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39. Tetsu Kashima: Titration in Nonaqueous Solutions. XV.[1] Direct Differential Potentiometric Titration by Glass-Glass Retarded Electrodes. (1).* Titration in Anhydrous Acetic Acid.

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Potentiometric titration in aqueous solution is usually carried out using glass and calomel electrodes with a salt bridge consisting generally of a saturated aqueous solution of potassium chloride. Of the two liquid junction potentials, the one between the unknown and saturated potassium chloride solution is assumed to change slightly during titration. On the other hand it has been shown from investigations on nonaqueous titrations[1~3] that maintaining the liquid junction potential constant is difficult when nonaqueous solutions are employed.

Since the solvent of an ordinary reference electrode is generally water, a boundary between aqueous and nonaqueous solutions cannot be avoided even if a salt bridge of nonaqueous solution[4] is adopted. The liquid junction potential at this boundary cannot be treated theoretically at all, because it would be influenced by the mobility of ions in different media. There is a large and uncertain potential between the nonaqueous medium and aqueous potassium chloride of the reference electrode, frequently of several hundred millivolts, fluctuating during titration. In an attempt to avoid the difficulties mentioned above, some reference electrodes of nonaqueous solvents have been studied,[5] but changes of liquid junction potentials cannot be reduced and maintained constant in the course of titration, particularly when a titrant is a solvent different from the solution to be titrated.

In this paper the author wishes to introduce a direct differential titration method[6,7] by glass-glass retarded electrodes to nonaqueous titrations in order to avoid fluctuations

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1) Parts XII, XIII, XIV: Eiseishikenjo Hôkoku, **73**, 103(1955); **74**, 9, 15(1956).
2) T. Kashima, *et al.*: Yakugaku Zasshi, **75**, 329, 332, 586, 1112(1955).
3) T. Kashima, K. Kano: *Ibid.*, **76**, 50, 931(1956).
4) N.F. Hall, J.B. Conant: J. Am. Chem. Soc., **49**, 3047(1927); J.B. Conant, T.H. Werner: *Ibid.*, **52**, 4436(1930); R.H. Cundiff, P.C. Markunas: Anal. Chem., **28**, 792(1956).
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6) D.A. MacInnes, *et al.*: J. Am. Chem. Soc., **48**, 2831(1926); *ibid.*, **53**, 555(1931); Z. physik. Chem., **130A**, 217(1927); A. Kirrmann, N. Daune-Dubois: Compt. rend., **236**, 1361(1953)(C.A., **47**, 9215 (1953)).
7) J.J. Lingane: "Electroanalytical Chemistry," Interscience Publ. Inc., New York (1953).

of the liquid junction potentials.

Experimental

Reagents—Acetic acid : Reagent grade, is distilled and subjected to fractional freezing. The solid separated is purified by redistillation with CrO_3, preferably with the addition of a quantity of Ac_2O corresponding to water content in the solvent. b.p. 118°. Blank of the solvent is one drop of titrant to 25 cc.

p-Dioxane : Reagent grade is distilled. The middle portion of the distillate is shaken with dried Amberlite IRC-50 for 24 hours,[8] refluxed over NaOH, and the aqueous layer removed. It is redistilled and refluxed for an extended period of time over Na, fresh Na being added from time to time. It is then distilled in the presence of Na. b.p. 100.5~101°.

Perchloric acid : Guaranteed reagent grade, 70%.

Perchloric acid titrant : 0.05*N* in AcOH, cited in a previous paper.[1]

Perchloric acid titrant : 0.05*N* in *p*-dioxane, prepared by diluting 4.2 cc. of 70% $HClO_4$ to 1,000 cc. with *p*-dioxane under cooling with water. These titrants are standardized against approximately 0.1 g. of potassium hydrogen phthalate (National Bureau of Standards, U.S.A.) dried at 110° to constant weight.

1-Phenyl-3-methyl-3-pyrazolin-5-one : Reagent grade, recrystallized three times from benzene, excluding light, to white needles or prisms, m.p. 127~128°.

Antipyrine (1-Phenyl-2,3-dimethyl-3-pyrazolin-5-one) : J.P. VI, recrystallized three times from benzene to colorless plates, m.p. 112~112.5°.

4-Aminoantipyrine : Reagent grade, recrystallized three times from benzene in the dark to slightly yellow plates or prisms, m.p. 109~109.5°.

Aminopyrine (4-Dimethylaminoantipyrine) : J.P. VI, recrystallized three times from benzene to colorless prisms, m.p. 108~108.5°.

Acid salts of diphenhydramine, cited in a former paper.[3]

Apparatus—Beckman pH meter, model G.

Glass electrodes : Type "42" of Beckman Instruments.

Calomel electrode : Type "fiber" of Beckman Instruments.

Karl Fischer titration apparatus with a three-necked flask.

Procedure—About 25 cc. of 0.02*M* AcOH solution of a sample is titrated with 0.05*N* $HClO_4$ titrant using Karl Fischer titration apparatus. Electromotive force of the titration cell is measured by Beckman pH meter with two glass electrodes of the same response and one of which serves as a "retarded electrode."[7] Because of the high electric resistance of the titration cell, e.g. about 500 megohm (10^6 ohm) at 20°, the surface of the flask, test tube, and electrodes are cleaned and coated with "Desicote" of Beckman Instruments, and the apparatus is shielded electrostatically. The reproducibility of values of electromotive force obtained is ±2 mV in a room of constant temperature.

Two identical glass electrodes are placed in the solution to be titrated, of which the retarded

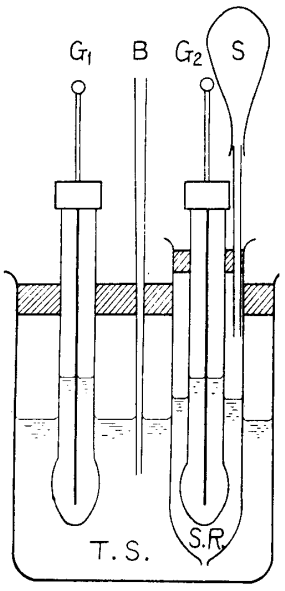


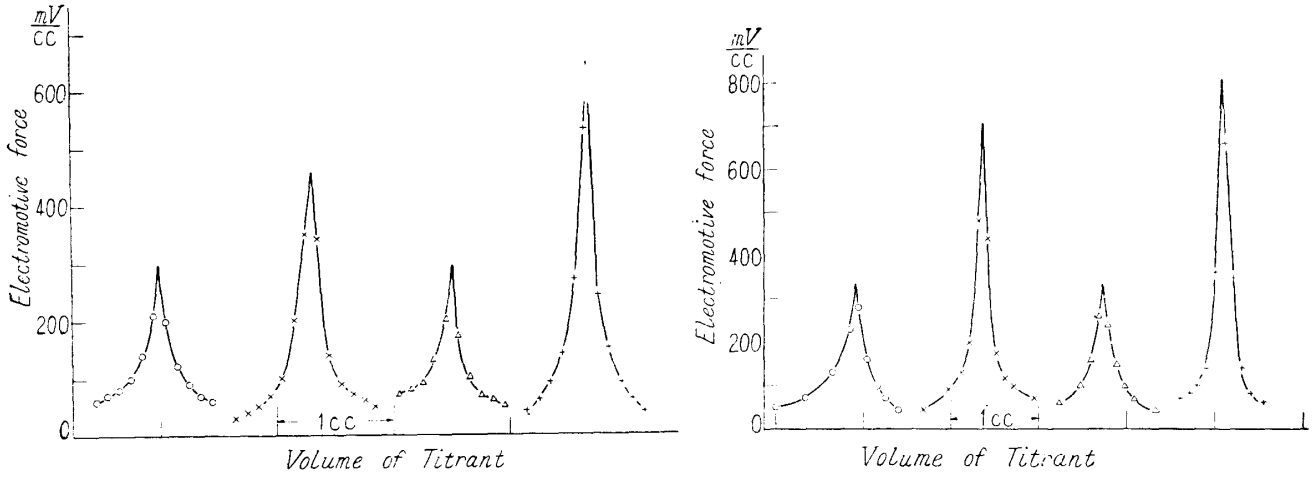
Fig. 1. Titration Cell Assembly

G_1, G_2 : Glass electrode
B : Buret
S : Squirt
T.S. : Test solution
S.R. : Solution of retarded electrode

8) L. Levi, I.G. Chatten, M. Pernarowski : J. Am. Pharm. Assoc., Sci. Ed., **44**, 61(1955).

electrode is in a small portion of solution separated from the main body of the solution, acting as a kind of reference electrode, and hence isolated from immediate contact with the titrant. The titration cell used is shown in Fig. 1, the retarded electrode being in a test tube with a small hole at the bottom, provided with a large squirt for flushing and refilling.

When each increment, ΔV, of the titrant is added to the solution, an electromotive force, ΔE, will be observed between the retarded electrode and the other glass electrode in the main body of the solution. After each measurement the solution around the retarded electrode is forced into the main body of the solution, and the test tube is washed several times by flushing and refilling. Accordingly at each stage of the titration the retarded electrode is kept behind the other electrode, and the difference in the composition between the solutions around two electrodes can be maintained as little as possible. The end point is, of course, indicated by a maximal value of ΔE, which increases rapidly near the end point.

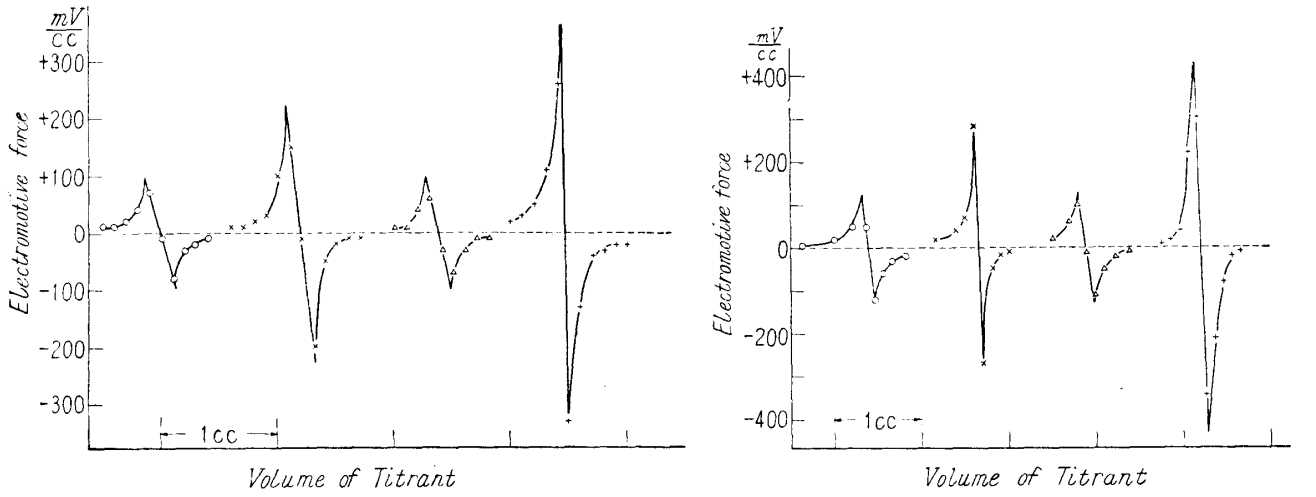


(a) Solvent of Titrant: Acetic Acid

(b) Solvent of Titrant: *p*-Dioxane

Fig. 2. Direct Differential Titration Curves of 1-Phenyl-3-methyl-3-pyrazolin-5-one Derivatives (0.02*M*, 25 cc.) with 0.05*N* Perchloric Acid by Glass-Glass Retarded Electrodes at 23°±1°C.

—○— 1-Phenyl-3-methyl-3-pyrazolin-5-one —△— 4-Aminoantipyrine
—×— Antipyrine —+— Aminopyrine



(a) Solvent of Titrant: Acetic Acid

(b) Solvent of Titrant: *p*-Dioxane

Fig. 3. Second Derivative Differential Titration Curves of 1-Phenyl-3-methyl-3-pyrazolin-5-one Derivatives

—○— 1-Phenyl-3-methyl-3-pyrazolin-5-one —△— 4-Aminoantipyrine
—×— Antipyrine —+— Aminopyrine

The direct differential titration curve is obtained by plotting the values of electromotive force, corrected for the usually existing small electromotive force between two electrodes, against the volume of titrant. The equivalence point is characterized by a maximal value of $\Delta E/\Delta V$, namely, the top of the curve, in Fig. 2. The end point can also be determined as the point where the second derivative, $\Delta^2E/\Delta V^2$, becomes zero and it is calculated readily as the difference of the two neighboring $\Delta E/\Delta V$, shown in Fig. 3.

Since the volume of solution around the retarded electrode is kept small compared to the total volume, no significant error results from withholding this small volume. Suppose 25 cc. of 0.02N test solution is titrated with 0.05N titrant solution (10 cc.) and the volume of solution around the retarded electrode is 1 cc. The error due to the fact that the last 0.1-cc. increment is added to only 34 cc. instead of the total 35 cc. will amount to $0.1\times1\div35=0.00286$ cc. of the titrant or only 0.0286%, which is certainly negligibly small and could not be detected with an ordinary buret.

Results

Direct differential titration curves for the derivatives of 1-phenyl-3-methyl-3-pyrazolin-5-one obtained by the present method are shown in Fig. 2, and the second derivative differential titration curves obtained from them are illustrated in Fig. 3. For comparison, conventional potentiometric titrations were carried out with the same substances under the same conditions except the use of glass-calomel electrode combination, and the titration curves thus obtained are presented in Fig. 4 and the former paper.[1] These results of the assays are summarized in Table I.

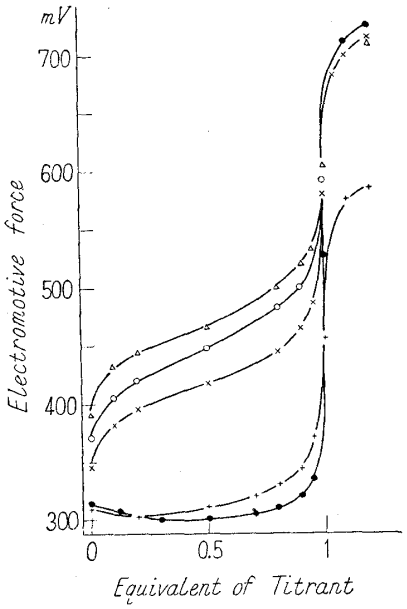


Fig. 4. Potentiometric Titration Curves of 1-Phenyl-3-methyl-3-pyrazolin-5-one Derivatives

0.02M in AcOH with 0.05N $HClO_4$ titrant in p-dioxane by glass-calomel electrodes at 23°±1°C

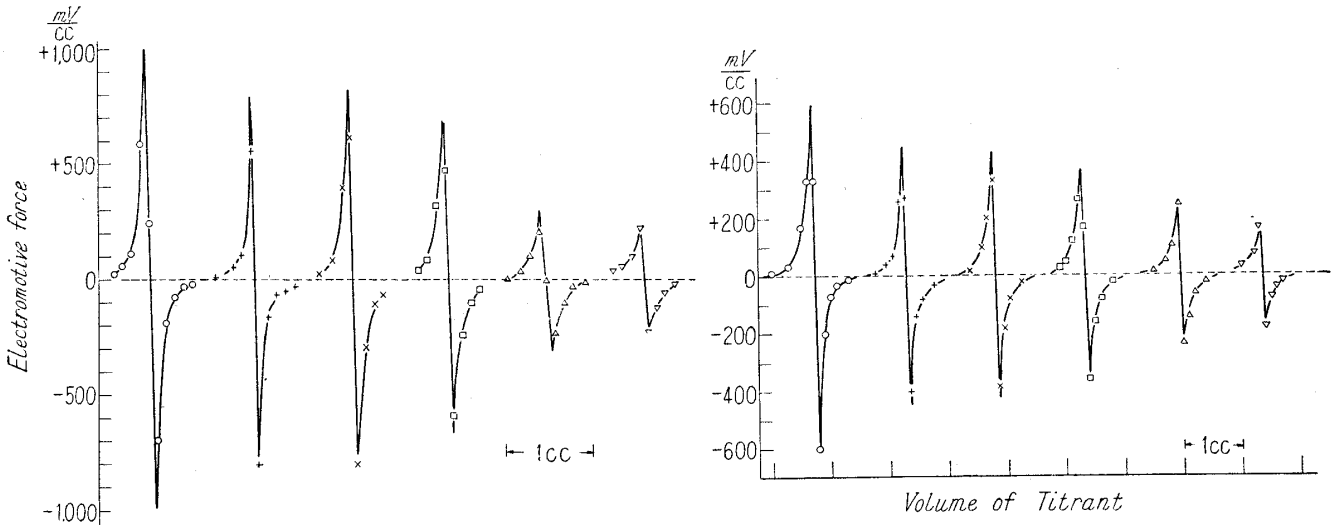
—○— 1-Phenyl-3-methyl-3-pyrazolin-5-one
—×— Antipyrine
—△— 4-Aminoantipyrine
—+— Aminopyrine
—•— Potassium hydrogen phthalate

Table I. Determination of 1-Phenyl-3-methyl-3-pyrazolin-5-one Derivatives by Direct Differential Potentiometric Titration or Potentiometric Titration in Anhydrous Acetic Acid

Base	Method	Acetic acid* Taken g.	Acetic acid* Found %	p-Dioxane* Taken g.	p-Dioxane* Found %
1-Phenyl-3-methyl-3-pyrazolin-5-one	D	0.0875	99.95	0.0760	99.6
	P	0.0833	99.6	0.0863	99.5
Antipyrine	D	0.0896	100.05	0.0946	99.7
	P	0.0953	99.65	0.0976	99.6
4-Aminoantipyrine	D	0.1036	100.0	0.0996	99.8
	P	0.0958	99.7	0.0985	99.6
Aminopyrine	D	0.1082	98.75	0.1141	98.6
	P	0.1163	98.55	0.1083	98.35

Each value is the average of two or three samples.
* Solvent of titrant.
D : Direct differential potentiometric titration method.
P : Potentiometric titration method.

The second differential titration curves of several acid salts of diphenhydramine are illustrated in Fig. 5. The effect of the acid residue of the salt in the titration of the sample will be seen from the curves (cf. previous papers[3]).



(a) Solvent of titrant : AcOH

(b) Solvent of titrant : *p*-Dioxane

Fig. 5. Second Derivative Differential Titration Curves of Acid Salts of Diphenhydramine (0.02 *M*) at 23°±1°C

—○— Succinate —×— Maleate —△— Nitrate
—+— Fumarate —□— Oxalate —▽— Phosphate

Discussion

The precision and accuracy of the differential titration method is said to be high, but this method is slower and less convenient than other electrometric technique of titration and electrode of the same response would not be obtained easily. One of the advantages of this method is that it does not require a reference electrode and this advantage would not be so important if the titration is carried out in aqueous solution, but of great importance in nonaqueous solution, because the liquid junction potential between two solutions of the same solvent is smaller and more stable than those between two solutions of different solvents.

Titration in aqueous solution is usually carried out in the next cell,

$$\underset{E_{g1}}{\text{Ag–AgCl, Cl}^-} \parallel \text{T. S. soln.} \mid \underset{E_{j2}}{\text{satd. KCl soln.}} \mid \underset{E_{j1}}{\text{Cl}^-, Hg_2Cl_2, Hg} \qquad (1)$$

and nonaqueous titration is frequently carried out in the cell,

$$\underset{E_{g2}}{\text{Ag–AgCl, Cl}^-} \parallel \text{T. S. nonaq.} \mid \underset{E_{j3}}{\text{satd. KCl soln.}} \mid \underset{E_{j1}}{\text{Cl}^-, Hg_2Cl_2, Hg} \qquad (2)$$

where E_{j1} and E_{j2} are small and stable, but E_{j3} is large and unstable, particularly when titration is carried out in a mixed solvent or in a solvent which is different from the medium of titrant, even if a salt bridge or a reference electrode of nonaqueous solution is used.

The cell for this direct differential titration (cf. Fig. 1) is as follows:

$$\underset{E_{g2}}{\text{Ag–AgCl, Cl}^-} \parallel \text{T. S. nonaq.} \mid \underset{E_{j4}}{\text{S. R. nonaq.}} \parallel \underset{E_{g3}}{\text{Cl}^-, \text{AgCl–Ag}} \qquad (3)$$

where the liquid junction potential, E_{j4}, is small and stable, because both the media and solutes of the solution in the main body and those of the solution around the retarded electrode are the same or similar to each other, even if the solvent of the titrant is

different from that of the solution to be titrated, or a mixed solvent is used. Glass electrode was found to function properly and stable in acidic solvents, and high accuracy and precision can be expected by this method.

If the solvent of titrant is *p*-dioxane instead of acetic acid, it can be determined more sensitively, especially when the basicity of the sample is rather stronger in the solvent (cf. Figs. 2, 3, and 5).

Estimating by the half-neutralization point of the potentiometric titration curve,[3] the effect on titration of the combined nitric acid residue of the diphenhydramine salt is larger than that of phosphoric acid, but by the differential titration curve the effect of the former is smaller than that of the latter. It would be caused by the effect of the second dissociation of phosphoric acid near the end point, so the end point of salt of organic base could not determine very accurately by ordinary method.

The author is indebted to Dr. T. Kariyone, Director of the Laboratory, Dr. K. Nagasawa and Dr. Y. Nozaki for their kind encouragements and advices, and wishes to thank Messrs. M. Tsuchiya and K. Kano for their valuable assistance in the preparation of the reagents.

Summary

Direct differential potentiometric titrations in nonaqueous solutions were carried out using two glass electrodes, one of which is used as a retarded electrode. One and the greatest disadvantages of nonaqueous potentiometric titrations employing a reference electrode whose solvent is different from that of the solution or of the titrant, the fluctuation of liquid junction potentials between the two solutions of different solvents, can be overcome by this method.

This method applied to the determinations of four derivatives of 1-phenyl-3-methyl-3-pyrazolin-5-one and several acid salts of diphenhydramine in anhydrous acetic acid solution with perchloric acid in acetic acid or *p*-dioxane as the titrant, was shown to give satisfactory and reproducible results.

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40. Tsukasa Kuraishi : 4,5-Substituted Pyridazines. IV.[1] The Effect of Some Substituents at the 4-Position on the Ultraviolet Absorption Spectrum of 3,6-Dichloropyridazine.

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Recently, studies of the near-ultraviolet absorption spectra of diazines have been extended by several workers. Particulary, much attentions have been paid to the weak absorption band arising from a non-bonding nitrogen electron transition.[2] In preliminary works the present writer studied the vibrational spectra of the diazines and electronic spectra of the weak absorption of pyrazine vapor.[3] In order to investigate the effect of some substituents at the 4-position of pyridazine ring on the ultraviolet absorption spectra, the absorption maxima of several compounds of the following type

* Showa-machi, Nagasaki (倉石 典).

1) Part Ⅲ : This Bulletin, **5**, 587(1957).
2) For discussion of $n-\pi^*$ and $\pi-\pi^*$ transition of the diazines, see F. Halverson, R.C. Hirt : J. Chem. Phys., **19**, 711(1951); R.C. Hirt, F.T. King, J.C. Cavagnol : *Ibid.* **25**, 574(1956); R.H. Hornig, E.D. Amstutz : J. Org. Chem., **20**, 1069(1955).
3) M. Ito, R. Shimada, T. Kuraishi, W. Mizushima : J. Chem. Phys., **25**, 574(1956); **26**, 1508(1957).