

# The electrochemical preparation of 3-bromothiophen

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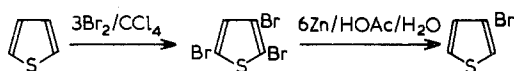
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The electrochemical reduction of 2,3,5-tribromothiophen to 3-bromothiophen may be carried out in good yield with a high current efficiency using a lead, mercury, zinc or graphite cathode in 70% dioxan/30% water containing sodium bromide (0.2 M) and a potential just positive to that for hydrogen evolution. The electrolysis may be designed to form free bromine at the anode or thiophen may be brominated in the anolyte; the product is 2-bromothiophen or 2,5-dibromothiophen which is resistant to further substitution in this solvent. Various strategies for the scale up of this synthesis are discussed.

## 1. Introduction

3-Bromothiophen cannot be made directly by the bromination of thiophen because substitution always occurs first at the 2-position. Hence it must be made by bromination of thiophen to 2,3,5-tribromothiophen under rather forcing conditions [1] and subsequent reduction of the tribromothiophen.\* This reduction is presently carried out chemically by refluxing with zinc and acetic acid [2, 3], although this reaction requires the use of a three-fold excess of zinc and leads to large volumes of effluent containing zinc ions.\*



This paper considers an electrochemical alternative for the reduction step carried out in dioxan/water containing sodium bromide and discusses the effect of cathode material, potential, solvent, concentration of substrate and temperature on the selectivity and current yield. The bromide electrolyte was selected so that the anode could be used (a) to generate free bromine, or (b) to brominate thiophen in the anolyte. This paper therefore also examines the anode reactions and considers the likely compatibility of the anode and cathode reactions in a working cell.

It may be noted that the chemical reduction with zinc metal is a type of Clemmensen reduction and that BASF in Germany have run several

electrochemical Clemmensen replacement reactions on a commercial scale [4, 5]; their electrolyte was generally sulphuric acid.

## 2. Experimental

### 2.1. Instrumentation

The *I-E* data were obtained with a Hi-Tek Instruments Potentiostat, Model DT 2101 and Waveform Generator, Model PPR1, and recorded on a Hewlett Packard *x-y* Recorder, Type 7035B. The controlled potential and controlled current electrolyses were carried out with either the Hi-Tek Potentiostat or a Thompson Associates Ministat, Model 251. Charges were measured with an integrator built in the laboratory.

### 2.2. Cells

Cyclic voltammograms and steady state curves were obtained using two-compartment, three-electrode cells. For Zn, Pb and graphite the electrodes were in the form of discs, of area 0.2 cm<sup>2</sup>, surrounded by a PTFE sheath while the mercury electrode was a pool and the Pt electrode a wire of similar area. The counter electrode was always a Pt wire spiral in the same compartment. The Radiometer type 401 SCE reference electrode was placed in a separate compartment separated from the working electrode by a Luggin probe.

In the cells for preparative electrolyses the working and counter electrodes were separated by a fine glass sinter. With Pb, Zn and graphite the working electrodes were in the form of discs, of

\* Data provided by Croda Synthetic Chemicals Ltd.

area  $2\text{ cm}^2$  mounted in PTFE machined to fit a B24 joint; these electrodes enter a 'tube-type cell' so that the electrode faces were vertical and were parallel to the sinter and, beyond, a Pt gauze counter electrode. The volume of the working electrode compartment was about  $10\text{ cm}^3$ . This cell had a water jacket through which water at controlled temperature could be passed. The mercury electrode was a pool in the base of a different cell. In this case the sinter and Pt gauze counter electrode were horizontal above the pool. All cells were fitted with a reference electrode compartment separated from the working electrode by a Luggin capillary.

All solutions were deoxygenated with oxygen-free  $\text{N}_2$  (BOC Ltd) before the commencement of the experiments and a stream of nitrogen was also used to stir the preparative scale electrolyses.

### 2.3. Chemicals

The solutions were prepared from distilled water and BDH Ltd dioxan. This was filtered before use. Sodium bromide and sodium perchlorate were BDH Ltd Analar grade.

Thiophen was obtained from BDH Ltd and 2-bromothiophen, 3-bromothiophen and 2,3,5-tribromothiophen were obtained from Croda Synthetic Chemicals Ltd. 2,3- and 2,5-dibromothiophen were prepared by bromination of 3-bromothiophen and 2-bromothiophen, respectively, using elemental bromine (BDH Ltd) in carbon tetrachloride. The structures of these products were confirmed by NMR spectroscopy using a Varian HA-100 spectrometer.

### 2.4. Analysis

Organic products were identified and estimated using GLC by the comparison of retention times and peak areas with those of reference samples. The identification of products was further confirmed by GLC mass spectroscopy and comparison of the spectra with those from reference samples. The electrolysis solution was injected directly into the chromatograph. The instruments used were a Pye Unicam GCD gas chromatograph with FID and a Kratos MS 30 mass spectrometer. The GLC column was 2% polyethylene glycol adipate at a tempera-

ture between 85 and  $120^\circ\text{C}$ . The carrier gas was nitrogen, flow rate  $60\text{ cm}^3\text{ min}^{-1}$ .

Bromine was determined by a standard volumetric procedure; excess potassium iodide was added and the iodine liberated was titrated with thiosulphate.

## 3. Results and discussion

### 3.1. The cathodic reduction of 2,3,5-tribromothiophen

Steady state and cyclic voltammetric experiments were carried out at a graphite, lead, mercury and zinc cathode for a solution of 2,3,5-tribromothiophen (10 mM) in 70% dioxan/30% water containing sodium bromide (0.2 M), a medium selected because it seemed to represent a reasonable compromise taking into account the solubility of the substrate and the conductivity of the solution.

The cyclic voltammograms show a single reduction process just positive to the potentials where hydrogen evolution occurs; the reduction is always irreversible and, indeed, there are no oxidation peaks before the dissolution of the metal (or bromine generation at graphite) on the potential sweep towards positive potentials. The reduction potential for the 2,3,5-tribromothiophen and the potential for the commencement of hydrogen evolution appear to depend on the cathode material and only on lead could a well-formed peak be observed on the cyclic voltammogram. The peak potential is  $-1.52\text{ V}$  versus SCE and the peak current density is proportional to the square root of the potential scan rate showing that the current beyond the peak is mass-transfer controlled. The slope of the linear  $I_p$  versus  $\nu^{1/2}$  plot may be used to estimate a value of  $D$  of  $1.0 \times 10^{-5}\text{ cm}^2\text{ s}^{-1}$  (assuming  $n = 4$ , see later).

The steady state  $I-E$  curves under the same conditions all show single reduction waves; they are, however, drawn out and have only poorly formed plateaux because of the proximity to the wave of the hydrogen evolution reaction. At all cathodes the limiting current density has a similar value indicating that these currents are also mass-transfer controlled.

At a lead cathode, the steady state current at

— 1.50 V was proportional to the concentration of 2,3,5-tribromothiophen (0.01 — 0.10 M) and with a concentration of 0.1 M, the current was  $30 \text{ mA cm}^{-2}$ . By increasing the temperature to  $60^\circ \text{ C}$  this current was increased to  $40 \text{ mA cm}^{-2}$ .

A few experiments with more acidic media, 70% acetic acid/30% water or 70% dioxan/30% acetic acid with sodium bromide (0.2 M) were unsuccessful in defining a reduction wave for 2,3,5-tribromothiophen presumably because of enhanced hydrogen evolution.

A series of controlled potential electrolyses were carried out to define how the products depend on the electrolysis parameters. The effects of cathode material and electrode potential are shown by the results in Table 1 for electrolyses in 70% dioxan/30% water containing sodium bromide (0.2 M); the products are reported when the electrolyses had been terminated after the passage of  $4 F \text{ mol}^{-1}$  of 2,3,5-tribromothiophen. It can be seen that at each of the cathode materials, it is possible to define a potential where both the current yield and the organic yield of 3-bromothiophen is high. Generally, however, this is only found over a narrow potential range corresponding to the limiting current region on the steady state  $I-E$  curves. At more negative potentials, hydrogen evolution occurs but while this

adversely affects the current efficiency it does not decrease the selectivity of formation of 3-bromothiophen. Indeed, in a further experiment carried out at a constant current density 50% above the limiting current for 2,3,5-tribromothiophen (100 mM) at lead, the current efficiency dropped to 44% but the organic yield of 3-bromothiophen was still 87%. At potentials below the limiting current region the selectivity for 3-bromothiophen is less good and significant quantities of dibromothiophens were observed amongst the products. At potentials in the foot of the waves 2,4-dibromothiophen becomes the major product, the yield being as high as 75% at graphite at  $-1.4 \text{ V}$ . In many of these electrolyses, the current was monitored as a function of charge passed; at potentials in the limiting current region these  $I-Q$  plots were linear and could be extrapolated to confirm that  $4 F \text{ mol}^{-1}$  are consumed in the reduction of 2,3,5-tribromothiophen.

The effect of solvent composition on electrolysis at a lead cathode is shown in Table 2. At  $-1.6 \text{ V}$ , an increase in the water concentration increases the selectivity but at a slightly decreased current efficiency. Above 70% dioxan, the selectivity of the reaction is seriously diminished and at 90% the electrolysis is difficult because of

Table 1. Products from the controlled potential reduction of 2,3,5-tribromothiophen (10 mM) in 70% dioxan/30% water + sodium bromide (0.2 M). Electrolyses terminated after the passage of  $4 F \text{ mol}^{-1}$  of 2,3,5-tribromothiophen

Electrode	Potential	Unreacted 2,3,5-tribromothiophen (%)	Organic yields (%)	
			3-bromothiophen	dibromothiophens
C	-1.4	5	10	82*
	-1.5	0	41	49
	-1.6	15	80	0
Hg	-1.3	7	0	73
	-1.5	2	15	75
	-1.6	0	80	15
	-1.7	0	92	0
Pb	-1.3	6	36	54
	-1.4	5	65	36
	-1.5	0	93	2
	-1.6	0	92	4
	-1.7	15	65	0
Zn	-1.5	1	54	43
	-1.55	0	88	8

\* 2,4-dibromothiophen (71%) + 2,3-dibromothiophen (11%). This ratio is typical.

Table 2. Electrolyses of 2,3,5-tribromothiophen (10 mM) at a lead cathode at  $-1.6$  V versus SCE in various dioxan/water mixtures containing sodium bromide (0.2 M). Products after  $4 F \text{ mol}^{-1}$

Solvent		Unreacted 2,3,5-tribromothiophen (%)	Organic yield (%)	
% $H_2O$	% dioxan		3-bromothiophen	dibromothiophens
50	50	18	71	0
30	70	0	92	4
20	80	23	52	23
10	90	100	no reduction	

low conductivity and no reduction is observed at  $-1.6$  V.

A preparative scale electrolysis requires a high current density and this is dependent on a high concentration of substrate. The solubility of 2,3,5-tribromothiophen is enhanced by increasing the percentage of dioxan or the temperature but is reduced by the presence of sodium bromide. 70% dioxan was selected on the basis of the data in Table 2 and electrolyses were carried out at various concentrations of 2,3,5-tribromothiophen up to a saturated solution. In one experiment at  $60^\circ \text{C}$ , the electrolyte concentration was 0.4 M (see later). The results are reported in Table 3. It can be seen that the yield of 3-bromothiophen is independent of the 2,3,5-tribromothiophen concentration and the maximum current density in the poor mass-transport conditions prevailing in the cell is  $50 \text{ mA cm}^{-2}$ .

During the experiments with 2,3,5-tribromothiophen (0.1 M) the concentrations of starting material and products were monitored during the electrolysis (see Fig. 1). At room tem-

perature, a significant concentration (up to 11% of the total thiophens) of 2,4-dibromothiophen is present in the electrolyte during the electrolysis although after the passage of  $4 F \text{ mol}^{-1}$  this dropped to a low value. At  $60^\circ \text{C}$  the concentration of the intermediate is always lower (the maximum is 4% of the total thiophens) and if a preparative electrolysis were to be carried out in a flow system without complete conversion of substrate to product, this temperature would lead to a better selectivity for 3-bromothiophen.

Electrolyses were also carried out when 2,3,5-tribromothiophen was present in excess, i.e. as a second phase in the catholyte. Under these conditions the current remains constant during the electrolysis and much of the organic product is extracted into the tribromothiophen. The results are reported in Table 4 for electrolyses after the passage of charge to convert 25% of the substrate to 3-bromothiophen. In these conditions more dibromothiophens are formed but the current yield of 3-bromothiophen is still 68–72%. The current densities are slightly lower than expected.

Table 3. Electrolyses at a lead cathode of 2,3,5-tribromothiophen in 70% dioxan/30% water + NaBr.  $4 F \text{ mol}^{-1}$  of substrate.  $-1.5$  V versus SCE

Concentration (M) 2,3,5-tribromothiophen	NaBr	T ( $^\circ \text{C}$ )	Initial current density ( $\text{mA cm}^{-2}$ )	% yield 3-bromothiophen	% yield dibromothiophen
0.01	0.2	20	3	93	2
0.1	0.2	20	35	92	4
0.15*	0.2	20	50	91	2
0.1	0.2	60	40	93	1
0.12*	0.4	60	45	92	2
0.17*	0.4†	20	60	80	4

\* Saturated solution.

† The catholyte was 0.4 M  $(\text{C}_4\text{H}_5)_4\text{NBr}$ . Some unchanged 2,3,5-tribromothiophen was found in the anolyte.

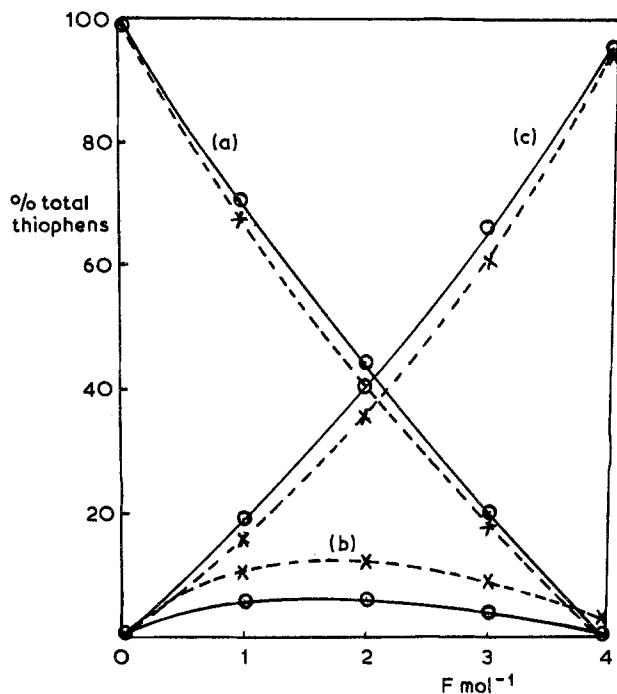


Fig. 1. Conversion of 2,3,5-tribromothiophen to product with charge passed during the electrolysis. (a) 2,3,5-tribromothiophen, (b) dibromothiophens, (c) 3-bromothiophen. --- 20° C; — 60° C.

The variation of products with potential and conversion under all conditions studied strongly suggest that although the  $I-E$  curves show only a single reduction wave, in reality there are two overlapping  $2e$  reduction processes and that the bromides are removed step-wise.

### 3.2. The counter electrode reaction

As long as the anode is made of an inert material, it is to be expected that the counter electrode reaction in the sodium bromide solution would be the formation of bromine. As a further part of this preliminary study of cell design for the production of 3-bromothiophen, it is, however, necessary to check the current efficiency for this process and the stability of bromine in the elec-

trolysis medium. It is also uncertain whether it would be desirable to isolate bromine and the alternative would be to brominate thiophen *in situ* in the anolyte. Moreover, there is the possibility of carrying out the electrolysis in an undivided cell if the bromination of 3-bromothiophen is slow. The experiments in this section were designed to answer these questions.

Fig. 2 shows a cyclic voltammogram for bromide ion ( $10^{-2}$  M) at a platinum electrode in 70% dioxan/30% water containing sodium perchlorate (0.2 M). It can be seen that there is a single well-formed oxidation peak  $E_p = 0.90$  V versus SCE, and the product is completely stable on the timescale of this experiment. The peak current for both the oxidation and the reverse process are proportional to the square root of

Table 4. Electrolysis of 2,3,5-tribromothiophen in two-phase conditions;  $1\text{ cm}^3$  2,3,5-tribromothiophen +  $9\text{ cm}^3$  70% dioxan/30% water containing sodium bromide.  $-1.6$  V. Thiophens present after charge of  $1\text{ F mol}^{-1}$  2,3,5-tribromothiophen.  $x + y = \%$  starting material in organic and aqueous layers, respectively.

$T$ (° C)	$I$ (mA cm <sup>-2</sup> )	Distribution of thiophens		
		3-bromothiophen	dibromothiophen	2,3,5-tribromothiophen
20	25	15 + 2	6 + 0	70 + 3
60	40	15 + 3	6 + 0	70 + 4

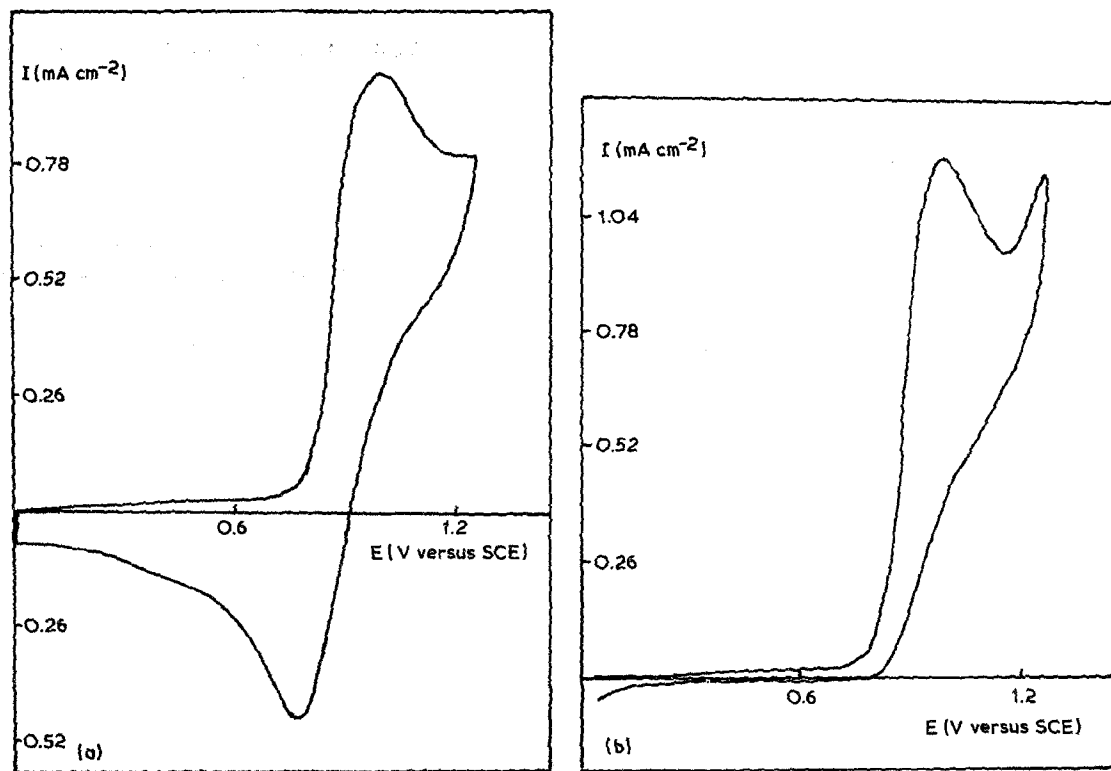


Fig. 2. (a) Cyclic voltammogram of bromide ( $10^{-2} M$ ) in 70% dioxan/30% water containing sodium perchlorate (0.2 M). Pt electrode, potential scan rate  $0.03 V s^{-1}$ . (b) As (a) + thiophen (1 M).

the potential scan rate. Table 5 reports the yields of bromine, determined volumetrically, from a series of constant current electrolyses at a graphite anode of solutions of sodium bromide (0.4 M) in 70% dioxan/30% water. The yield depends only slightly on the current density and the concentration of bromine (0.1 M) decreased about 20% on standing in the anolyte overnight. Hence it is clear that the reaction of bromine with dioxan is very slow in solutions such as those used for these electrolyses. At the highest current

Table 5. Current efficiencies for bromine generation at a graphite anode in 70% dioxan/30% water + sodium bromide (0.4 M) after the passage of charge required for 50% conversion of bromide ion to bromine

Current density ( $mA cm^{-2}$ )	Current efficiency (%)
10	99
25	97
50	92
100	87

densities, the current efficiency for bromine formation is sensitive to a decrease in bromide ion concentration, and for example, the current efficiency with 0.2 M sodium bromide was poor at  $100 mA cm^{-2}$ .

Fig. 2 also shows the cyclic voltammogram for bromide ion in the presence of a high concentration of thiophen and it is clear that bromine reacts with thiophen. The apparent rate constant for the reaction between bromine and thiophen could be estimated by increasing the potential scan rate and decreasing the thiophen concentration. The value obtained and those for the reactions of other thiophens with bromine are reported in Table 6. It can be seen that while the bromination of thiophen is relatively rapid, the monobromothiophens brominate further only slowly.

These data are in accord with the results of some preparative scale electrolyses of thiophen (10 mM) + sodium bromide (0.2 M). At very low current densities (i.e. slow electrolysis) the yield of 2-bromothiophen after the passage of  $2 F mol^{-1}$

Table 6. Apparent rate constants\* for the reactions of bromine with thiophens in 70% dioxan/30% water + sodium perchlorate 0.2 M, determined by cyclic voltammetry

	$k_{app}^*$ (mol <sup>-1</sup> s <sup>-1</sup> )
Thiophen	105
2-bromothiophen	$8.2 \times 10^{-2}$
3-bromothiophen	$7.0 \times 10^{-2}$
2,5-dibromothiophen	0 <sup>†</sup>

\*  $k_{app} = k_1 + k_2 K [Br^-]$  where  $k_1$  and  $k_2$  are the actual rate constants for the reaction of the thiophen with bromine and tribromide ion, respectively, and  $K$  is the equilibrium constant,  $K = [Br_3^-] / [Br_2] [Br^-]$ .

† Based on preparative experiments.

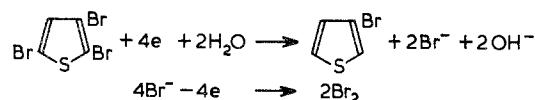
of thiophen is 94% but at higher current densities ( $> 5 \text{ mA cm}^{-2}$ ) it is necessary to leave the anolyte standing for a short period after the electrolysis for the reaction to go to completion. When the electrolysis was continued to  $4F \text{ mol}^{-1}$  of thiophen, the yield of 2,5-dibromothiophen was only 4% immediately after the electrolysis but this was increased by an extended period at room temperature and after refluxing the anolyte for 3 h, the yield of 2,5-dibromothiophen was 80% along with 2-bromothiophen (10%). The further bromination of 2,5-dibromothiophen did not occur in the electrolysis conditions and, indeed, it was not possible to find conditions where 2,3,5-tribromothiophen could be prepared in 70% dioxan/30% water. Normally it is prepared by bromination in carbon tetrachloride but it is necessary to reflux the solution, and periodically, to remove the hydrobromic acid formed in the reaction. Certainly, in any electrolysis where there is an excess of thiophen in the anolyte, only 2-bromothiophen would be formed.

### 3.3. Strategies for scaling up the electrolytic preparation of 3-bromothiophen

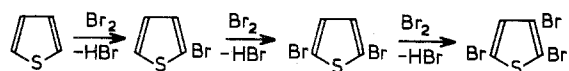
The results in the previous sections show that a process for the conversion of 2,3,5-tribromothiophen to 3-bromothiophen with the formation or use of bromine at the counter electrode is chemically feasible. The cathode reaction, the reduction of 2,3,5-tribromothiophen to 3-bromothiophen, takes place with high organic yield and current efficiency provided the

electrolysis is carried out under conditions where the current is mass-transfer limited and the electrode potential is not so negative as to allow hydrogen evolution. In practice, in a commercial cell it might be difficult to control the current this closely but the use of a current density above the critical value would not lead to a loss in organic yield. Furthermore, it is possible to carry out the reaction to 100% conversion without loss of performance; indeed it is advantageous since it avoids the low percentage of dibromothiophens at intermediate conversions. The major problem with the cathode reaction in the solutions used in this study concerns the current density. In this work the maximum value was  $50 \text{ mA cm}^{-2}$  although since the reduction is mass-transport limited, it is to be expected that this could be increased by standard techniques in a flowing system.

The anode reaction is also satisfactory. Bromine may be formed in excellent current yields and there is no evidence for the reaction of the bromine with the solvent at a significant rate. Hence the electrolysis may be carried out to form elemental bromine, extracted or distilled from the electrolyte. The electrode reactions are;



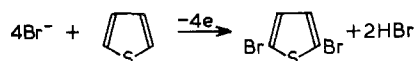
The bromine may then be used to prepare further tribromothiophen in the solvent of choice, i.e. carbon tetrachloride



It may be noted that if the cathode reaction is run at 100% current efficiency, there is not a bromine balance; the anode reaction forms only two thirds of the bromine required for the formation of 2,3,5-tribromothiophen. However, it seems possible to run the process deliberately at a high cathode current density (i.e. at  $1.5I_L$ ) in order that the organic reduction has a current efficiency of only 67%; the bromine would then be in balance and the excess current at the cathode would evolve hydrogen gas. The possibility of running such an electrolysis in an undivided cell should also be considered; the rate constant for the reaction of bromine with 3-bromothiophen is low and provided the bromine is removed from

the electrolyte continuously, the back reaction should not be important.

The alternative electrolyses would make use of the *in situ* bromination of thiophen in the anolyte. If excess thiophen is present in the electrolyte, 2-bromothiophen would be formed. Moreover, it would be formed at twice the rate that 2,3,5-tribromothiophen is consumed at the cathode. Hence it would seem more sensible to control the thiophen concentration in the anolyte feed in such a way that 2 mol bromine/mole thiophen are formed in the cell and to pass the anolyte extract to a holding tank to form 2,5-dibromothiophen. The net anode reaction would then be



However, we were not able to add the third bromine in dioxan/water and thus it would be necessary to extract the 2,5-dibromothiophen for further bromination. This reaction route would require a divided cell because the bromination of 3-bromothiophen would compete with that of 2-bromothiophen. If, however, the electrolysis was run to form only 2-bromothiophen at the anode, an undivided cell again becomes possible.

Hence the preparation of 3-bromothiophen in 70% dioxan/30% water containing sodium bromide deserves further study. Further consideration should be given both to cells where

bromine is isolated and to cells where an organic reaction is carried out in the anolyte. The best electrode materials will depend on this choice but the use of an elevated temperature (i.e. 60°C) always seems advantageous. It may be noted that in our laboratory cells, the optimum concentration of sodium bromide for the cathode reaction is not the same as that for the anode process. In a commercial cell with flowing electrolyte this may not remain a problem. In any case it may be overcome by using the more expensive salt tetrabutylammonium bromide (0.4 M)

### Acknowledgement

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