SHORT COMMUNICATION

Electrochemical synthesis of erythrosin from fluorescein*

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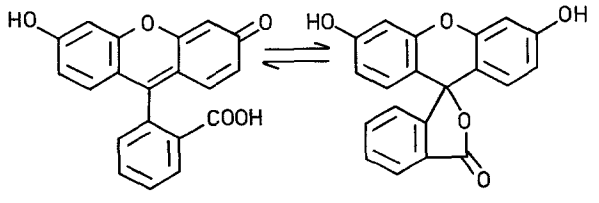
1. Introduction

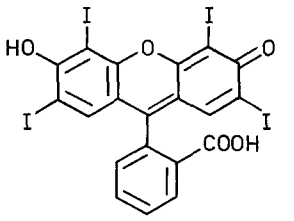
Erythrosin (disodium salt of 2,4,5,7-tetraiodo-9-*o*-carboxyphenyl-6-hydroxy-3-isoxanthone or tetraiodofluorescein or iodescein) is an important xanthene dye. It has been classified under FD and C colours, i.e. those certifiable for use in food colouring, drugs and cosmetics according to the Federal Food, Drug and Cosmetic Act of 1938 [1]. It has the trade name Red 3 and is a reddish brown powder. It stands as one of the seven permitted food colours, it is used as a sensitizer of photographic plates and, finally, it is used to distinguish live and dead yeast cells because the latter absorb the dye much more quickly. Erythrosin is employed in the cotton and paper industries. It is used as a sensitizer in photoelectric experiments and in the irradiation of ergosterol. It is an indicator in analysis. In fact, small doses of iodine may be ingested by eating erythrosin, the colouring matter used in making ice cream, cake mix, syrups, maraschino cherries, rose milk, candy and confectionery products (when they do not contain oils and fats) bakery products and cereals, puddings, aqueous drug solutions, tablets and toothpaste. It also serves as a biological stain [2–5]. It has an acceptable daily intake (ADI-related to kilograms of body weight) value of 0–2.5 mg kg^{-1} day^{-1} [6]. The electrosynthesis of eosin (disodium salt of 2,4,5,7-tetrabromofluorescein), an important colouring dye, was reported earlier [7].

Iodination of fluorescein (1), which exists in the two tautomeric forms shown below, using iodine in hot dilute acetic acid yields erythrosin (2) [8]. Treatment of a comparatively cool alkaline solution of fluorescein and sodium iodide with ammonium or potassium persulphate also yields erythrosin. In the above



FLUORESCEIN (1)

Structure 1.



TETRAIODOFLUORESCEIN (2)

Structure 2.

methods, contamination of erythrosin by the di and triiodinated fluorescein was observed. Use of the acetic acid medium involves pollution; and use of costly ammonium persulphate renders the second process uneconomical on a large scale. Hence an alternate route using electrochemical means was sought for the production of erythrosin. An earlier patent describes the electrochemical production of erythrosin by electrolysis of an alkaline solution of fluorescein containing a small excess of iodine [9].

2. Experimental details

Preliminary experiments on the electrolysis of fluorescein were carried out in a two litre beaker using 500 or 1000 ml of an electrolyte (depending on other conditions employed) containing 10 g of fluorescein and 15.3 g of powdered iodine using a TSIA/graphite anode and a stainless steel cathode. The different electrolytic media and the anode current densities used are listed in Table 1. Nylon cloth (two rounds wound around the cathode) served as the separator. The electrolyte was agitated by means of an overhead stirrer. A charge of 8 faraday per mole of fluorescein was passed. 50 to 100% excess charge was necessary for the completion of electrolysis. The electrolysed solution was then neutralized with HCl, when erythrosin precipitated along with other iodination products, if any. The product was then filtered, dried and weighed. Different electrolytes, including binary electrolyte mixtures were employed (Table 1) in an attempt to improve the solubility of fluorescein.

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 ethyl methyl ketone (20 ml), acetone (5 ml) and ammonia (5 ml), served as the eluant. Clear, well separated bands were observed for fluorescein, mono, di, tri, and tetraiodofluorescein.

The optimum conditions for obtaining maximum yield of erythrosin were found and were employed

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Table 1.

S	Parameter	Experimental conditions
1a	Electrolytes and their pH	5–10% $NaHCO_3$ (pH 8.62–8.64), 20% CH_3COONa (pH 9.0), 10% NH_3 (25% solution) (pH 10.98), 1% NaOH (pH 13.21), 10% anh. Na_2CO_3 (pH 10.8)
b	Mixed electrolytes	10% CH_3COONa; 5% $NaHCO_3$
2	Anode	TSIA, graphite
3	Anode current density	2.5–7 A dm^{-2}

for scale-up to larger cells. Scale-up to a 23.5 A cell was carried out by electrolysing 120 g of fluorescein and 183.6 g of iodine contained in 4 dm^3 of 10% NH_3 solution, in a 5 dm^3 glass beaker consisting of two graphite anodes (area: 4.69 dm^2) and three stainless steel cathodes (area: 4.93 dm^2) with a Nylon separator, (the cathodes and anodes being alternately placed with an interelectrode distance of 1 cm) at a current density of 5 A dm^{-2}. Scale-up to a 45.3 A cell was carried out by electrolysing 250 g of fluorescein and 382.5 g of iodine contained in 6 dm^3 of 10% anhydrous Na_2CO_3 in a Perspex cell (19.6 cm × 19.6 cm × 24.4 cm) consisting of two expanded TSIA anodes (area: 9.05 dm^2) and three stainless steel cathodes (area: 9.64 dm^2) covered with a Nylon separator (two rounds), the cathodes and anodes being alternately placed with an interelectrode distance of 1 cm, at a current density of 5 A dm^{-2}.

The yield of erythrosin 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 triiodinated fluorescein were also found. More precise information about the purity of erythrosin is obtained from its dye content (determined by u.v.–visible spectrophotometry or gravimetry). The absorptivity of the disodium salts in 1 g^{-1} cm^{-1} (measured at the corresponding wavelength in nanometres) of fluorescein, 4-iodo, 2-iodo, 4,5-diiodo, 2,5-diiodo, 2,7-diiodo, 2,4,5-triiodo, 2,4,7-triiodo and 2,4,5,7-tetraiodofluorescein are 228(491–493), 154(497–500), 193(501–503), 122(507–509), 145(509–511), 179(511–513), 116(516–519), 140(517–520), and 108(527–530), respectively [1]. In the gravimetric method [1], 0.5 g of the sample was treated with 25 ml of 1:49 HCl, boiled and kept on a steam bath for several hours. It was then cooled to room temperature and the precipitate was transferred to a tared Gooch crucible with 1:99 HCl, washed with water, dried for 3 h at 135 °C, and finally weighed. The percentage of pure dye is given by the formula: % of pure dye = $W(f)100/w$ where W and w are the weights of the precipitate and the sample in grams, respectively, and f is the gravimetric conversion factor (= 1.074 for erythrosin). A 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.

3. Results and discussion

The results on the effect of varying the experimental parameters on the yield of erythrosin ($T = 40 \pm 5°$ C) are shown in Table 2. It is seen that in $NaHCO_3$ medium, at the TSIA anode the yield of erythrosin obtained is not good (S. nos. 1–4). The erythrosin content is poor, indicating that in this medium, the tetraiodination is incomplete and that the medium is not suitable for the synthesis of erythrosin. These results are in contrast to those obtained in the case of eosin where $NaHCO_3$ was very suitable for obtaining

Table 2. Effect of variation in the experimental parameters on the yield of erythrosin (Separator-Nylon; $T = 40 \pm 5°$ C)

S	Electrolyte	Anode	Anode c.d./A dm^{-2}	Cell current/A	Cell voltage/V	Yield‡/%	Erythrosin content/%
1	5% $NaHCO_3$	TSIA	5	3.6	6.5	68.0	46.8
2	10% $NaHCO_3$	TSIA	3	2.1	5.0	74.0	58.3
3*	10% $NaHCO_3$	TSIA	5	3.5	6.0	81.4	63.4
4	10% $NaHCO_3$	TSIA	7	5.0	7.0	74.0	52.0
5	20% CH_3COONa	TSIA	5	3.5	6.0	44.0	40.4
6	10% CH_3COONa; 5% $NaHCO_3$	TSIA	5	3.5	6.0	71.3	34.4
7	1% NaOH	TSIA	5	3.5	7.0	55.0	31.8
8*	10% anh. Na_2CO_3	TSIA	5	3.5	6.0	91.2	99.0
9	5% NH_3	TSIA	5	3.5	6.5	82.3	78.7
10	10% NH_3	TSIA	3	2.1	4.5	88.0	67.0
11*	10% NH_3	TSIA	5	3.5	6.0	91.2	85.1
12	10% NH_3	TSIA	7	5.0	7.0	89.0	67.0
13	10% NH_3	Graphite	2.5	2.0	5.5	88.0	31.8
14*	10% NH_3	Graphite	5	4.2	7.0	90.2	51.0
15	10% NH_3	Graphite	5	23.5	8.0	87.0	–
16	10% anh. Na_2CO_3	TSIA	5	45.3	8.0	83.0	85.7
17*	CS†						76.0

* Erythrosin content determined by gravimetry at Chemical Testing and Analytical Laboratory, Guindy.
† Commercial sample (CS) of erythrosin.
‡ Yield based on erythrosin assumed as the exclusive product.

Table 3. Absorption maxima for the electrolysis products in different media

S	*Medium*	*Anode*	λ_{max}	*Main product*
1	$NaHCO_3$	TSIA	511	Mono and diiodofluorescein
2	CH_3COONa	TSIA	509	Diiodofluorescein
3	NaOH	TSIA	507	Monoiodofluorescein
4	Anh. Na_2CO_3	TSIA	525	Tetraiodofluorescein
5	NH_3	TSIA	522	Tri and tetraiodofluorescein
6	NH_3	Graphite	514	Mono and diiodofluorescein

maximum yield of eosin with a high eosin content [7]. In the 20% CH_3COONa medium (S. no. 5), the yield and erythrosin content values are still lower, in contrast to the excellent results obtained for eosin in this medium. The use of mixed electrolyte of 10% CH_3COONa and 5% $NaHCO_3$ is also not satisfactory. It is likely that the pH values of these media, which are in the range 8.6–9.0, are very low for the reaction to occur. Hence 1% NaOH as a medium was tried (S. no. 7). Here, too, the yield and dye content values are very low, indicating that the pH is too high. Formation of iodate is likely, which reduces the iodination reaction. Excellent results are obtained with 10% anh. Na_2CO_3 as the medium (S. no. 8), where the pH values lie between those considered above. The yields of erythrosin in the NH_3 medium (S. nos. 9–12) at the TSIA are quite good and the erythrosin content is higher at a current density of 5 A dm^{-2}. At higher current densities, oxygen evolution is a competing reaction; this reduces the yield and CE. With the use of graphite anodes in NH_3 medium (S. nos. 13–15), the yield is high. However, the erythrosin content is low indicating that the tetraiodination reaction is incomplete at this electrode. It is likely that, at graphite, competitive oxygen evolution is responsible for lowering the yield and erythrosin content.

The absorption maxima for the products obtained in different media are given in Table 3. It is seen that with TSIA, when Na_2CO_3 is used, the only product is tetraiodofluorescein. In 10% NH_3, the triiodofluorescein is also formed to some extent. With $NaHCO_3$, CH_3COONa and NaOH as the electrolytes, the mono and/or diiodinated products predominate. This suggests the necessity for strict pH control. Also in NH_3 medium, with a graphite electrode, only the di and triiodinated products are formed. It is also seen from Table 2 that the cell voltage is lower when TSIA is used than when graphite is used, other conditions being similar. This indicates that TSIA catalyses iodine oxidation. It has been reported that TSIA(Ti/TiO_2, RuO_2) is a catalyst for such reactions [10]. From the above results, it is seen that the best yield of erythrosin is observed for the iodination carried out at TSIA in 10% anh. Na_2CO_3 medium. Hence scale-up under this condition to 45.3 A was carried out (S. no. 16, Table 2), the results of which indicate that the yield of erythrosin and the erythrosin content are little affected upon scale-up. A comparison of the erythrosin content obtained as above with that of the commercial sample of erythrosin (S. no. 17, Table 2) indicates the superiority of the electrochemical method (as reflected in a higher erythrosin content). Hence the reaction can be conveniently further scaled up in this medium. Further scale-up studies are being carried out.

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