14. Morizo Ishidate and Masaichiro Masui: High Frequency Titration. XI. Non-Aqueous Titration by High Frequency Method. (3)[1]. Titration of Salts of Organic Acids.

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Although a few papers[2] have been published regarding determinations of salts of organic acids in non-aqueous medium with chemical indicators or by potentiometric methods, none can be found on conductometric or high frequency methods. As reported in the previous paper[1], anhydrous sodium carbonate yielded fair results in the standardization of 0.1 *N* perchloric acid-acetic acid solution by the high frequency method. Consequently, it was considered that this method is also useful for the determination of the salts of organic acids.

The present study was undertaken in order to apply the high frequency titration in non-aqueous solutions to the salts of organic acids recorded in the Japanese Pharmacopoeia.

As was pointed out in the previous paper[1], it was necessary to add as much as about 32±12% of methanol in titrating solutions, if ordinary high frequency titrator, not the one for use in dielectric constant measurements, was to be used. After the respective samples were dissolved in methanol or in acetic acid, and heated if necessary, benzene was added to make the necessary volume. With the exception of sodium oxalate, the most satisfactory results were obtained with sodium salts which were easily dissolved by this method and directly titrated with perchloric acid solution in acetic acid (Fig. 1). Sodium oxalate was difficult to dissolve in the above solvents, and was therefore dissolved in excess of perchloric acid and back titrated with sodium acetate solution. Precipitation of sodium oxalate after passing the equivalence point

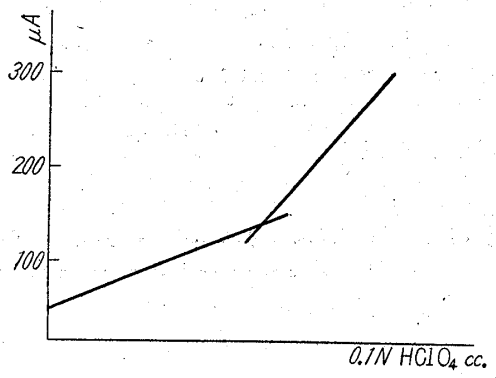

Fig. 1.
Direct titration curve of Na benzoate, Na salicylate, Na citrate, with 0.1*N* $HClO_4$ in CH_3COOH.
Solvent: $CHO_3H + (CH_3COOH) + C_6H_6$

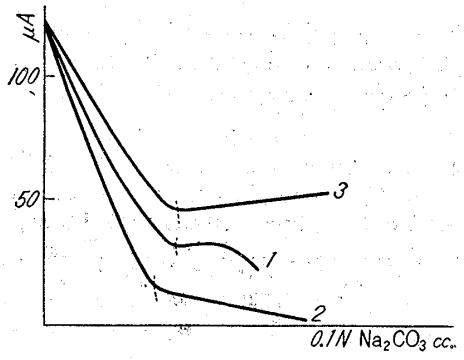

Fig. 1′.
Back titration curves of Na oxalate with 0.1*N* Na_2CO_3 in AcOH.
Solvent: $CH_3OH + C_6H_6 + (CH_3COOH)$ ……Curve (1)
$CH_3OH + C_6H_6 + (CH_3COOH)$
Ethylene glycol…Curve (2), (3)

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1) Part 2: J. Pharm. Soc. Japan, 73, 1011 (1953).
2) P. C. Markunas, J. A. Riddick: Anal. Chem., 23, 337 (1951); C. W. Pifer, E. G. Wollish: *Ibid.*, 24, 519 (1952).

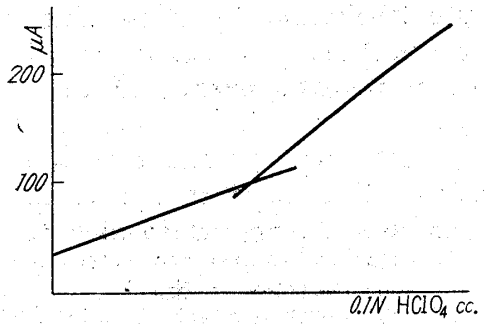

Fig. 2.
Back back titration curve of K bicarbonate and KNa tartrate, with 0.1N $HClO_4$.
Solvent: $CH_3OH+C_6H_6+CH_3COOH$.

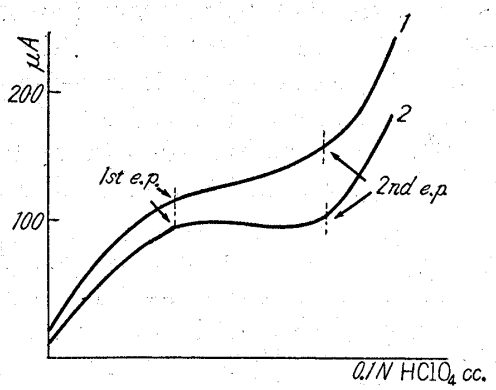

Fig. 3.
Direct titration curves of Pb acetate (1), Ca lactate, and Ca gluconate (2), with 0.1N $HClO_4$ in AcOH.
Solvent: $CH_3OH+C_6H_6+$ (CH_3COOH)

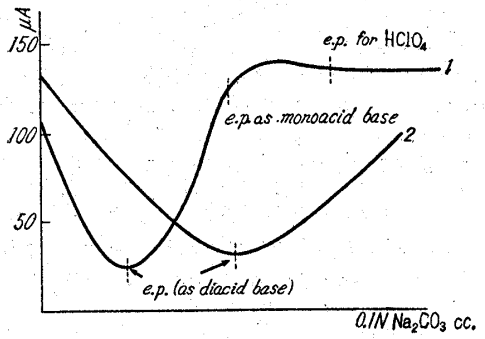

Fig. 4.
Back titration curves of Ca lactate and Ca gluconate, with Na_2CO_3 in AcOH.
Solvent: $CH_3OH+C_6H_6+$ (CH_3COOH)

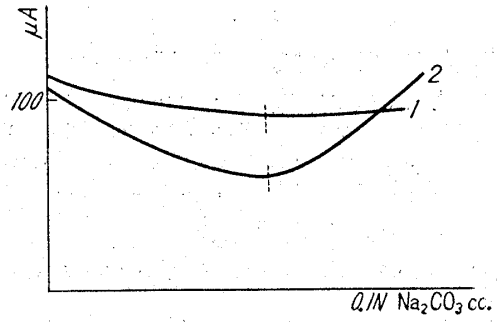

Fig. 5.
Back titration curves of Pb acetate with 0.1N Na_2CO_3 in AcOH.
Solvent: $CH_3OH+C_6H_6+$ (CH_3COOH) ··· (1)
(1) +Ethylene glycol ····· (2)

could be avoided by the addition of a small amount of ethylene glycol (Fig. 1′). Potassium salts were soluble in the above solvents, but potassium perchlorate was insoluble, hence its precipitation occurred after each addition of the titrant, therefore a long time elapsed until the moving of the meter ceased. In order to carry out this titration in a shorter period, excess perchloric acid was added, heated for a short time, and after adding excess sodium acetate, titrated with perchloric acid (Fig. 2). The addition of excess of the reagent was very easily observed because the moving of the meter made it possible to discern approximately when it passed the equivalence point.

Quite different results were obtained with lead and calcium salts. The curves shown in Fig. 3 were observed by the direct titration of these salts and it was difficult to make determinations from these curves. However, calcium salts were determined fairly accurately by back titration (Fig. 4). In the case of back titration of lead salts, no measurable break appeared (Fig. 5, curve 1) but by the addition of a small amount of ethylene glycol a feasible curve for the determination was obtained (Fig. 5, curve 2).

As are apparent from the procedures and the forms of the titration curves, best precision and accuracy were obtained with sodium salts, with an accuracy of about

0.2~0.3%, followed by potassium salts with an accuracy of about 0.4%, and with about 0.4~0.7% for lead and calcium salts.

In the present study, it was found that a mixture of methanol and benzene and, if necessary, acetic acid and ethylene glycol, was an excellent solvent for the salts to be tested, and perchloric acid and sodium acetate were satisfactory titrants in the high frequency titration of the salts of organic acids.

Experimental

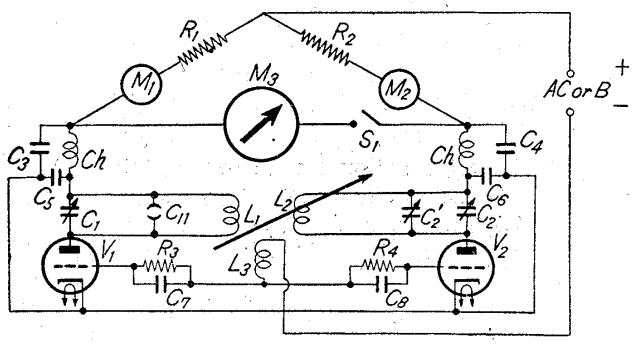

Fig. 6.
Circuit Diagram of High Frequency Oscillator and Accessory Circuit.
V_1, V_2; 6*SN*7 L_1, L_2: 3 turns (dia. 2.5 cm., 1.0 cm. apart) L_3: 4 turns (dia. 2.5 cm., 1.0 cm. apart) Ch: 90μH C_1, C_2: ca 90$\mu\mu$F C_2': ca 10$\mu\mu$F C_3, C_4: 0.01μF C_5, C_6: 0.1μF C_7, C_8: 0.01μF R_1, R_2: 1.5kΩ R_3, R_4: 10kΩ C_{11}: for titration cell S_1: switch M_1, M_2: 15mA ammeter M_3: 300μA ammeter

Apparatus—The apparatus used is the same as that reported in the previous paper[3] and its circuit diagram is shown in Fig. 6.

Reagents—Perchloric acid solution, 0.1*N*, prepared by adding 70% perchloric acid (G.R.) reagent to glacial acetic acid, in the usual manner; acetic anhydride was not used. After a few days the solution was standardized against standard anhydrous sodium carbonate.

Sodium acetate solution, 0.1*N*, prepared by dissolving standard anhydrous sodium carbonate, weighed accurately, in glacial acetic acid and made up exactly to the necessary volume.

Solvents—Methanol, benzene, and glacial acetic acid were used after purification. Ethylene glycol, first grade reagent*, was used without purification.

Samples—Sodium oxalate was Merck's "pro Analyse," and potassium hydrogen carbonate (over 99.9%) and potassium sodium tartrate were standard reagents of JIS.* Other chemicals used were Japanese Pharmacopoeae grades. Further purification was not carried out but determinationof their purity according to the Japanese Pharmacopoeia VI was carried out at the same time.

Procedures—Direct titration: 10~100 mg. of sample was weighed accurately and dissolved in 2~5 cc. of acetic acid or in 10~30 cc. of methanol, if necessary under heating. Methanol and benzene were added to the methanol solution as described in the table (usually 32±5%), and titrated with 0.1*N* perchloric acid solution by high frequency titration.

Back titration: 10~50 mg. of sodium oxalate was dissolved in excess 0.1*N* perchloric acid solution (1~15 cc.), methanol and benzene were added as described above, 2 cc. of ethylene glycol added, and then titrated. 20~100 mg. of calcium or lead salt was dissolved in 2~5 cc. of acetic acid and 10~30 cc. of methanol, further amounts of methanol and benzene added, and 0.1*N* perchloric acid solution was added dropwise observing the meter (Fig. 6, M_3) which moved as shown in Fig. 3. After the latter steep slope was observed, 1~4 cc. more of the acid was added and titrated with sodium acetate solution. In the case of lead salts, 0.2~2 cc. of ethylene glycol was added.

Back back titration: Excess 0.1*N* perchloric acid solution was added to potassium salts and potassium perchlorate was precipitated by slightly boiling for about 30 seconds. Methanol and benzene were added as described above and then 0.1*N* sodium acetate was added until it was 1~2 cc. in excess under observation of the meter. This excess sodium acetate was titrated with 0.1*N* perchloric acid solution.

Correction of 0.1*N* perchloric acid and sodium acetate solutions for the temperature difference between the time of titration and of standardization was made by the same coefficient of expansion as acetic acid, viz. 0.0011 per 1°C.

3) J. Pharm. Soc. Japan, 73, 921 (1953).
* Reagent grades are those of Japanese Industrial Standard (JIS).

Table I

Compound	Purity by other method (%)	Amount (mg.)	Solvent (cc.)				Purity found (%)		
			AcOH	MeOH	Ethylene glycol	Benzene	Direct titrn.	Back titrn.	Back back titrn.
Na oxalate	99.95	11.95～46.65	0～2	10～17	1.8～2	35		100.14 s*=0.56	
Na benzoate	99.69**	23.76～83.60	0～7	15～18		35	99.73 s*=0.28		
Na salicylate	99.50**	37.72～102.59	0～5	15～17		35	99.50 s=0.05		
Na citrate	99.47**	29.89～69.47	5	17		35	99.56 s=0.33		
Pb acetate	102.9**	37.78～92.81		15～22	0.2～2	35		103.21 s=0.45	
Ca lactate	98.62**	19.87～52.13	5	12～17		35～43		99.29 s=0.72	
Ca gluconate	100.41**	30.24～93.79	3～5	17		35		100.25 s=0.68	
K bicarbonate	99.9	21.66～81.39	5	17～18		35			99.75 s=0.44
K Na tartrate	97.7**	22.72～44.44	3～4	17		35			98.14 s=0.40
	101.1**	22.72～88.10	3～5	17		30～35			100.74 s=0.37

* $\sqrt{\frac{1}{n-1}\sum(x_1-\bar{x})^2}$

** Determined by the method described in the Japanese Pharmacopoeia VI Ed.

Summary

Salts of organic acids, mainly Pharmacopoeiae chemicals, were determined by the high frequency titration in non-aqueous solutions, in a mixture of methanol and benzene, and, if necessary, acetic acid and ethylene glycol, with perchloric acid or sodium acetate in acetic acid. Sodium salts were generally titrated directly with perchloric acid, and accuracy was 0.2%. Potassium salts were titrated by back back titration, giving accuracy of 0.4%, while calcium salts were titrated with an accuracy of 0.4～0.7%.

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15. Itiro Yosioka and Hirotaka Otomasu: Studies on Phenazines. VI.[1] Synthesis of Iodinin Isomers. (3). Syntheses of 1,3-, 1,4-, and 2,3-Dihydroxyphenazine Di-N-oxides.

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The synthesis of dihydroxyphenazine di-N-oxides, the iodinin isomers, whose hydroxyl

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1) Part V: This Bulletin, 2, 25 (1954).