by using NaBr, wherein bromine can be generated in situ at the anode. Use of NaBr is preferred to that of KBr as the former is cheaper (which would reduce cost considerably when scale up studies are made) and has higher solubility in aqueous media than the latter. Use of NaOH, costly K₂S₂O₈ and I₂ can also be avoided, in case of iodination, wherein NaI or KI can be used.

Advantages of flow reactor with a batch recirculation as compared to a batch reactor for electrochemical halogenation are

* Blocking of the expanded anode surface by product/products is avoided in the flow method as the electrolyte flow is perpendicular to the expanded anode surface.

TABLE V: Effect of current density on the yield and λ_{\max} of the product for the iodination of fluorescein in a flow reactor with batch recirculation

CD (A/dm ²)	Yield (%)	λ_{\max} (nm)
2.5	*	516
5.0	90	525
7.5	*	515

* Yield not determined as the product erythrosin is contaminated with di and triiodofluorescein

- * Reactor to reservoir volume ratio being smaller prevents heating up of the electrolyte solution and hence loss of Br_2/I_2 .
- * Scaling up is more convenient with a batch recirculation system. Continued electrolysis can be carried out adjusting the bromide/iodide concentration and by adding fluorescein batchwise.

The probable mechanism of bromination of fluorescein was discussed in detail in an earlier communication [8]. Bromination of fluorescein occurred by the anodically generated bromine or by the reaction of cation radical of fluorescein with bromide ion. During the progress of bromination, only fluorescein and eosin were found in different proportions. However, in the case of iodination, the results of UV-visible spectral studies showed that the reaction proceeded via the intermediary iodination products—mono, di and triiodofluorescein. This is evident from the Fig. 1 wherein with the progress of electrolysis in the case of iodination of fluorescein in a batch reactor, the λ_{max} value for the product shifts to that for mono, di and triiodofluorescein correspondingly during the progress of electrolysis, and finally, tetraiodofluorescein is formed.

One reason for the above observation may be that the bromination is much faster than the iodination. Secondly, a different mechanism may be operative in the two cases. It is due to larger atomic size and greater electropositive nature of iodine that generation of positive iodine species (I^+ , I_2^+)

is easier as compared to that in case of bromide and chloride. The formation of such species is likely to be catalysed at a DSA, which can attack fluorescein as an electrophile to yield erythrosin. It may be mentioned here that the mechanism of electrochemical halogenation of organic substrates in general is still unclear and is yet to be established.

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REFERENCES

1. *Encyclopedia of Industrial Chemical Analysis*, eds F D Snell and L S Ettre, Interscience, New York, **10** (1970) 447-547
2. *Thorp's Dictionary of Applied Chemistry*, eds J.F Thorpe and M A Whiteby, Longman's green, London, **4** (1946) 316
3. *The Merck Index, An Encyclopedia of Chemicals, drugs and biologicals*, 11th ed, S Budavari, Merck and Co, New Jersey (1989) 564
4. G G Hawley, *The condensed chemical dictionary*, 8th edn, Van Nostrand Reinhold, New York (1971) 349
5. M Gomberg and D L Tabern, *J Ind Eng Chem*, **14** (1922) 1115
6. D Vasudevan and P N Anantharaman, *J Appl Electrochem*, **23** (1993) 808
7. D Vasudevan and P N Anantharaman, *J Appl Electrochem*, **24** (1994) 1188
8. D Vasudevan and C A Basha, *J Ind Chem Soc*, **75** (1998) 165