

SCIENTIFIC SECTION

DIETHYLPHTHALATE V.*

BY J. A. HANDY AND L. F. HOYT.¹

Introduction.—The new qualitative test for phthalate described in our paper Diethylphthalate IV (1) has been further investigated. This test depends upon the formation of characteristic needle-like crystals of potassium phthalate when a phthalate is saponified with alcoholic potash. The solubility of potassium phthalate in several alcohols has been determined and a quantitative method has been developed for estimating phthalates in essential oils and synthetic perfume materials.

Review of the Literature.—Leffmann and Trumper (2) have made a study of several published methods for detecting diethylphthalate and found that the phenolphthalein test could be improved by using a prepared phenolsulphonic acid reagent. Leffmann and Trumper claim that in applying the fluorescein type test the procedure recommended by Andrew (where the condensation is carried out at not over 100° C.) gives negative blanks with substances, particularly acetaldehyde, which at a higher temperature of condensation give a temporary positive result. *Note:* Our own experience has been similar in regard to blanks, and it is true that in the absence of interfering substances very small amounts of diethylphthalate, *i. e.*, 0.2 mg., can be easily and positively detected by the Andrew test. We have found, however, by carefully controlled condensations on small amounts of phthalates at different temperatures that a larger yield of fluorescein, and consequently a more intense and more sensitive test is obtained when the condensation is carried out at 150–160° C. (Diethylphthalate III. JOUR. A. PH. A., 14, 226. Diethylphthalate IV. JOUR. A. PH. A., 15, 445–6.)

Thoms (3),(4) describes qualitative methods for detecting diethylphthalate in alcohol and essential oils which depend on the familiar fluorescein reaction. He states that his procedure will detect 0.5 mg. of diethylphthalate in 50 cc. of alcohol, but gives no details of the sensitiveness of his procedure as applied to its detection in essential oils. A method of isolating the ester from 500 ml. quantities of alcohol is outlined.

Reid (5) has patented the manufacture of certain butyl esters of phthalic acid, *i. e.*, dibutyl, monobutyl, benzyl butyl and ethyl butyl phthalates, and states that these esters may be used as solvents for terpenes, esters, aldehydes etc., such as are used in perfumery.

STUDY OF THE QUALITATIVE POTASSIUM PHTHALATE CRYSTAL TEST.

1. Saponification tests were made on esters of a number of acids in the following manner: 5 drops if liquid, or 0.1 Gm. if solid, of the acid or its ester was added to 5 cc. alcoholic potash (40 Gm. KOH per liter of *absolute* ethyl alcohol) in a test-tube and the mixture heated under reflux for 30 minutes, or for a lesser time if crystals appeared.

* Read before Scientific Section, A. PH. A., Philadelphia meeting, 1926.

¹ Laboratories of Larkin Co., Inc., Buffalo, N. Y.

The acids chosen were those which are either (1) reported to occur free or as esters in essential oils, or (2) whose esters like those of phthalic acid are liable to be added to essential oils or (3) acids whose esters are in commercial use as solvents or plastisizers in the lacquer industry and which might at some time be used, as the phthalic acid esters are now used, in essential oils. (This included diamyl and dibutyl phthalates, diethyl carbonate, dibutyl tartrate, diethyl oxalate and tricresyl phosphate.) In case the potassium salt of an acid is insoluble in alcohol, as is potassium phthalate, identical crystals of potassium phthalate will of course be obtained by the saponification of the various esters, such as amyl, butyl, ethyl, etc., with alcoholic potash.

Table I shows the results. It is to be noted that all of the acids tested in the acetic series yield potassium salts which are freely soluble in absolute alcoholic potash. The potassium salt of myristic acid and the corresponding soaps, potassium palmitate and stearate are insoluble in cold alcoholic potash, but freely soluble in hot alcoholic potash.

Notes: The concentration of the potassium salt was approximately 2% in each case. In some cases, such as diethyl oxalate and dibutyl tartrate, saponification takes place almost instantaneously in the cold. The result with tricresyl phosphate was rather surprising but there is no question that the ester was saponified readily as shown by the development of a pronounced cresol odor in the mixture hitherto free from any odor of cresol. Even after boiling under reflux for 2 hours no insoluble residue of potassium phosphate appeared and hence this salt must be soluble (to the extent of 2% at least) in absolute alcoholic potash.

It is an interesting fact that the diamyl and dibutyl esters of phthalic acid are practically tasteless, in sharp contrast to diethylphthalate which has an intensely bitter taste. Dibutyl tartrate on the other hand is very similar in taste to diethylphthalate; diethyl oxalate has a sharp sour taste similar to that of oxalic acid; diethyl carbonate both in taste and odor is similar to ethyl ether. Tricresyl phosphate is entirely tasteless and odorless.

MICROSCOPICAL EXAMINATION OF CRYSTALS.

The crystal structure of the potash salts which are insoluble in alcohol was critically examined, and photomicrographs were taken at magnifications of 100 \times . These photomicrographs show that potassium carbonate is similar in appearance to potassium phthalate, and these two salts can of course be readily distinguished by the addition of any dilute acid which would cause vigorous effervescence with the carbonate. Potassium citrate also crystallizes in needles which are generally similar to those of potassium phthalate, although in the course of repeated preparation of both the citrate and the phthalate crystals it was observed that the citrate crystals were invariably smaller and finer than those of potassium phthalate. It is of course extremely unlikely that an organic citrate would be present in any sample which was being tested for phthalates.

The fluorescein test could be readily applied to crystals of any potassium salt of unknown composition, to determine whether or not the crystals consisted of, or contained, potassium phthalate. The solution containing the crystals should be filtered, the crystals washed with alcohol, and heated to 150° C. for about 3 min. with 1-2 cc. resorcinol—sulphuric acid reagent (2.5 Gm. resorcinol

in 100 cc. 1.84 H_2SO_4). After cooling the mixture should be diluted with distilled water and made distinctly alkaline. A persistent yellowish green fluorescence is proof that the crystals consisted of, or contained, potassium phthalate.

Incidentally the potassium phthalate crystal test furnishes a means of separating a phthalate, from the sample containing it, with a minimum of impurities and facilitates the application of a reliable fluorescein test for phthalates.



Fig. 1.—Potassium Phthalate. $\times 100$.



Fig. 2.—Sodium Phthalate. $\times 100$.

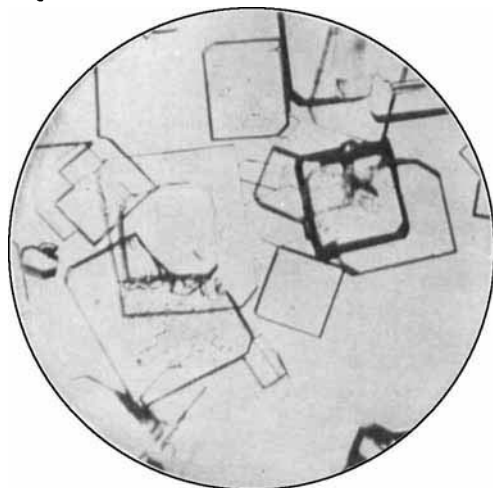


Fig. 3.—Potassium Anthranilate. $\times 100$.

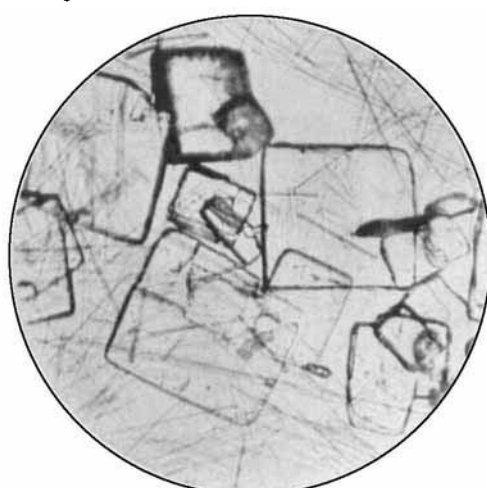


Fig. 4.—Mixture: 8 parts Potassium Anthranilate, 1 part Potassium Phthalate. $\times 100$.

The photomicrographs show that the potassium salts of oxalic, succinic, and tartaric acid as prepared by alcoholic saponification of their esters are virtually amorphous. The potassium salts of anthranilic, anisic, benzoic and cinnamic acids all have distinctive crystalline forms.

¹ It was found impractical to use a beautiful color plate, taken with polarized light, in the JOURNAL.

The photomicrographs show that potassium phthalate can be readily distinguished even in a mixture containing a large excess of potassium anthranilate, benzoate, or cinnamate.

The crystals of potassium phthalate retain their characteristic size and form in all three of these mixtures. The potassium anthranilate crystals in mixture with potassium phthalate, also show a crystal form and size identical with that of the pure crystals. The characteristic crystalline forms of potassium benzoate and potassium cinnamate when prepared in mixture with potassium phthalate appear to be altered from those of the pure benzoate and cinnamate crystals, although the phthalate is clearly distinguishable in these mixtures.

Since potassium carbonate and citrate were found to have a crystal form similar to that of potassium phthalate it was considered worth while to investigate the crystalline structure of the corresponding sodium salts. A quantity of alcoholic soda (40 Gm./liter of NaOH in absolute ethyl alcohol) was prepared and the sodium salts of phthalic, benzoic, carbonic and citric acid were prepared by saponification of suitable esters.

Sodium phthalate was found to crystallize poorly in minute scale-like crystals with a pearly luster. A photomicrograph was taken of these crystals which are markedly different from those of the corresponding potassium salt. The benzoate, carbonate and citrate of sodium, as prepared by saponification in absolute alcoholic sodium hydroxide were all found to be amorphous.

These crystals are best prepared for microscopical examination by placing on a clean slide a drop of the alcoholic liquid containing the crystals, covering with a circular cover glass and sealing the edge of the cover glass with warm commercial glucose slightly diluted with water (1 volume of water to 10 of commercial glucose or corn syrup).

TABLE I.—SOLUBILITY OF POTASSIUM SALTS IN ABSOLUTE ETHYL ALCOHOL.

Group 1. Acids whose potassium salts are insoluble in absolute ethyl alcohol.		Group 2. Acids whose potassium salts are soluble in absolute ethyl alcohol (<i>i. e.</i> , to a concentration of 2% or more).	
Esters used.	Acids.	Esters used.	Acids.
(Ethyl)	Anisic	(Ethyl)	Formic
(Benzyl)	Benzoic	(Ethyl)	Acetic (C ₂)
di-(Ethyl)	Carbonic	(Amyl)	Butyric (C ₃)
(Methyl)	Cinnamic	(Benzyl)	Propionic (C ₄)
tri-(Ethyl)	Citric	(Amyl)	Valeric (C ₅)
di-(Ethyl)	Oxalic	Caproic (C ₆)
di-(Amyl) } di-(Butyl) } di-(Ethyl) }	o-Phthalic	(Methyl)	Lauric (C ₁₂)
.....		Myristic (C ₁₄)	
(Methyl)		Salicylic	
di-(Ethyl)	Succinic	(Ethyl)	Lactic
di-(Butyl)	Tartaric	tri-(Cresyl)	Phosphoric
(Methyl)	Anthranilic	Phenylacetic

SOLUBILITY OF POTASSIUM PHTHALATE IN ALCOHOLS.

A quantity of potassium phthalate was prepared by saponifying diethyl-phthalate with alcoholic potash. The white silky needle-like crystals were found to be highly hygroscopic and very soluble in water. Even at 50% relative humidity and 25° C. potassium phthalate will absorb about one-half of its weight

of water and will liquefy in the absorbed moisture. At 85-90% relative humidity this same phenomenon takes place within 15 to 20 minutes.

The solubility of potassium phthalate in several alcohols at 20° C. was determined with the results shown in Table II.

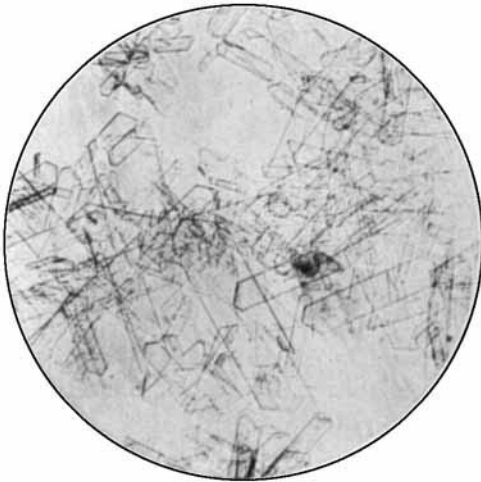


Fig. 5.—Potassium Benzoate. × 100.

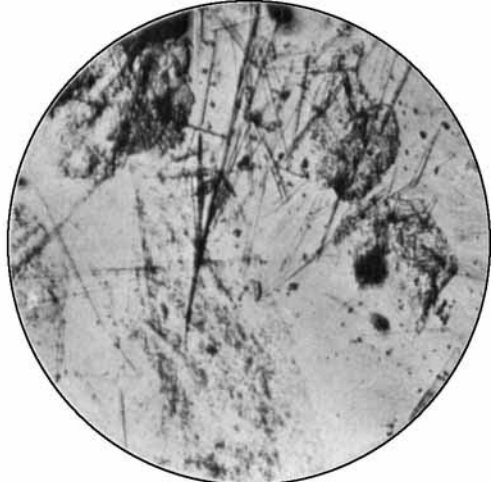


Fig. 6.—Mixture: 8 parts Potassium Benzoate, 1 part Potassium Phthalate. × 100.



Fig. 7.—Potassium Cinnamate. × 100.



Fig. 8.—Mixture: 8 parts Potassium Cinnamate 1 part Potassium Phthalate. × 100.

TABLE II.—SOLUBILITY OF POTASSIUM PHTHALATE IN ALCOHOL, 20° C.

Alcohol used.	Milligrams per 100 cc.	Parts per million (by wt.).
Absolute Ethyl Alcohol.....	16.1	203
95% Ethyl Alcohol (Cologne Spirits).....	25.2	308
Specially denatured alcohol No. 30 (10 vols. of purified CH ₃ OH added 100 vols. of 95% C ₂ H ₅ OH).....	72.8	890
Absolute Methyl Alcohol.....	792	9940

The fact that the methyl alcohol used was absolute was verified by means of its refractive index which was taken with the Zeiss Immersion Refractometer and found to be 6.35° at 17.5° C., corresponding to 99.8% methyl alcohol by volume. On account of the relatively high solubility of potassium phthalate in absolute methyl alcohol (*i. e.*, nearly 50 times the solubility in the corresponding absolute ethyl alcohol) it is impractical to use absolute methyl alcohol in the quantitative method subsequently described. The solubility of potassium phthalate¹ in boiling alcohol, S. D. No. 30, was found to be 210 mg. per 100 cc. or nearly 3 times its solubility at 20° C.

3. QUANTITATIVE DETERMINATION OF PHTHALATES.

The fact that potassium phthalate is so slightly soluble in ethyl alcohol, either 95% or absolute, suggested the idea that based on this insolubility of potassium phthalate a quantitative method could be worked out for determining phthalates in essential oils, synthetic perfume ingredients and other anhydrous or nearly anhydrous substances.

In order to minimize solubility corrections, absolute ethyl alcohol was used, in the subsequent quantitative work, for making alcoholic potash (40 Gm. KOH per liter) and for washing the crystals of potassium phthalate.

Data for the conversion of diethylphthalate to potassium phthalate is as follows:

Diethylphthalate, $(C_2H_5)_2C_8H_4O_4$, mol. wt. 222.17

Potassium Phthalate, $K_2C_8H_4O_4$, mol. wt. 242.27

$$\text{Factor: } \frac{K_2C_8H_4O_4}{(C_2H_5)_2C_8H_4O_4} = 1.0905; \quad \frac{(C_2H_5)_2C_8H_4O_4}{K_2C_8H_4O_4} = 0.9170$$

It was found that diethylphthalate was saponified readily by alcoholic potash at ordinary temperatures. While saponification takes place very rapidly in boiling alcohol there is considerable unavoidable bumping of the boiling solution if there is much diethylphthalate present and saponification at 25° C. or 37° C. is preferable for quantitative work. Several tests were made to determine the recovery when diethylphthalate (approx. 0.2 Gm.) was saponified at 25° C. and 37° C. for various periods of time with 10 cc. absolute alcoholic potash, with the results shown in Table III.

TABLE III.—SAPONIFICATION OF DIETHYLPHTHALATE.
10 cc. Alcoholic Potash (40 Gm./Liter in Absolute Ethyl Alcohol).

Temp. ° C.	Time. Hrs.	Wt. of diethyl- phthalate used. Gram.	Equiv. amt. of $K_2C_8H_4O_4$. Gram.	Wt. of found $K_2C_8H_4O_4$. Gram.	No. of cc. wash alcohol.	% recovery.	
						(a) Uncor.	(b) Cor. for sol. of $K_2C_8H_4O_4$ in wash alc.
25°	4	0.2020	0.2203	0.2136	20 cc.	97.8%	98.5%
25°	24	0.2019	0.2202	0.2184	21 cc.	99.3%	100.7%
37°	$2\frac{1}{2}$	0.2064	0.2251	0.2208	22 cc.	98.2%	99.4%
37°	24	0.1980	0.2159	0.2141	20 cc.	99.2%	100.7%
37°	50	0.2020	0.2203	0.2196	21 cc.	99.8%	101.2%

¹ Sodium phthalate was found to be less hygroscopic than potassium phthalate. Its solubility in absolute ethyl alcohol at 20° C. was found to be 16.4 milligrams per 100 cc., which is almost exactly the same as that of the corresponding potassium salt. Owing to the fact, however, that the crystalline form of sodium phthalate renders it difficult and very slow to filter it was considered that potassium phthalate was distinctly preferable in the following quantitative estimation of phthalates.

These results show that saponification of 0.2 Gm. diethylphthalate by 10 cc. absolute alcoholic potash is virtually complete after $2\frac{1}{2}$ hours at 37° C., and that after standing 24 hours at either 25° C. or 37° C. a recovery of slightly over 100% is obtained. *Note:* The higher results, *i. e.*, over 100%, obtained on prolonged standing are due probably to a gradual absorption of carbon dioxide by the

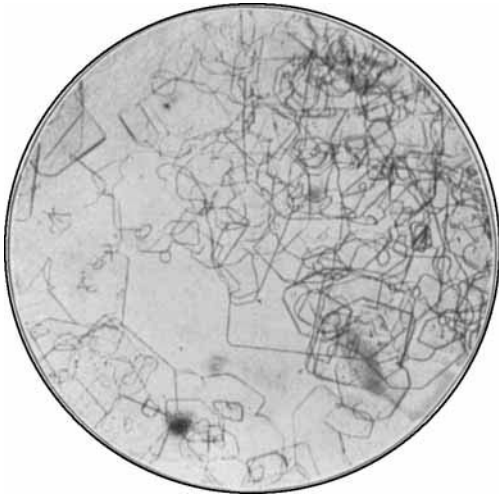


Fig. 9.—Potassium Anisate. $\times 100$.

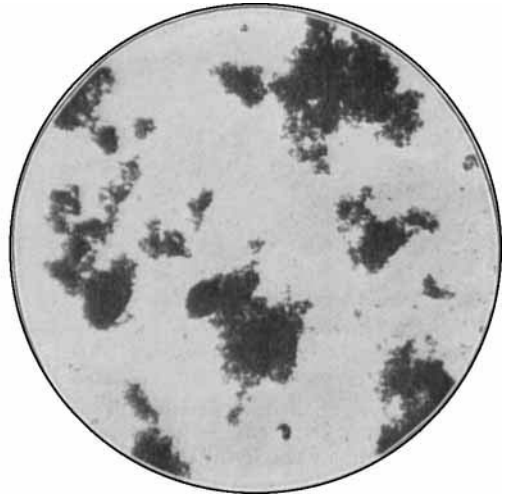


Fig. 10.—Potassium Oxalate. $\times 100$.

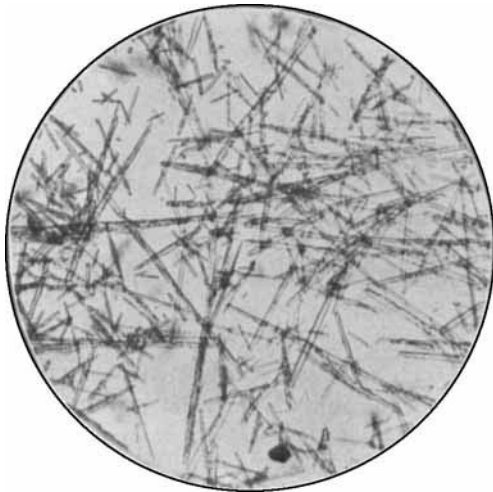


Fig. 11.—Potassium Carbonate. $\times 100$.

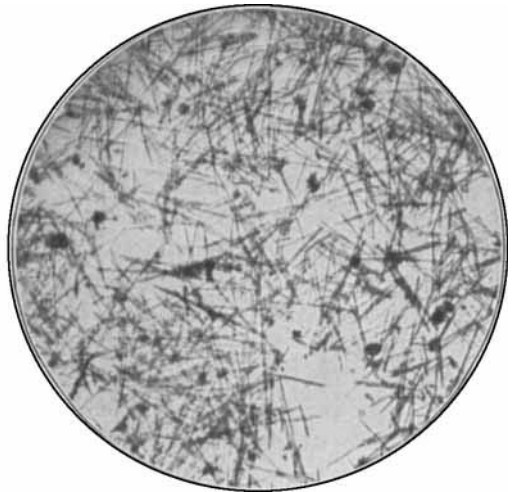


Fig. 12.—Potassium Citrate. $\times 100$.

excess caustic and precipitation of the highly insoluble potassium carbonate which is formed.

The Quantitative Method for Phthalates, *i. e.*, saponification with absolute alcoholic potash, and weighing of the resulting potassium phthalate, was applied to the determination of varying amounts of diethylphthalates in essential oils with the results shown in Table IV.

TABLE IV.—QUANTITATIVE DETERMINATION OF DIETHYLPHTHALATE IN ESSENTIAL OILS.

Wt. of ess. oil used.	Wt. of diethyl-phthalate added.	% of diethyl-phthalate in mixture.	Equiv. wt. of $K_2C_8H_4O_4$.	Wt. of $K_2C_8H_4O_4$ found.	Cc. wash alcohol used.	% recovery.		
						(a) No correction.	(b) Cor. for wash alc.	(c) Cor. for blank on oil and for wash alc.
Oil of Ylang-Ylang								
1.025	None	None	None	.0022*
1.007	.0141	1.38%	.0154	.0141	23	91.5%	115.6%	101.2%
1.343	.0702	4.97%	.0766	.0771	33	100.8%	107.5%	103.5%
1.142	.1496	11.60%	.1632	.1567	38	95.9%	99.7%	98.3%
Oil of Rose								
0.785	None	None	None	.0032*
1.130	.0282	2.44%	.0308	.0303	25	98.3%	111.6%	96.8%
1.050	.2067	16.48%	.2254	.2330	25	103.4%	105.2%	103.5%
Absolute Rose								
1.038	None	None	None	.0069*
1.050	.0281	2.61%	.0306	.0348	20	113.6%	124.1%	101.2%
1.090	.2047	15.81%	.2232	.2310	26	103.6%	105.5%	102.1%
Rose Liquid Pomade								
0.503	None	None	None	.0119*
1.120	.0283	2.46%	.0309	.0476	27	154%	88.0%
1.040	.2050	16.50%	.2185	.2356	34	107.6%	99.2%

* Weight of alcoholic insoluble from blank control test.

Details of the Quantitative Method for Determining Phthalates are as follows:

Reagents.—1. Absolute Alcoholic Potash; 40 Gm. KOH per liter of absolute ethyl alcohol. Filter and preserve in a tightly-stoppered bottle.

2. Absolute ethyl alcohol, for wash purposes.

Apparatus.—1. Small stoppered flasks; 50- or 100-cc. glass stoppered Erlenmeyer flasks are convenient though any small flask with cork or rubber stopper may be used.

2. Filtering Crucibles; preferably Jena glass filtering crucibles, porosity 5-7 (*Note:* These Jena glass crucibles are obtainable from the Empire Laboratory Supply Co. of New York; either of their No. 8000 or No. 8002 styles of crucibles are satisfactory). Gooch crucibles with prepared asbestos may be used if desired.

3. Graduate, equipped as a wash bottle; convert a 50 ml. or 100 ml. glass stoppered graduate into a wash bottle, using small glass tubing of 2-3 mm. inside diameter, with a tip drawn to a fine point.

Procedure.—Size of sample to use; for essential oils or synthetic perfume ingredients use 1 to 2 Gm., and weigh to 0.0001 Gm.; for specially denatured alcohols or perfumes use approximately 8 to 10 Gm. and weigh to 0.01 Gm.

To the weighed sample add 10 ml. absolute alcoholic potash, stopper the flask tightly and set aside for any convenient time between 6 and 24 hours at 25° C. or, if available, in a bacteriological incubator at 37° C. Filter rapidly, using suction, through a weighed Jena glass crucible or Gooch crucible. Wash flask and crucible with repeated small amounts of absolute ethyl alcohol (20 to 35 ml. is usually sufficient) and note the total number of ml. of wash alcohol used. (*Caution:* Do not expose the potassium phthalate crystals to the air or to suction any longer than is absolutely necessary. Prolonged suction, drawing humid air through the crystals in the crucible, will result in absorption of moisture, liquefaction of the crystals and possible loss. Transfer the crucible to the drying

oven *at once*, after filtration is completed.) Dry the crucible in an oven at 105–110° C. for 1 hr., cool in a desiccator and weigh. To the final weight of potassium phthalate, add 0.000161 Gm. for each ml. of wash alcohol used. Calculation: Weight of potassium phthalate \times 0.917 = weight of phthalates *expressed as diethylphthalate*.

Notes: (1) Experiments have indicated that more accurate results will be obtained by deducting, from the final corrected weight of potassium phthalate, 0.0030 Gm. per Gm. of sample. This value is a fair average of the alcohol-insoluble “blanks” per Gm. of essential oil. In case the “blank” for the particular oil in question is accurately known it should of course be used in place of 0.0030 Gm.

(2) Any acid of Group I, Table I, or its esters, if present in the sample in appreciable amounts would be liable to cause high results. If any of these acids are suspected of being present the crystal residue in the crucible should be

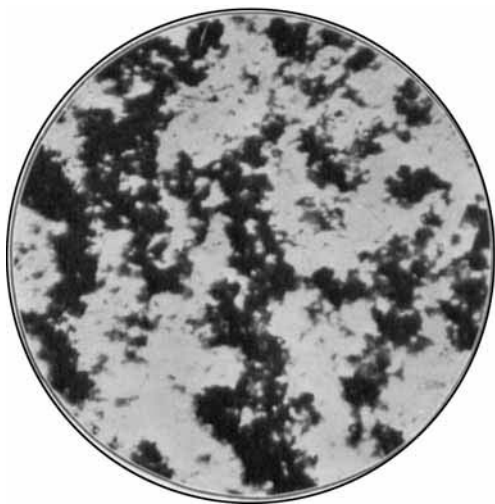


Fig. 13.—Potassium Succinate. \times 100.

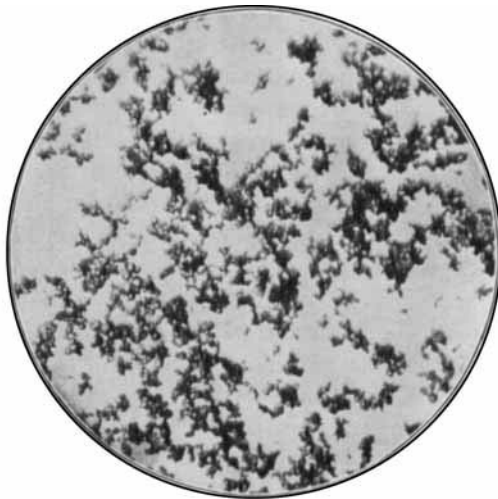


Fig. 14.—Potassium Tartrate (neutral). \times 100.

examined under the microscope; mounting the crystals in 95% or absolute ethyl alcohol and protecting from evaporation by “ringing” the cover glass with commercial glucose. Lack of time has prevented accurate determinations of the degree of solubility in absolute alcohol of the potassium salts of the acids of Group I, but in view of their qualitative behavior the solubilities are believed to be comparable to that of potassium phthalate.

The results of Table IV show that diethylphthalate added to certain essential oils in amounts ranging from 1.38% to 16.50% may be quantitatively recovered from such a relatively small sample as 1 gram of oil with a satisfactory degree of accuracy. The sample of Rose Liquid Pomade used gave a very high “blank” equivalent to 0.0237 Gm. per Gm. of sample and was found to already contain some diethylphthalate. With the exception of one low result obtained with this oil, the per cent recovery (Column “C”) on 8 other quantitative tests ranged from 96.8% to 103.5% and averaged 100.7%.

The general applicability of the quantitative method for phthalates to the estimation of diethylphthalate has been investigated.

With the aid of Gildermeister and Hoffmann's "The Volatile Oils" a list was made up of essential oils known to, or reported to, contain esters of acids of Group I, *i. e.*, acids whose potassium salts are insoluble in absolute alcohol. Where available these essential oils or resins have been subjected to saponification with alcoholic potash to determine whether or not such oils or resins, free from diethylphthalate, would give such a large "blank" that quantitative determination of any added diethylphthalate would be impractical. The results are shown in Table V.

In most cases the alcohol-insoluble "blank" material is amorphous. From the Tuberose Liquid Pomade, however, there were obtained definite crystals of the same microscopical appearance as potassium benzoate, and it is quite probable that they were derived from the saponification of the natural benzyl benzoate which this product is stated to contain.

In the case of the 3 resins tested, large blanks were obtained, amounting to from 12.6% to 27.6% of the weight of the resins taken. In this class of natural product the accurate quantitative determination of added diethylphthalate by the potassium phthalate method would be impractical. Of the 11 essential oils examined, which would be expected to give the largest blanks because they are reported to contain acids or esters of acids of Group I, only 3 gave "blanks" whose weight was 1 per cent or more of the weight of the sample used, and 6 of the 11 gave blanks amounting to 0.41 per cent or less of the weight of the sample. The quantitative estimation of diethylphthalate in such oils can be made with a fair degree of accuracy. The larger the amount of diethylphthalate present the more accurate the determination since the influence of the blank will be proportionally less, the larger the weight of the alcohol insoluble matter obtained by saponifying the sample with alcohol potash.

TABLE V.—"BLANKS" ON ESSENTIAL OILS.

Weight of Alcohol—Insoluble Matter Produced by Saponification of Essential Oils by Alcoholic KOH.

All data calculated to basis of grams insoluble per gram of essential oil.

Oil.	Wt. alc. insol. per gram.	Oil.	Wt. alc. insol. per gram.
Angelica	0.0231	Santal Citrin	0.0032
Cassie	0.0096	Tuberose (Liquid pomade)	0.0107
Geranium	0.0038	Vetivert	0.0164
Jasmin (Liquid pomade)	0.0014	Ylang-Ylang (Bourbon)	0.0022
Neroli	0.0035	Liquid Amber (Honduras balsam)	0.2765
Oil of Rose	0.0041	Resin Benzoin	0.1262
Absolute Rose	0.0066	Balsam Peru	0.1328

QUANTITATIVE DETERMINATION OF DIETHYLPHTHALATE IN SPECIALLY DENATURED ALCOHOL.

In alcohols, containing no other interfering substances, it would be possible to determine diethylphthalate quantitatively by means of its saponification number (505.09 mg. KOH per Gm., theoretical; 500.8 to 504.2 mg. KOH per Gm. on average commercial samples).

Analyses were made, however, to determine the applicability of the quanti-

tative potassium phthalate method to the estimation of diethylphthalate in specially denatured alcohols 39-B and 39-C.

The sample of 39-B used was made up in the laboratory. The formula calls for the addition of $2\frac{1}{3}$ volumes of diethylphthalate to 100 volumes of ethyl alcohol. The quantities used were 2.50 cc. (2.8005 Gm.) of diethylphthalate sp. gr. $15.6/15.6 = 1.1222$ to 100 cc. 190 proof ethyl alcohol, sp. gr. = 0.816. The mixture, *i. e.*, S. D. alcohol No. 39-B, contains 3.325% of diethylphthalate by weight. The sample of S. D. alcohol No. 39-B used was a commercial sample, made with 192 proof ethyl alcohol and should contain 1 volume of diethylphthalate added to 100 volumes of ethyl alcohol. The theoretical ester content would be 1.36% by weight.

The results were as follows:

TABLE VI.—SPECIALLY DENATURED ALCOHOL.

	No. 39-B.	No. 39-C.
Weight of sample used.....	10.00	10.00
Weight of diethylphthalate in sample.....	0.3325 (actual)	0.1362 (theoretical)
Equivalent wt. of potassium phthalate....	0.3628	0.1485
Amount of alcoholic potash used (40 Gm./l. in absolute EtOH).....	10 cc.	10 cc.
Amount of absolute ethyl alcohol used in washing.....	31 cc.	32 cc.
Weight of $K_2C_8H_4O_4$ found.....	0.3578	0.1285
Weight of $K_2C_8H_4O_4$, corrected for solubility in wash alcohol.....	0.3628	0.1317
Recovery.....	100.06%	88.7%

In view of the fact that it was possible to recover the ester practically 100 per cent from the S. D. alcohol No. 39-B of known composition, the analysis indicates that the commercial sample of S. D. alcohol 39-C contained less than the specified amount of diethylphthalate.

SUMMARY.

1. The potassium phthalate crystal test has been further investigated and a large number of acids have been classified as to the solubility of their potassium salts in absolute ethyl alcohol. Photomicrographs have been taken of the alcohol insoluble potassium salts of a number of acids.

2. The solubility of potassium phthalate in different alcohols has been determined and a quantitative gravimetric method for estimating diethylphthalate, or other phthalates, in essential oils or perfume raw materials, alcohol, or other anhydrous substances has been worked out. The results of a number of analyses indicate that diethylphthalate added to or present in a large number of essential oils in amounts ranging from 1.3% to 15% or more can be recovered practically quantitatively.

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THE ASSAY OF SALICYLATES AND BENZOATES, SECOND PAPER.

BY A. H. CLARK.

The United States Pharmacopœia (referred to hereafter as U. S. P. VIII, IX, or X as the case may be) has described a number of benzoates and salicylates. The U. S. P. X describes the benzoates of ammonium and sodium and the salicylates of ammonium, bismuth (basic), mercury (basic), sodium, strontium and physostigmine. Phenyl and methyl salicylates also are described. The U. S. P. IX described quinine salicylate and the U. S. P. VIII lithium benzoate and salicylate. This list is practically complete in so far as medicinally useful benzoates and salicylates are concerned.

The writer pointed out some time ago¹ that it is desirable to have a uniform or general method for the assay of these medicaments and suggested a method for the assay of sodium salicylate and sodium and ammonium benzoates¹ which he showed to be entirely satisfactory and very simple and time-saving. This method in principle consists in acidulating a solution of the salt in question and extracting the benzoic or salicylic acid with chloroform, evaporating the chloroform under stated conditions and weighing the acid obtained.

The present paper deals with the application of the above-mentioned method to the assay of the substances listed in the opening paragraph. In the previous paper the testing of the accuracy of the method on samples of undoubted purity was the prime object. In the present work this is considered proven and when the method gave concordant results on the commercial samples used the result was taken as final. A few observations which do not have a direct bearing on the question of assay but concern interesting points observed are appended in certain cases.

In any method of assay for a medicinal substance one always thinks of the therapeutically active radical or group as being the one that should be assayed. This may be a good principle to follow providing first of all that one knows which is the active part of a given substance. Obviously, convenience and accuracy should play a very important part in deciding on a method of analysis. If it is desirable to have a general method for a number of medicaments such a method should be sought regardless of any questions of therapeutic activity of the portion assayed. If it is more convenient, for example, to assay mercuric salicylate on the basis of its content of salicylic acid this should be done. Tests can be devised for the elimination of undue amounts of foreign metals and perhaps more readily than for undue amounts of foreign organic acids. If we carry the argument of relative therapeutic value very far we come to the point where we may consider all salicylates alike, or all sodium salts alike, or all mercury salts alike, and therefore why have official more than one salicylate, sodium compound, mercury compound, etc.? The absurdity of this argument should be apparent to any one, therefore why allow the question of therapeutics to enter into the matter?

¹ *JOUR. A. PH. A.*, January 1926, p. 6.