

# Polarographic Study of Iodothiophenes

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Eight iodothiophenes were polarographed in two different solvents, *N,N*-dimethylformamide and 2-ethoxyethanol and the half-wave potential for each wave was calculated. The reduction of the iodothiophenes at the dropping mercury electrode was found to be essentially the same as reduction of the iodothiophenes by chemical methods. Reaction mixtures obtained in the preparation of some iodothiophenes were polarographed and the information obtained was found to be useful in determining the iodothiophenes present and their relative amounts. A study of the wave heights *vs.* concentration of 2-iodothiophene in *N,N*-dimethylformamide and in 2-ethoxyethanol was conducted and the diffusion current was shown to be proportional to the concentration.

THIOPHENE has been of interest in the field of organic synthesis because it possesses chemical characteristics similar to those of benzene and has been substituted for benzene and other aromatic nuclei in the synthesis of intermediates of pharmaceutical compounds and thiophene derivatives with therapeutic activity.

It was the intent of this project to make a polarographic study of iodothiophenes to provide additional information relative to the characteristics of the thiophene nucleus and to give an insight into the reactions taking place at the dropping mercury electrode.

Polarography has been used to compare the reactivities of the thiophene and benzene nucleus. Day and Blanchard (1) have studied the polarography of phenyl-2-thienyl ketone and 2,2'-dithienyl ketone in buffered solutions ranging from pH 1 to 13. Elving and Callahan (2) have studied the polarographic behavior of thenoyltrifluoroacetone and related compounds. Tirouflet and co-workers (3) have studied the polarographic behavior of thiophene derivatives and similarly substituted benzene derivatives. They compared 2-nitrothiophene, 2-iodothiophene, 2-thiophenealdehyde and other compounds with the corresponding benzene derivatives.

Since a direct correlation between the half-wave potential of corresponding benzene and thiophene derivatives had been shown, Tirouflet and Chane (4) studied the half-wave potential increments due to substituent *X* in the 5-position in 2- and 3-nitrothiophene and found them to be equal within experimental error with the corresponding increments in nitrobenzene with *X*-substituent in the *para* and *meta* position. The Hammett equation, which relates structure to both equilib-

rium constants and rate constants for the reactions of *meta*- and *para*-substituted benzene derivatives, was thus shown to hold for the thiophene series and sigma values were shown to be of the same order of magnitude. Further work by these same workers has shown that an extension of the Hammett equation to the thiophene series was possible in most cases, but must be carefully evaluated. Imoto and co-workers (5) have studied the effects of the benzene and thiophene nucleus on the polarographic half-wave potentials of the aromatic aldehydes and nitro compounds and concluded that Hammett's law is applicable to the half-wave potential of the thiophene derivatives.

## EXPERIMENTAL

**Polarographic Procedure.**—A manual polarograph (Sargent polarograph model III) equipped with a standard mercury capillary electrode and a saturated calomel reference electrode in an H-type cell was used for the determinations. Nitrogen was passed through each solution of iodothiophene for 30 minutes to remove the oxygen from the solution before being polarographed.

All determinations were conducted in a constant temperature bath at  $25 \pm 0.5^\circ$ . The current readings *vs.* voltage were plotted on graph paper and a smooth curve was drawn through the points. The half-wave potential was obtained from the graph by taking the mid-point of what appeared to be the most symmetrical curve.

The characteristics of the capillary in *N,N*-dimethylformamide with 0.05 *M* tetrabutylammonium iodide as the electrolyte were measured at  $25 \pm 0.5^\circ$  with a mercury height of 60 cm. and are reported in Table I.

TABLE I.—CHARACTERISTICS OF CAPILLARY IN *N,N*-DIMETHYLFORMAMIDE

Volts	Time, sec.	<i>m</i> , mg./sec.
0.0	7.44	0.8588
1.0	6.86	0.8586
2.0	4.35	0.8680

The characteristics of the capillary in 2-ethoxyethanol with 0.05 *M* tetrabutylammonium iodide as

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the electrolyte were measured at  $25 \pm 0.5^\circ$  with a mercury height of 60 cm. and are reported in Table II.

TABLE II.—CHARACTERISTICS OF CAPILLARY IN 2-ETHOXYETHANOL

Volts	Time, sec.	m, mg./sec.
0.0	7.39	0.8658
1.0	7.12	0.8626
2.0	4.67	0.8714

**Purification of Solvents.**—*N,N*-Dimethylformamide was dried over anhydrous potassium carbonate and distilled through a 90-cm. Fenske column. The fraction that distilled at  $152\text{--}153^\circ$  was collected.

Cellosolve (2-ethoxyethanol) was refluxed for 30 minutes with exsiccated ferrous sulfate and distilled through a 90-cm. Fenske column. The fraction that distilled at  $135^\circ$  was collected.

Tetrabutylammonium iodide was twice crystallized from ethyl acetate, suction filtered and 10-Gm. quantities placed in green glass containers. The containers were placed in a vacuum desiccator for 1 hour, then sealed and stored in a dark place.

**Preparation of Iodothiophenes.**—Tetraiodothiophene, 2-iodothiophene, 2,5-diiodothiophene, 3-iodothiophene, and 3,4-diiodothiophene were prepared essentially by the methods described in *Thiophene and its Derivatives* by Hartough (6). 2,3,4-Triiodothiophene, 2,3,5-triiodothiophene, and 2,3-diiodothiophene were prepared essentially by the methods described by Steinkopf (7).

**Polarographic Results.**—The eight iodothiophenes were polarographed in *N,N*-dimethylformamide and in 2-ethoxyethanol to obtain the half-wave potentials as shown in Tables III and IV

The polarograms for all the prepared compounds, some mixtures of these compounds and several unknowns were plotted and analyzed but only a selected few of these polarograms are shown in this paper.

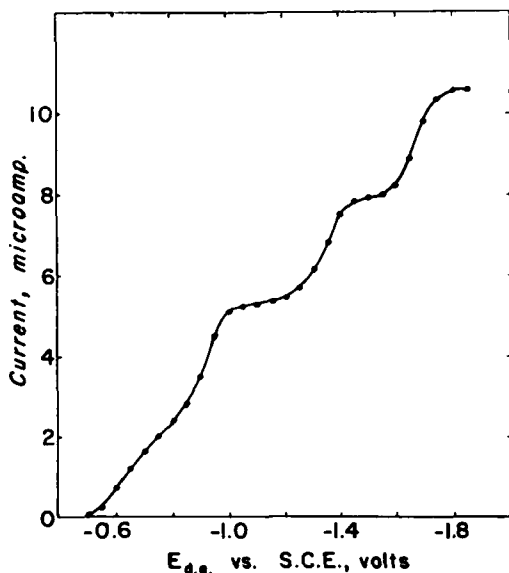


Fig. 1.—Polarogram of 1.0 millimolar tetraiodothiophene in *N,N*-dimethylformamide containing 0.05 *M* tetrabutylammonium iodide as electrolyte.

Four waves were obtained in the curve of the polarogram of tetraiodothiophene with the first two waves almost merging into one single large wave. The four waves were all of approximately the same height as shown in Fig. 1. 3-Iodothiophene, when polarographed, gave a single wave which corresponded to the last wave in tetraiodothiophene, consequently the last wave in tetraiodothiophene was judged to be caused by the iodine in the 3-position. To get a smooth wave from 3-iodothiophene, the concentration was maintained at about 0.5 millimolar because larger concentrations caused an inflection at the top of the wave as shown in Fig. 2. The polarogram of 2-iodothi-

TABLE III.—HALF-WAVE POTENTIALS IN *N,N*-DIMETHYLFORMAMIDE

Compound	Position of Iodine Causing Wave			
	5	2	4	3
2-Iodothiophene	...	-1.21	...	...
2,3-Diiodothiophene	...	-0.89	...	-1.68
2,3,4-Triiodothiophene	...	-0.68	-1.32	-1.67
		-0.91		
2,3,4,5-Tetraiodothiophene	-0.67	-0.92	-1.34	-1.67
2,3,5-Triiodothiophene	-0.73	-0.97	...	-1.67
2,5-Diiodothiophene	-0.91	-1.23	...	...
3-Iodothiophene	...	...	...	-1.65
3,4-Diiodothiophene	...	...	-1.28	-1.66

TABLE IV.—HALF-WAVE POTENTIALS IN 2-ETHOXYETHANOL

Compound	Position of Iodine Causing Wave			
	5	2	4	3
2-Iodothiophene	...	-1.16	...	...
2,3-Diiodothiophene	...	-0.88	...	-1.74
2,3,4-Triiodothiophene	...	-0.74	-1.27	-1.67
2,3,4,5-Tetraiodothiophene			Insoluble	
2,3,5-Triiodothiophene	-0.74	-0.93	...	-1.67
2,5-Diiodothiophene	-0.88	-1.21	...	...
3-Iodothiophene	...	...	...	-1.61
3,4-Diiodothiophene	...	...	-1.23	-1.67

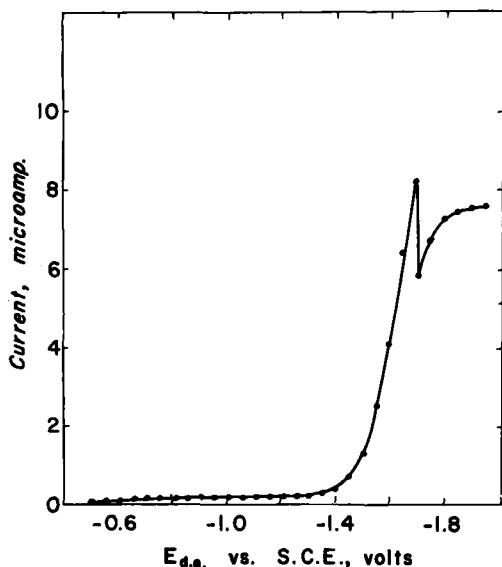


Fig. 2.—Polarogram of 1.78 millimolar 3-iodothiophene in 2-ethoxyethanol containing 0.05 *M* tetrabutylammonium iodide as electrolyte.

phene showed a single wave which corresponded with the second wave of tetraiodothiophene but it, too, gave an inflection when concentrations greater than 0.55 millimolar were used. Two maximum suppressors, Triton X-100 and methyl red, were added to the more concentrated solutions of 2-iodothiophene in an attempt to eliminate the inflections, but the suppressors had no effect on the inflections.

The curves of 2,3,5-triiodothiophene were similar to those of tetraiodothiophene except that the wave of the 4-position iodine was missing from the curves.

2,5-Diiodothiophene was polarographed to obtain a normal two-wave curve. In conjunction with this work a mixture of 2-iodothiophene and 2,5-diiodothiophene was polarographed and in the polarogram there was observed a short 5-position iodine wave and an extended 2-position iodine wave to indicate the ratio of these two substitutions. The polarograms of 3,4-diiodothiophene and 2,3-diiodothiophene were normal two-wave curves with the waves well distinguished from one another but with some shifting of the 2-position wave to a less negative potential in the case of the 2,3-diiodothiophene.

When 2,3,4-triiodothiophene was polarographed in *N,N*-dimethylformamide, four waves were produced but only the expected three waves were produced when polarographed in 2-ethoxyethanol. The sum of the wave heights of the first two waves of the curve of 2,3,4-triiodothiophene in *N,N*-dimethylformamide was equal to a single wave of the other two waves in the curve. Also, since only three waves were observed on the polarogram of 2,3,4-triiodothiophene in 2-ethoxyethanol, it was concluded that the first two waves of 2,3,4-triiodothiophene in *N,N*-dimethylformamide were caused by the single iodine in the 2-position. As the concentration of 2,3,4-triiodothiophene in *N,N*-dimethylformamide was decreased, the height of the first wave of the polarogram increased while the second wave decreased.

In one attempt to prepare 2,3,5-triiodothiophene

by iodinating 3-iodothiophene in the 2 and 5 position, only an oil was obtained instead of solid 2,3,5-triiodothiophene. A polarogram was run with this oil and the curve in Fig. 3 was obtained. This curve showed that the reaction had not been run long enough since only a small amount of triiodothiophene was evident from the curve.

In the course of this study an experiment was conducted to determine the linearity of wave heights vs. concentration of 2-iodothiophene in *N,N*-dimethylformamide and in 2-ethoxyethanol. The results, shown in Fig. 4, indicated that the diffusion current was proportional to the concentration.

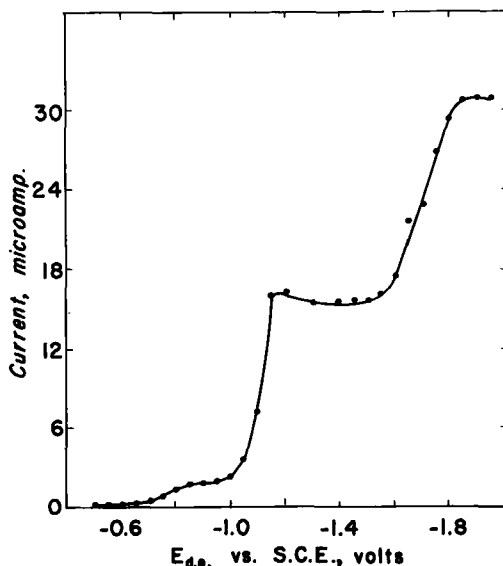


Fig. 3.—Polarogram of the oil obtained in preparing 2,3,5-triiodothiophene (3 drops per 50 ml. of *N,N*-dimethylformamide containing 0.5 *M* tetrabutylammonium iodide).

## DISCUSSION

In order for data obtained from polarography to be of the utmost use to the chemist, a correlation between the normal chemical reaction and the reaction at the dropping mercury electrode should be obtained. Some researchers in this field suggest that the potential gradient near the surface of the mercury drop causes organic halides to approach the mercury surface with the halogen atom away from the drop and that this places the backside of the carbon holding the halogen in position to accept electrons, unless this is sterically interfered with by the presence of other groups. In addition, a large field effect should aid alkyl halide dissociation at all potentials. Lambert and Kobayashi (8) have studied the half-wave potentials of alkyl halides and cycloalkyl halides. They found good correlation between  $S_N2$  reactivity and half-wave potential for many of these compounds which react by  $S_N2$  reaction.

If the iodothiophenes approach the mercury surface with the iodine atoms away from the surface of the mercury, then it would seem that the polaro-

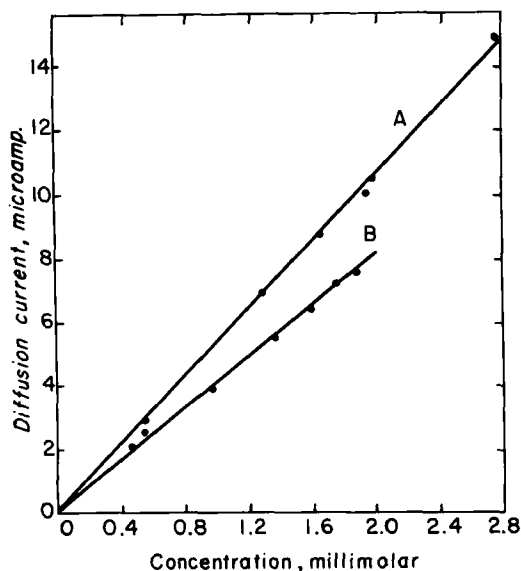
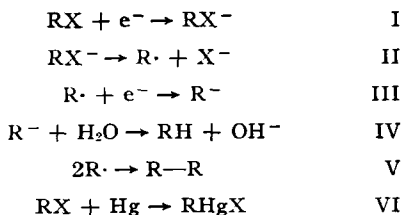


Fig. 4.—Plot of concentration *vs.* diffusion current of 2-iodothiophene in (A) *N,N*-dimethylformamide and (B) 2-ethoxyethanol.

gram of a compound such as 2,5-diiodothiophene would show a greater first wave height than second wave height since there are two identical carbons from which the removal of the first iodine atom can be made. In this study, the wave height produced by each iodine in a polyiodothiophene was approximately the same. Also, the position in which 2-iodothiophene approached the mercury surface would probably be different than the position in which 2,5-diiodothiophene approached the surface because they would have different dipole moments, yet in this study the half-wave potential of 2-iodothiophene corresponded fairly well with the 2-position iodine in 2,5-diiodothiophene. Levin and Fodiman (9) have shown earlier that a molecule such as the benzene nucleus containing *n* chlorine atoms was reduced at a potential independent of whether this molecule was introduced as such or was formed in the solution by reduction of a molecule richer in chlorine. It might be speculated then, in the case of the iodothiophenes, that the first electron could be added to the aromatic ring causing one of the ring electrons to shift to the iodine that is most easily reduced.

Marple, Hummelstedt, and Rogers (10) studied the polarographic reductions of benzyl halides. They proposed the following for the mechanism of reduction of benzyl halides at the dropping mercury electrode.



It was generally assumed that addition of the first

electron was the slow step and that reactions II, III, and IV were relatively rapid because only one wave was usually observed for each halogen atom replaced. Reactions V and VI were possible side reactions. They also found that benzyl iodide underwent two widely separated one-electron reduction steps at concentrations of less than  $10^{-4}$  *M*. At higher concentrations, adsorption phenomena were encountered between the two waves due to the presence of bibenzyl, a by-product of the first reduction step. Judging from Marple and co-workers work, bithienyl might possibly have been formed as a side reaction and produced an adsorption wave causing the inflection observed in higher concentrations of 2-iodothiophene and 3-iodothiophene.

The behavior of 2,3,4-triiodothiophene in *N,N*-dimethylformamide in which a single iodine in the 2-position caused a double wave was probably an example of the kinetics of the reaction varying with the concentration.

The plot of concentration *vs.* diffusion current in Fig. 4 indicates that there exists a linear relationship between diffusion current and concentration of 2-iodothiophene in *N,N*-dimethylformamide and in 2-ethoxyethanol but that the diffusion current is higher in *N,N*-dimethylformamide than in 2-ethoxyethanol.

## SUMMARY

Eight prepared iodothiophenes were reduced at a dropping mercury electrode of a manual polarograph in two different solvents, *N,N*-dimethylformamide and 2-ethoxyethanol, and their half-wave potentials were determined. The polarograms of the iodothiophenes in the two solvents were compared and discussed.

Polarograms were run on some of the reaction mixtures obtained in preparing the iodothiophenes in order to determine their composition. The information gained in these polarograms was of value in determining the length of time that the reaction should be run under the conditions used.

A study of the wave heights *vs.* concentration of 2-iodothiophene in *N,N*-dimethylformamide and in 2-ethoxyethanol was conducted and the diffusion current was shown to be proportional to the concentration; consequently a quantitative estimation of this compound could be obtained from its diffusion current.

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