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Electrochemical synthesis of eosin from fluorescein

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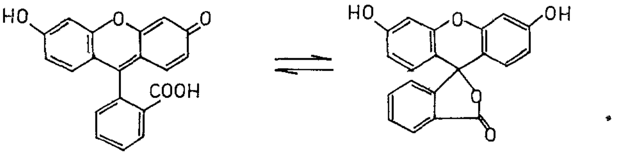
Electrosynthesis of eosin has been carried out by brominating fluorescein in different media such as $NaHCO_3$, CH_3COONa, NH_3, etc., and also in several binary electrolyte mixtures at stationary/rotating anodes at different current densities and temperatures. Based on the results of the yield and dye content obtained in different media, the best conditions for the electrosynthesis of eosin have been selected. The yield of eosin was extremely sensitive to electrolyte pH. $NaHCO_3$ and CH_3COONa were found to be suitable media. TSIA(Ti/TiO_2, RuO_2) was found to be most suitable in the production of eosin. An attempt at reuse of electrolyte was successful in $NaHCO_3$ medium with the dye being isolated as its sodium salt. A plausible mechanism for the bromination of fluorescein has been discussed. Scale-up studies on eosin are in progress.

1. Introduction

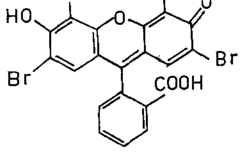
Eosin (disodium salt of 2,4,5,7-tetrabromo–9-*o*-carboxyphenyl–6-hydroxy–3-isoxanthone or tetrabromofluorescein) is an important colouring dye. It has been classified under 'D and C' colours – those certifiable for use in colouring drugs and cosmetics intended for internal application or ingestion according to the Federal Food, Drug and Cosmetic Act (1938) [1]. It is used commercially in the manufacture of red inks; to a lesser extent as a dye for silk, paper, cotton, wool and cellulose esters and in the cosmetic industry for lipstick and nailpolish colouring (except for use in the eye area) and also in colouring motor fuel [2–4]. Red 21 and Red 22 are the trade names for tetrabromofluorescein and eosin, respectively. Erythrosin (disodium salt of 2,4,5,7-tetraiodofluorescein), an analogue of eosin, is useful in colouring foods, drugs and cosmetics [1].

Bromination of fluorescin (**1**), which exists in two tautomeric forms as shown below, using bromine in glacial acetic acid [2] or alcohol [5] medium yields eosin (**2**). It is prepared on a large scale by acidifying an alkaline solution of fluorescein, also containing bromide and bromate, dissolving the precipitated dye in aqueous K_2CO_3 and evaporating to crystallize [2].



Fluorescein (1)

In the chemical methods, contamination of eosin by the di and tri-brominated fluorescein was observed. Hence an alternate route using electrochemical means was thought of for the production of eosin. It is important to mention here that there are no reports available to date on the electrochemical synthesis of eosin.



Tetrabromofluorescein (2)

A plausible mechanism of bromination of fluorescein has also been suggested.

2. Experimental details

Preliminary experiments on the electrolysis of fluorescein were carried out in a $1/2\,dm^3$ beaker using 500/1000 ml of an electrolyte containing 10/20 g of fluorescein and 25.32/50.64 g of KBr using a stationary or rotating anode and stainless steel cathode. The different electrolyte media and anode materials employed and the anode current densities used are listed in Table 1. The experiments were carried out both with and without a diaphram. A ceramic porous pot (containing all constituents of the anolyte except fluorescein, and the cathode) or nylon cloth (two rounds wound around the cathode) served as a diaphram. The electrolyte was agitated by means of an overhead stirrer or by a rotating anode, the rate of which was controlled by means of a dimmerstat. A current of 8 Faraday per mole of fluorescein was passed. Fifty to 100% extra current in addition to theoretical current was necessary for the completion of electrolysis. The electrolysed solution was then neutralized with HCl when eosin precipitated along with other bromination products, if any. The product was then filtered, dried and weighed.

Table 1

S	*Parameter*	*Experimental conditions*
1a	Electrolytes and their pH	5–17% $NaHCO_3$ (pH 8.62–8.64), 20% CH_3COONa (pH 9.0), 10% NH_3 (≈ 25% solution) (pH 10.98), 10% $(NH_4)_2CO_3$ (pH 8.55), 5% $Na_2B_4O_7$ (pH 9.74)
b	Mixed electrolytes	10% CH_3COONa; 5% $NaHCO_3$, 5% CH_3COONa; 1% NH_3, 20% CH_3COONa; 2.5% $Na_2B_4O_7$, 10% CH_3COONa; 0.2% NaOH
2	Anode	Expanded TSIA, graphite, rotating TSIA, rotating PbO_2/graphite
3	Anode current density/A dm^{-2}	3–9 (stationary), 10–20 (rotating)

Different electrolytes including binary electrolyte mixtures were employed (Table 1) in an attempt to improve the solubility of fluorescein. It was quite low in CH_3COONa medium where the electrolyte was used as a suspension. However, as eosin began to form, it went into solution.

The progress of electrolysis was followed by paper chromatography. A Whatman paper No. 1 was used as the adsorbent and a solvent-mixture consisting of methyl ethyl ketone (42.5 ml), acetone (10 ml), water (1.8 ml), and ammonia (5 ml), served as the eluant. Clear, well separated bands with retention factors (R_f) of 0.01, 0.08, 0.22, 0.31 and 0.64 were observed for fluorescein, mono, di, tri, and tetrabromofluorescein, respectively. The colour of the band also varied from dark yellow, orange, light orange, orange–rose to rose.

The optimum conditions for obtaining maximum yield of eosin were found and were employed for scale up to a higher amperage cell. Scale up to a 29 A cell was carried out by electrolysing 120 g of fluorescein (added in six equal instalments) contained in 3 dm^3 of 10% $NaHCO_3$ solution, with the required amount of KBr, in a PVC cell (19.4 cm × 12 cm) consisting of three expanded TSIA (area: 5.75 dm^2) and two stainless steel cathodes (area: 5.90 dm^2) with nylon diaphram, alternately placed with an interelectrode distance around 1 cm. Similarly, scale up to a 24.5 A cell was carried out by electrolysing 100 g of fluorescein contained in 5 dm^3 of 20% CH_3COONa solution with the required amount of KBr, in a perspex cell (19.6 cm × 19.6 cm × 24.4 cm) consisting of two expanded TSIA (area: 4.89 dm^2) and three stainless steel cathodes (area: 4.70 dm^2) wound with nylon cloth (two rounds).

The yield of eosin reported is based on the amount of solid isolated at the end of electrolysis. However, under certain experimental conditions, some unreacted fluorescein, and mono, di, and tribrominated fluorescein were also found. More precise information about the purity of eosin is obtained from its dye content (determined by u.v.–visible spectrophotometry or gravimetry).

The absorptivity, in l g^{-1} cm^{-1} (measured at the corresponding wavelength in nanometres) of fluorescein, 4-monobromo, 2,4- or 2.5-dibromo, 4,5-dibromo, 2,4,5-tribomo and 2,4,5,7-tetrabromo fluorescein are 258(492), 206(498), 188(506), 163(504), 157(512) and 149(518), respectively [1]. A test certificate was issued for the dye content of some samples determined gravimetrically by the Chemical Testing and Analytical Laboratory, Guindy, Madras-32, India.

All experiments were carried out at 40 ± 5° C except for one carried out in the range 82–86° C).

3. Results and discussion

Preliminary studies on the effect of variation of fluorescein : KBr ratio on the product yield showed that only when the ratio was 1 : 8 did complete conversion of fluorescein to eosin occur. The effect of varying the experimental parameters on the yield of eosin, in 10% $NaCHO_3$ was studied and the results are presented in Table 2. The best result was observed for the electrolysis in 10% $NaHCO_3$ using TSIA at a current density of 5 A dm^{-2} with nylon as diaphram (S2 in Table 2). At current densities greater than 5 A dm^{-2} the decrease in the yield of eosin may be due to competing oxygen evolution (S3 and 4). With 5% and 17% $NaHCO_3$, though the yields were slightly higher, the dye contents were lower (S5 and 6). It is also seen that the yield, as well as the dye content, were much lower at a graphite anode than with a TSIA and a

Table 2. Effect of variation in the experimental parameters on the yield of eosin in $NaHCO_3$ medium (diaphram: nylon; $T = 40 + 5°$ C)

S	*% $NaHCO_3$*	*Anode*	*Anode c.d. /A dm^{-2}*	*Cell current /A*	*Cell voltage /V*	*Yield*† */%*	*Dye content /%*
1*	10	TSIA	3	2.7	4.5	75.6	93.3
2*	10	TSIA	5	4.6	5.5	94.2	94.5
3*	10	TSIA	7	6.4	6.0	92.7	87.8
4	10	TSIA	9	8.2	6.5	82.5	64.7
5	5	TSIA	5	4.6	6.0	96.3	89.3
6	17	TSIA	5	4.6	5.5	94.8	56.9
7	10	TSIA	5	29.0	7.0	92.7	89.0
8	10	Graphite	5	4.1	6.0	83.0	52.6
9	10	Rotating TSIA	10	4.7	4.0	93.7	94.5
10	10	Rotating PbO_2/graphite	10	8.0	7.0	90.7	31.4

*Dye content determined by gravimetry.

†Yield based on eosin assumed as the exclusive product.

Table 3. Effect of variation in the experimental parameters on the yield of eosin in 20% CH_3COONa medium ($T = 40 + 5°$ C)

S	*Anode*	*Diaphram*	*Anode c.d.* /A dm^{-2}	*Cell current* /A	*Cell voltage* /V	*Yield*† /%	*Dye content* /%
1*	TSIA	Porous pot	5	6.2	8.0	80.0	91.9
2*	TSIA	–	5	4.6	5.5	83.5	88.5
3*	TSIA	Nylon	5	4.6	5.5	87.0	92.6
4	TSIA	Nylon	5	19.2	6.0	86.9	–
5	TSIA	Nylon	5	24.5	6.0	85.0	–
6‡	TSIA	Nylon	5	4.6	4.0	88.2	–
7	Rotating TSIA	Nylon	10	6.3	4.5	87.2	92.5
8	Rotating PbO_2/graphite	Nylon	10	8.0	4.5	82.8	61.3

*Dye content determined by gravimetry.
†Yield based on eosin assumed as the exclusive product.
‡$T = 82–86°$ C.

rotating PbO_2/graphite anode than with a rotating TSIA (S2, 8, 9 and 10). Choosing the optimum conditions from Table 2 (S2), scale up of the cell to 29 A was carried out (S7). The results showed a good yield of eosin with a high dye content. In view of the considerable solubility of fluorescein and high solubility of eosin in 10% $NaHCO_3$ media instalment additions of fluorescein were made to saturate the dye as its sodium salt.

The results on the effect of variation of different experimental parameters in 20% CH_3COONa on the yield of eosin are shown in Table 3. Best results are observed with a TSIA or rotating TSIA, with nylon as diaphram (S3 and 7). The yield and dye content of eosin were reduced considerably when the porous pot was used, or when no diaphram was used (S1 and 2). The low porosity of the porous pot offers considerable resistance to the current. This was evident from the higher cell voltage. When no diaphram was used, some of the brominated product was debrominated at the cathode, thereby reducing the yield and dye content. On scale up to a 19.2 A or 24.5 A cell, the yield of eosin was only slightly reduced (S4 and 5). Also, as the temperature was raised from 40° C to 82–86° C, the yield of eosin was little affected (S6). The yield and the dye content of eosin were much lower at a rotating PbO_2/graphite anode as compared to those at a rotating TSIA (S7 and 8).

The results showing the effect of electrolyte medium on the yield of eosin (for the electrolysis of fluorescein with TSIA and with nylon as diaphram) are shown in Table 4. In the case of electrolytes, NH_3, $(NH_4)_2CO_3$, and $Na_2B_4O_7$ (S1–3), the dye content was quite poor indicating that bromination was incomplete. The pH values for NH_3 and $Na_2B_4O_7$ are much higher than those for $NaHCO_3$(8.64) and CH_3COONa(9.0). It is likely that at higher pH, bromide was irreversibly oxidized to bromate, which caused a loss in the bromine content available for bromination. In the case of binary electrolyte mixtures (S4–7), the dye content was very low, for the same reasons as stated above. In the case of $(NH_4)_2CO_3$ (pH 8.55, S2), during the course of electrolysis, the electrolyte became hot, thereby causing its decomposition to NH_3 and CO_2. Formation of NH_3 raises the pH and, hence, lowers the dye content. $(NH_4)_2CO_3$ melts at 58° C with decomposition [7].

An attempt was also made to synthesize dibromofluorescein by passing half the current as that required for eosin, with TSIA or graphite anode in 20% CH_3COONa. With TSIA, eosin was the major product along with unreacted fluorescein. However, with graphite anode, mixtures of various brominated products, as well as unreacted fluorescein, were found at the end of electrolysis.

The absorption maxima for the products obtained in different media are given in Table 5. It can be seen that with TSIA and with $NaHCO_3$ or CH_3COONa as electrolyte, tetrabromofluorescein was the exclusive product (S1 and 2). With other electrolytes, the bromination was incomplete and intermediary bromination products predominated (S3–5). This suggests the necessity for strict control of pH. Also, use of graphite instead of TSIA, in $NaHCO_3$ medium resulted in the formation of dibromo-

Table 4. Effect of variation in the electrolyte medium on the yield of eosin (anode: TSIA; diaphram: nylon; anode c.d.: 5 A dm^{-2}; $T = 40 + 5°$ C)

S	*Electrolyte*	*Cell current* /A	*Cell voltage* /V	*Yield** /%	*Dye content* /%
1	10% NH_3	4.6	5.5	92.9	53.2
2	10% $(NH_4)_2CO_3$	4.6	5.5	92.9	53.0
3	5%$Na_2B_4O_7$	9.2	6.5	87.0	59.6
4	10% CH_3COONa; 5% $NaHCO_3$	9.2	6.5	87.0	50.3
5	5% CH_3COONa; 1% NH_3	9.2	6.5	87.0	61.3
6	20% CH_3COONa; 2.5% $Na_2B_4O_7$	9.2	8.0	91.9	66.3
7	10% CH_3COONa; 0.2% NaOH	9.2	6.5	89.4	68.8

*Yield based on eosin assumed as the exclusive product.

Table 5. λ_{max} *values for the electrolysis products in different media*

S	*Medium*	*Anode*	λ_{max}	*Main product*
1	$NaHCO_3$	TSIA	517.6	Tetrabromofluorescein
2	CH_3COONa	TSIA	517.2–517.6	Tetrabromofluorescein
3	$(NH_4)_2CO_3$	TSIA	500.8	Mono and dibromofluorescein
4	$Na_2B_4O_7$	TSIA	500.8	Mono and dibromofluorescein
5	20% CH_3COONa; 2.5% $Na_2B_4O_7$	TSIA	498.8	Monobromofluorescein
6	$NaHCO_3$	Graphite	505.0	Dibromofluorescein
7	CH_3COONa	Rotating PbO_2/graphite	517.2	Tetrabromofluorescein
8	CS*	–	514.4	Tri and tetrabromofluorescein

*Commercial sample (CS) of eosin.

fluorescein as the main product (S6). In CH_3COONa medium, with the PbO_2/graphite anode (S7), though the tetra product predominated, much unreacted fluorescein was seen even after passing double the theoretical current. Further, in this medium, the PbO_2 coating was found to peel off after 2–3 runs. A commercial sample of eosin (S8) was found to be contaminated by tribromofluorescein (and also dibromofluorescein to some extent).

In conclusion, $NaHCO_3$ and CH_3COONa media are suitable for the synthesis of eosin with high dye content. In the former medium, due to higher solubility of fluorescein and also that of eosin, isolation of the dye as its disodium salt has proved successful. TSIA or rotating TSIA is found to be superior to graphite/PbO_2 over graphite anode for the production of eosin. At graphite, competitive oxygen evolution is responsible for lowering the yield. It is also seen from Tables 2 and 3 that the cell voltage is lower when TSIA/rotating TSIA was used than when graphite/PbO_2 over graphite was used, indicating that TSIA catalyses bromine evolution. It has been reported that in the electrolysis of NaBr or HBr solutions, Ti/TiO_2, RuO_2 surface is a catalyst [8]. Further scale-up studies are being carried out.

3.1. *Mechanism of bromination*

The following may be suggested as the mechanism for bromination:
At the anode

$$2Br^- \rightarrow Br_2 + 2e^- \qquad (1)$$

At the cathode

$$2H_2O + 2e^- \rightarrow 2OH^- + H_2 \qquad (2)$$

In the solution

$$Br_2 + H_2O \rightleftharpoons HBrO + H^+ + Br^- \qquad (3)$$

$$HBrO \rightleftharpoons H^+ + BrO^- \qquad (4)$$

$$\text{Fluorescein} + 4Br_2 \rightarrow \text{Eosin} + 4HBr \qquad (5)$$

The probable side reactions are:
At the anode

$$6BrO^- + 3H_2O \rightarrow 2BrO_3^- + 4Br^-$$

$$+6H^+ + \tfrac{3}{2}O_2 + 6e^- \qquad (6)$$

$$2H_2O \rightarrow O_2 + 4H^+ + 4e^- \qquad (7)$$

$$BrO_3^- + H_2O \rightarrow BrO_4^- + 2H^+ + 2e^- \qquad (8)$$

At the cathode

$$BrO^- + H_2O + 2e^- \rightarrow Br^- + 2OH^- \qquad (9)$$

In solution

$$2HBrO + BrO^- \rightarrow BrO_3^- + 2Br^- + 2H^+ \qquad (10)$$

$$Br_2 + Br^- \rightleftharpoons Br_3^- \qquad (11)$$

The estimated bromate content in the electrolysed solution was negligible (less than 1%) for the electrolysis in $NaHCO_3$ and CH_3COONa media, but was considerable with other electrolytes, including binary electrolyte mixtures, where the pH was above 9. This is due to the occurrence of Reactions 6, 8 and 10 at $pH > 9$ [9]. The debromination reaction, Reaction 9, was predominant when no diaphram was used, as reflected in the lower dye content. Oxygen evolution, Reaction 7, is competitive to bromine evolution and causes a decrease in the current efficiency: 20–50% and 50–100% extra current was necessary for complete conversion to eosin in CH_3COONa and $NaHCO_3$ media, respectively. At $pH < 9$, Reaction 11 is practically negligible [10].

The results clearly indicate the superiority of the electrochemical method over the chemical method. So, a mechanism involving homogeneous bromination by the anodically generated bromine alone cannot explain the above fact. Nucleophilic attack of the bromide ion on the cation radical of fluorescein [11], or the possibility of $Br_2^{\cdot-}$ as the brominating species under electrochemical conditions are also possible [12]. The need for excess bromide and extra current could be due to adsorption of Br^- on the anode which could block surface oxidation to some extent [13].

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