11:29 AcC, 0.001 mg. Little effect.
11:32 PD-2, 0.1 mg. Blood pressure rose from 142 to 208 mm. Rapid return to normal.
11:35 PD-1, 0.1 mg. Blood pressure rose from 144 to 164 mm. Traube–Hering waves. Transitory respiratory stimulation.
11:38 PD-2, 0.2 mg. Blood pressure rose from 154 to 236 mm. Traube–Hering waves. Transitory respiratory stimulation.
11:43 PD-1, 0.2 mg. Blood pressure rose from 148 to 184 mm. Traube–Hering waves. Transitory respiratory stimulation.

The authors wish to express their appreciation and thanks to Professor George B. Wallace, in whose laboratory most of the experiments were performed.

Summary

1. Methods of preparation of tertiary amino alkyl thiols are described.

2. Thioethyldimethylamine and its β-methyl derivative have been acylated and the resulting thioesters converted into quaternary ammonium derivatives yielding thioesters of choline and β-methylcholine.

3. The acetyl derivatives of thiocholine and the acetyl derivative and methyl thioether of β-methylthiocholine have been tested pharmacologically for their acetylcholine, "stimulating" and "paralytic nicotine" and "curare" actions.

NEW YORK, N. Y. RECEIVED MAY 27, 1938

[A COMMUNICATION FROM THE LABORATORY OF CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

Effects of Solvents on Polarographic Wave Heights

BY EDMOND S. PERACCHIO[1] AND VILLIERS W. MELOCHE

Since the discovery of the polarograph by Heyrovsky, many contributions have been made to the literature involving the use of the instrument. Aside from describing the process at the dropping mercury capillary electrode and developing equations for the polarographic curve, most papers were concerned with proof of reduction or qualitative detection of a great variety of substances. Actual applications of the method to quantitative analysis were few in number and often the procedures were poorly defined. Heyrovsky, Ilkovic and others have mentioned variables which affect wave height and its relationship to concentration of a given ion. In this connection they have included the mobility of the reducible ion as an important consideration. When one examines several papers which have appeared in the literature,[2] it may seem that a given amount of one reducible substance will give a wave height equal to that of an equivalent amount of another reducible substance or that differences between the wave for equivalent amounts of two different ions are not significant in quantitative analysis. From our studies it became evident that this was not necessarily true. At the same time it is true that the order of magnitude of these differences could be changed by the addition of various reagents to the solution of the sample.

Since in a preliminary investigation we found that the wave for lithium chloride was defined better in a solution containing ethyl alcohol than it was in water, it was decided to extend the study of the polarographic wave heights to systems containing high concentrations of non-aqueous solvents.

The purpose of this investigation is to illustrate the differences in wave heights which exist for equivalent weights of the alkali metals in certain aqueous solutions and to show how these differences are affected by the introduction of certain organic solvents.

Apparatus.—The usual Heyrovsky[3] polarographic system was used. A few changes were made in the manipulation and construction of the dropping mercury cathode. In the usual construction of the cathode, a mercury reservoir is suspended about 15 inches (38 cm.) above the capillary tip and is connected to the tip by means of gum rubber tube. This arrangement was not satisfactory even when the tube received special treatment. For our experiments, a 100-ml. dropping funnel was used as the reservoir, Fig. 1. The glass tube below the stopcock was long enough so that the distance from the surface of the mercury in the reservoir to the capillary tip afforded a mercury pressure of about 15 to 20 inches (38–51 cm.). The capillary was attached to the glass tube from the reservoir by a short piece of rubber tube which had been conditioned by

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[1] This paper is offered in partial fulfilment of the requirements for the degree of Doctor of Philosophy. The work was supported by a grant from the Wisconsin Alumni Research Foundation.

[2] References on wave height discrepancies: Heyrovsky and Nejedly, *Coll. Czech. Chem. Comm.*, **3**, 126 (1931); Suchy, *ibid.*, **3**, 358 (1931); Prajzler, *ibid.*, **3**, 408 (1930); Ilkovic and Semerano, *ibid.*, **4**, 176 (1932); Tokuoka, *ibid.*, **4**, 452 (1935); Rylich, *ibid.*, **7**, 290 (1935).

[3] Hohn, *Z. Elektrochem.*, **43**, 127 (1937); Winkle and Proske, *Angew. Chem.*, **50**, 18 (1937).

boiling in dilute sodium hydroxide, washing with hydrochloric acid and finally with water. Thermometer tube, 5.0 mm. o. d. and 0.5 mm. i. d., was used for the capillary tips, the tubes being drawn in such a manner that they had a long gradual taper. To prepare a tip for use, it was attached to the reservoir as described and immersed in water. Successive small portions were broken off until the mercury droplet barely formed. Using a solution 0.1 N in tetramethylammonium hydroxide and 0.001 N potassium chloride, the necessary connections were made preparatory to electrolysis and the trolley was set for a voltage nearly equal to the reduction potential for the potassium. Successive small portions were again broken from the tip until the oscillations of the galvanometer were at a minimum for a given voltage. Such a tip produces a smooth curve when used in the analysis of the alkali metals. The drop rate is usually about 1 drop every two seconds.

A straight-walled vessel was used instead of the usual Erlenmeyer type used by Heyrovsky and others (Fig. 2). The rubber stopper in the vessel had two holes. In one there was a glass tube which was slightly larger than the capillary tip and through which the tip could move freely as through a sleeve. The other hole provided for a tube through which hydrogen could be passed over the surface of the solution. The whole cathode, Fig. 1, was supported on a ring stand in such a manner that it could be raised or lowered by adjustment of a screw. In ordinary cases the hydrogen used for removing the dissolved oxygen from the solution of the sample was purified by passing it through alkaline pyrogallol and then through sulfuric acid. When the solution to be examined contained a highly volatile substance, the hydrogen was saturated by passing it through a portion of the solution before it passed through the sample in the vessel. This minimized the change of concentration caused by loss of the volatile substance.

Materials.—Tetramethylammonium hydroxide was used as the supporting electrolyte for all of the work with the alkali salts. It was prepared as follows: 17 g. of silver nitrate was dissolved in about 150 ml. of water. Four grams of sodium hydroxide was dissolved in about 150 ml. of water and poured with vigorous stirring into the silver nitrate solution. The precipitated silver oxide was washed 12 to 15 times by decantation using about 300 ml. of distilled water, mixing thoroughly each time and draining as completely as possible. Fifteen and six-tenths grams of tetramethylammonium bromide was dissolved in about 100 ml. of water and the solution poured with vigorous stirring into the washed silver oxide. After mixing, the solution was decanted and allowed to stand for several days. During this time most of the very fine particles of silver bromide settled. The solution was filtered through hard paper, diluted to 200 ml. and was ready for standardization.

Sodium chloride was prepared from a sample of fused sodium chloride by saturating a solution of the fused salt with hydrogen chloride, forcing the sodium chloride out of solution. The sodium chloride thus obtained was recrystallized from water.

Potassium chloride was prepared by treatment of analytical reagent potassium carbonate with hydrochloric acid and subsequent recrystallization of the potassium chloride.

Rubidium and cesium chlorides were prepared from analytical reagent quality materials. The chlorides were further purified according to the method of Wells and Stevens[4] for the separation of the alkali metals.

Lithium chloride was prepared from lithium metal and freshly prepared hydrochloric acid. The lithium chloride was extracted with pyridine to separate it from any of the other alkalies. Finally it was recrystallized from water.

Rochelle salt used as the supporting electrolyte in the cadmium and lead systems was reagent quality.

The alcohols used, methyl, ethyl, and propyl, were dried over calcium oxide and then fractionated. The fraction collected boiled over a 1° range. Ethylene glycol, trimethylene glycol, and glycerol were treated in a similar manner.

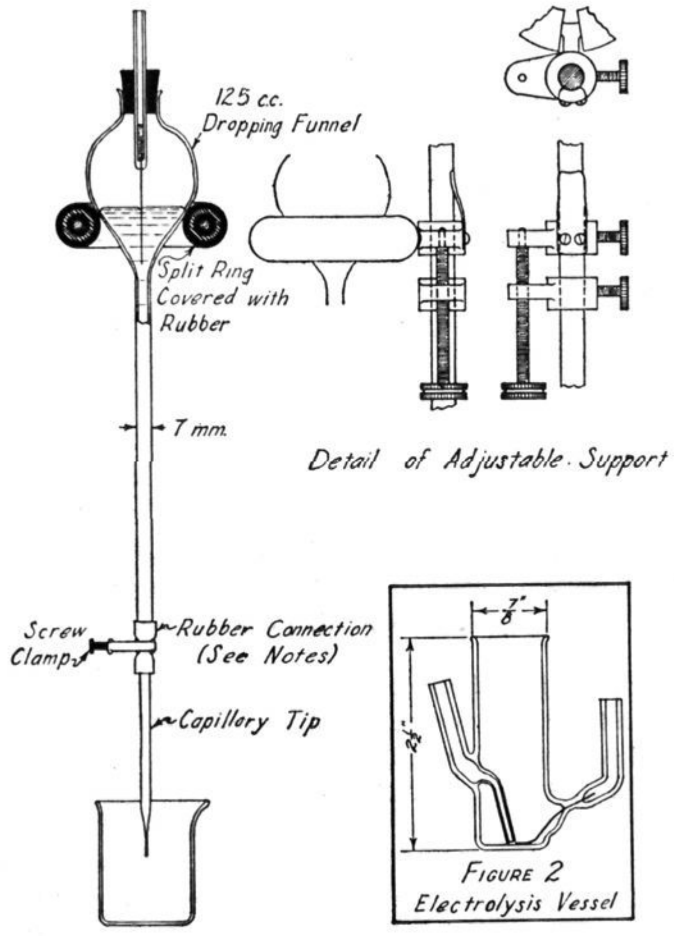

Fig. 1. Fig. 2.

1,4-Dioxane was dried over sodium metal and fractionated. Only freshly distilled product could be used. Apparently, on standing, the dioxane tends to form peroxides and these react with the mercury in the polarographic vessel. Freshly distilled dioxane did not do this.

Water was redistilled in a copper still and only the middle third collected for use.

The mercury used for the cathode and anode was aerated under a solution of sodium hydroxide, washed in a tower with 3% nitric acid, and finally with water. The dry mercury was distilled under reduced pressure.

Method.—Fairly concentrated stock solutions were prepared so that by taking a definite aliquot of each reagent and mixing them together the resulting solution contained each constituent in the desired concentration. The solutions used for electrolysis were made 0.001 N to the reducible ion, *i. e.*, sodium, potassium, etc., and 0.1 N to

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[4] Wells and Stevens, *Ind. Eng. Chem., Anal. Ed.*, **6**, 439 (1934).

the supporting electrolyte, tetramethylammonium hydroxide.

The concentration of the organic solvent was generally 80% except in a few cases where the concentration is specified. A sufficient quantity of the solution was prepared so that a portion of it could be placed in the saturation vessel and a portion in the cell used for electrolysis. Oxygen-free hydrogen was passed through the two solutions until the oxygen was removed from the solutions. This operation required three to five minutes. The solution was then ready for electrolysis. Wave heights were measured according to the method described as A_4B_4 by Borcherdt, Meloche and Adkins.[5] There was a slight exception in that the slope of the base of the curves was more nearly horizontal than illustrated. Therefore an application of the method A_1B_1 would not alter the results very much.

Wave Heights in Aqueous Systems.—In the course of our polarographic investigations, it was observed that the wave heights for equivalent weights of sodium and potassium were not equal. An illustration of this difference appears in Fig. 3. The first four curves represent 0.001 *N* sodium chloride, the second four 0.001 *N* potassium chloride, and the last two represent a 1–1 mixture of sodium chloride and potassium chloride, the total concentration of the mixture being 0.001 *N*. The average wave height for sodium is 0.755″ (19.1 mm.) and the average for potassium is 0.858″ (21.8 mm.). An average value for the 1–1 mixture of sodium and potassium as represented in the last two curves of Fig. 3 is 0.823″ (20.9 mm.) and this is 0.068″ (1.7 mm.) more than the equivalent wave height for sodium. Since the reduction potentials for the alkali metals are close to each other, the polarograph does not register them separately. One might expect that the wave height for a 1–1 mixture of 0.0005 *N* sodium and potassium would give a wave height half-way between the equivalent height for 0.001 *N* sodium and 0.001 *N* potassium. The curves which illustrate this point actually show a difference of 0.103″ (2.6 mm.) between sodium and potassium, and the wave height for the mixture is 0.068″ (1.7 mm.) greater than the sodium, showing that the wave height for the mixture did not fall half-way between the height for the sodium and the potassium but nearly so. It did not seem that these differences were small enough to be ignored; hence this study was extended to include rubidium and cesium.

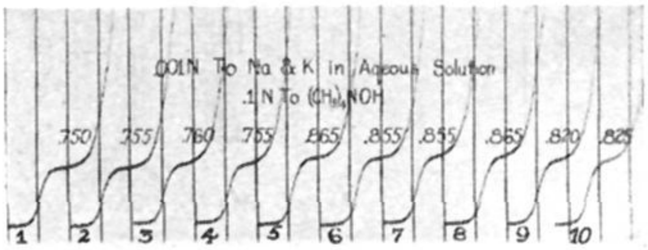

Fig. 3.—Curves 1, 2, 3, 4 for 0.001 *N* NaCl; curves 5, 6, 7, 8 for 0.001 *N* KCl; curves 9 and 10 for 0.0005 *N* NaCl and 0.0005 *N* KCl.

Solutions of equivalent weights of sodium, potassium, rubidium, and cesium chlorides were prepared and electrolyzed under conditions identical to those illustrated by the polarograms in Fig. 3. A representative set of curves for such a series is shown in Fig. 4. Direct comparison of the magnitude of the wave heights in Figs. 3 and 4 cannot be made because the sensitivity was different for each series and the tip also was different. By comparing the average wave heights in Fig. 4 one observes that the difference between sodium and potassium is 0.127″ (3.2 mm.), between potassium and rubidium 0.042″ (1.1 mm.), and between rubidium and cesium 0.067″ (1.7 mm.). The order of magnitude of the wave heights increases in the order sodium, potassium, rubidium, and cesium.

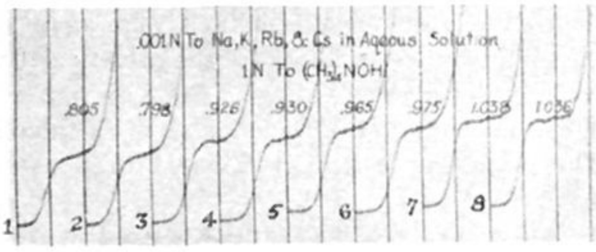

Fig. 4.—Curves 1 and 2 for 0.001 *N* NaCl; curves 3 and 4 for 0.001 *N* KCl; curves 5 and 6 for 0.001 *N* RbCl; curves 7 and 8 for 0.001 *N* CsCl.

Curves for lithium are not included in Fig. 4. This is due to the fact that the saturation wave for lithium is imperfectly, if at all, defined in aqueous systems.

In comparing the differences in wave heights for equivalent weights of elements of the alkali group, there is a variation in atomic weight from sodium to cesium. It is desirable to examine other elements not only to provide an element having a higher atomic weight but to provide two elements which are reduced at different potentials. Cadmium and lead were chosen for the purpose. For an electrolysis, it was found that 0.06 *N* Rochelle salt was satisfactory. The reducible ions, cadmium and lead, were 0.001 *N*. Representative results from this study are shown in Fig. 5. It can be seen that a difference does exist between the wave heights for equivalent weights of cadmium and lead. For a 1–1 mixture of the salts, the total equivalent weight being equal to that of the previous curves, the two waves did not appear in a ratio of 1–1 but appeared in heights nearly proportional to the differences shown in the two previous curves.

In the introduction we mention articles[2] that seem to indicate that equivalent amounts of cadmium, lead, and bismuth gave wave heights which were practically identical. While we will show that it is possible to change the environment in such a manner that the wave heights for equivalent amounts of different elements are the same, it did not seem that equal normal solutions necessarily should give equal wave heights for cadmium, lead, and bismuth when lithium nitrate and nitric acid were used as the supporting electrolyte in an aqueous system. Heyrovsky and Suchy[2] used lithium nitrate and nitric acid as supporting electrolytes when they studied the polarographic behavior of cadmium, lead, and bismuth. Since we had not used this particular supporting electrolyte, we repeated our experiments on cadmium, lead, and bismuth, duplicating as nearly as possible the conditions described by the above authors in their papers. Our results are shown in Fig. 6. It is observed that the differences in wave heights for cad-

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(5) Borcherdt, Meloche and Adkins, THIS JOURNAL, **59**, 2171 (1937).

mium and lead in this system are even greater than they appeared in Fig. 5 when Rochelle salt was used as the electrolyte. The second curve in Fig. 6 illustrates the addition of bismuth to the mixture. So far as the sensitivity of this system is concerned, the addition of bismuth did not seem to alter the differences which were previously observed between cadmium and lead.

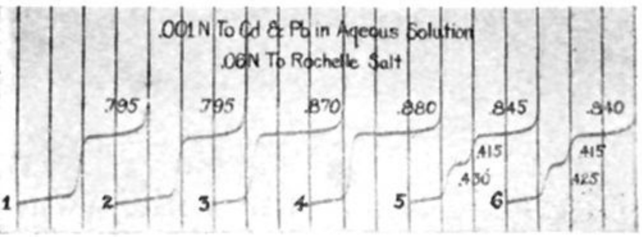

Fig. 5.—Curves 1 and 2 for 0.001 *N* $Cd(NO_3)_2$; curves 3 and 4 for 0.001 *N* $Pb(NO_3)_2$; curves 5 and 6 for 0.0005 *N* $Cd(NO_3)_2$ with 0.0005 *N* $Pb(NO_3)_2$.

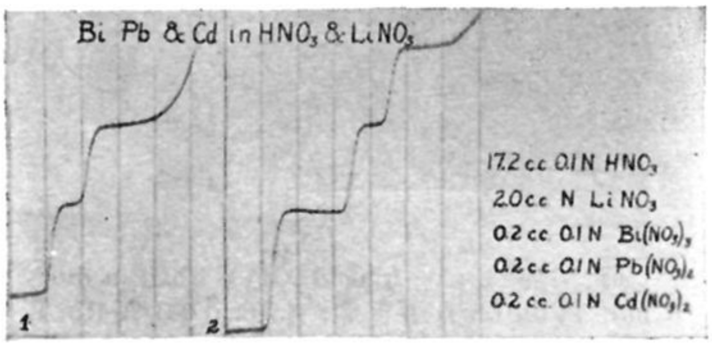

Fig. 6.—Curve 1 for 0.001 *M* $Cd(NO_3)_2$ with 0.001 *M* $Pb(NO_3)_2$; curve 2 for 0.001 *M* $Cd(NO_3)_2$; curve 2 for 0.001 *M* $Cd(NO_3)_2$, 0.001 *M* $Pb(NO_3)_2$ and 0.001 *M* $Bi(NO_3)_3$.

This information further substantiates the differences found for the elements of the alkali group, and indicates that when dealing with more than one element in solution, one cannot assume that equal wave heights of different elements mean equivalent concentration.

Wave Heights in Water–Alcohol Systems.—We know that aside from such factors as the capillary tip and temperature, we can alter the wave height for a given substance by changing the chemical environment. In the following experiments the effect of organic solvents on polarographic wave heights is described. A concentration of alcohol was selected which would easily change the character of the solution and yet not cause too great a difficulty in dissolving the salts of the alkali metals. Figure 7 represents the electrolysis of solutions containing the alkali chlorides 0.001 *N*, ethyl alcohol 80%, and tetramethylammonium hydroxide 0.1 *N*. Several important differences can be noticed. In the water–alcohol system lithium now shows a reproducible saturation wave. The order of the differences in wave height is lithium, sodium, potassium, rubidium, and cesium. Differences in wave height for equivalent amounts of these elements are less in alcohol–water than in pure water.

Table I gives the order of magnitude of decrease in wave height for sodium or potassium in various concentrations of alcohol as well as the relative wave heights for equivalent weights of sodium or potassium in different alcohols. A graph of percentage alcohol against wave height reveals that, in general, wave height decreases as the concentration of the alcohol increases. An equivalent weight of sodium or potassium in 70% ethyl or methyl alcohol gives wave heights of about the same magnitude. For a solution of propyl alcohol, the wave heights are decidedly lower.

TABLE I

Conversion factor inches to mm. = 25.4

Curve	% alcohol	Wave height, inches		
		Methyl alc.	Ethyl alc.	Propyl alc.
		Sodium Chloride		
1	0	1.38	1.40	1.37
2	10	1.27	1.33	1.14
3	20	1.18	1.21	0.99
4	30	1.17	1.16	.89
5	40	1.10	1.09	.81
6	50	1.13	1.00	.78
7	60	1.01	0.99	.68
8	70	1.08	1.00	.56
		Potassium Chloride		
1	0	1.165	1.175	1.185
2	10	1.08	1.110	1.075
3	20	1.045	1.065	1.00
4	30	0.995	1.03	0.92
5	40	.915	1.03	.90
6	50	.945	1.02	.765
7	60	.92	0.975	.70
8	70	.935	.99	.68

Since we know that the differences in wave heights for sodium and potassium are greater in the water system than in the water–alcohol system, it seemed desirable to extend this study to certain other organic solvents. We therefore included ethylene glycol, trimethylene glycol, and glycerol.

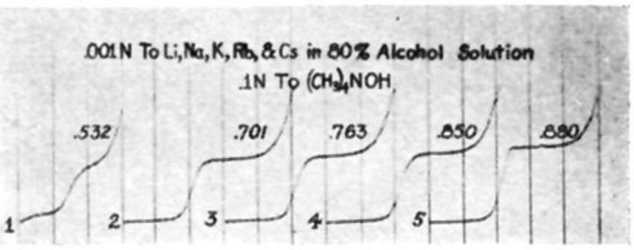

Fig. 7.—Curve 1 for 0.001 *N* LiCl; curve 2 for 0.001 *N* NaCl; curve 3 for 0.001 *N* KCl; curve 4 for 0.001 *N* RbCl; curve 5 for 0.001 *N* CsCl.

Polarograms for equivalent weights of sodium and potassium chlorides in ethylene glycol, trimethylene glycol, and glycerol are shown in Fig. 8. In curve 1 of Fig. 8, we have shown an equivalent weight of sodium chloride in water as a reference. Curve 2 shows sodium chloride in 80% ethyl alcohol; curve 3, sodium chloride in 80% ethylene glycol; curve 4, sodium chloride in 80% trimethylene glycol; curve 5, sodium chloride in 80% glycerol. Figure 9 represents a similar series for potassium. It will be noted that the wave heights for both sodium and potassium in these solvents decrease in the order mentioned, namely, water, ethyl alcohol, ethylene glycol, trimethylene glycol, and glycerol. As previously mentioned, in the water system, a given concentration of potassium gives a higher wave than an equivalent concentration of sodium. Equivalent concentrations of sodium and potassium give lower wave heights in 80% alcohol than in the water system, and the differences in height for sodium and potassium are less in the alcohol–water system than they are in pure water. While the wave height in 80% ethylene glycol is less than that in 80% ethyl alcohol, there is still a perceptible difference shown for equivalent weights of sodium and potassium. Wave heights in trimethylene glycol are only slightly smaller than those in ethylene glycol, and the differences shown for equivalent weights of sodium and potassium are almost imperceptible.

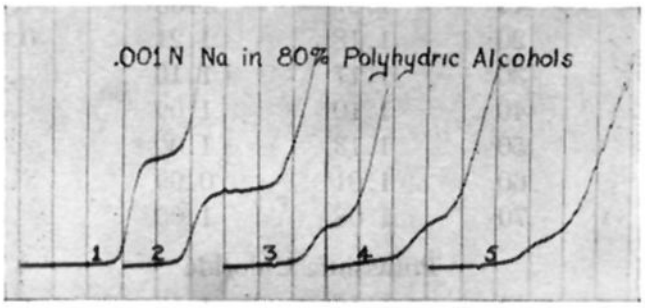

Fig. 8.—Curve 1 for 0.001 N NaCl in water; curve 2, same in ethyl alcohol; 3, in ethylene glycol; 4, in trimethylene glycol; 5, in glycerol.

The wave heights for equivalent weights of sodium and potassium in a solution containing glycerol are lowest of all, and there is no perceptible difference in the two wave heights. However, it will be noticed that while the shape of the curves for samples containing alcohol was almost ideal for quantitative measurements, the waves for the last three curves in Fig. 8 and Fig. 9 are successively less well defined. In this connection it may be observed that the viscosities of the last three media are relatively high.

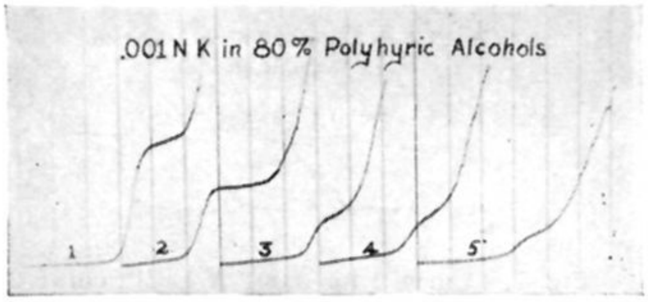

Fig. 9.—Curve 1 for 0.001 N KCl in water; 2, same in ethyl alcohol; 3, in ethylene glycol; 4, in trimethylene glycol; 5, in glycerol.

Wave Heights in Dioxane–Water System.—Figure 10 shows four curves, the first two of which represent equivalent weights of sodium and potassium in water and the second two represent the same weights of sodium and potassium in 70% dioxane. While the waves are less well defined in the dioxane system, it is important to note that the waves for sodium and potassium are practically identical. Figure 11 shows curves for equivalent weights of sodium, potassium, rubidium, and cesium in 80% dioxane. In this system the curves, so far as measurement is concerned, are identical. Since the curves in Fig. 10 are made with a different tip, they cannot be compared with curves in Figs. 8, 9, and 11. However, it may be mentioned that an equivalent weight of sodium or potassium in 80% dioxane gives a smaller wave height than it does in either water or alcohol systems.

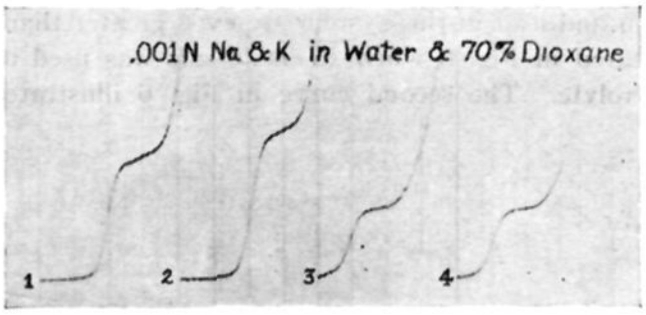

Fig. 10.—Curve 1 for 0.001 N NaCl in water; 2, 0.001 N KCl in water; 3, 0.001 N NaCl in dioxane; 4, 0.001 N KCl in dioxane.

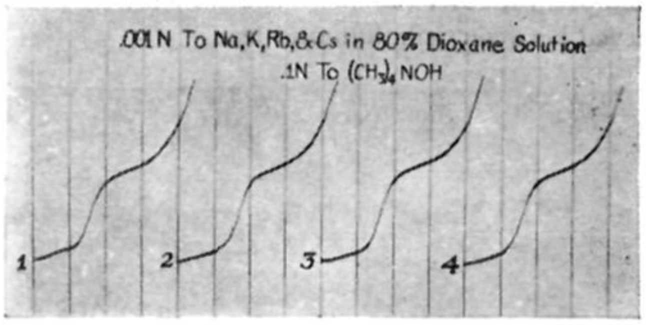

Fig. 11.—Curve 1 for 0.001 N NaCl in dioxane; 2, for 0.001 N KCl; 3, for 0.001 N RbCl; 4, 0.001 N CsCl.

Conclusion

In a preliminary paper before the Wisconsin Academy of Science[6] we reported that when solutions of sodium chloride and potassium chloride which are 0.001 N to chloride and 0.1 N to tetramethylammonium hydroxide are examined by means of the polarograph, the wave heights are not the same. In the present paper we have shown that the wave heights are different not only for equivalent concentrations of sodium and potassium chloride but also for all of the alkali chlorides. The wave heights increase in magnitude from sodium to cesium. These differences are not small enough to be ignored and therefore interfere with the application of the polarograph to quantitative analysis. In the usual procedure for the estimation of one element in an unknown an internal standard is used. The unknown is prepared in a suitable solution with a supporting electrolyte and a polarogram is recorded. Then a known amount of the element to be determined is added and another curve is recorded. The increase in wave height caused by the added standard is measured and from this the relationship

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(6) Peracchio and Meloche, *Wisconsin Acad. Sci.*, April 17, 1936.

between wave height and concentration of the element is calculated. By this procedure a reasonably precise value is obtained.

When there is more than one reducible ion in solution, one cannot presume that if the relationship between wave height and concentration is established for one, it will also hold for the others. In the precise application of the polarograph to chemical analysis, one is faced therefore, with the necessity of correcting for the discrepancies which exist or eliminating them.

In reporting the effect of the addition of certain non-aqueous solvents to solutions used in polarographic analysis we have shown that the wave heights for equivalent concentrations of alkali chlorides were lowered and that the differences between the wave heights for the alkalies were lessened. We also indicated that in solutions which contained 80% dioxane the wave heights for equivalent weights of alkali chlorides were the same. From these data one might assume that in cases where more than one element is to be determined one should use dioxane in the solution. This is by no means the case. Certainly, at present there is no one set of conditions which satisfy all samples. Information must be collected for the case at hand.

Ilkovic, Heyrovsky, Kemula, and Maas[7] have reported studies on the limiting current and have suggested the dependence on the diffusion constant, on the rate of dropping and the size of the drops at the dropping mercury cathode. Little emphasis has been placed on the importance of mobility in the application of the polarographic method to quantitative analysis. The few papers in this field have ignored the existence of differences in mobility and consequent differences in wave heights. This would be permissible if the highest degree of precision is not attempted. However, wave height differences cannot be ignored if the application of the technique is to be precise.

Summary

Polarograms are shown for sodium, potassium, rubidium, and cesium chloride in aqueous solutions and differences in wave height are shown to exist for equivalent concentrations of the chlorides.

Contrary to indications in the literature, it is shown that equivalent concentrations of cadmium, bismuth and lead chlorides do not give equal wave heights.

It is shown that the presence of various alcohols lowers the wave heights exhibited in aqueous solutions. Differences between the wave heights for equivalent concentrations of alkali chlorides are lessened.

Addition of certain polyhydric alcohols to the aqueous solutions of the alkali chlorides also lowered the wave heights but in cases of the more viscous solutions the curves were poorly defined.

When dioxane was added to aqueous solutions of the alkali chlorides, the wave heights for equivalent concentrations of the salts were the same. Although the shape of the curves was not ideal, the wave heights could be measured and the curves were suitable for quantitative analysis.

While the universal use of organic solvents in solutions prepared for the polarograph is not recommended, there are many cases where the use of such systems is desirable and in some cases even mandatory.

MADISON, WISCONSIN

RECEIVED APRIL 4, 1938

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(7) Information on limiting current: Ilkovic, *Coll. Czech. Chem. Comm.*, **6**, 498 (1934); Heyrovsky, *ibid.*, *loc. cit.*; Kemula, Congress Pure and Applied Chemistry, Madrid, 1934; Maas, *Coll. Czech. Chem. Comm.*, **10**, 42 (1938).