[CONTRIBUTION FROM CHEMICAL LABORATORY OF JOHNS HOPKINS UNIVERSITY.]

STUDIES IN IDENTIFICATION.

IV. THE IDENTIFICATION OF ALCOHOLS.

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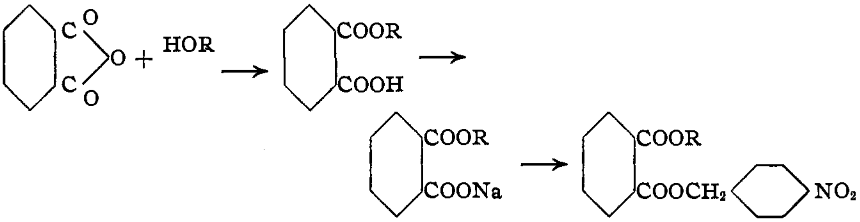
Introduction.

While the identification of alcohols by phenylurethanes and naphthylurethanes leaves little to be desired, yet there are special cases in which other methods may be of use.

The present method has the advantage of combining the separation of the alcohol with its identification and, furthermore, a primary alcohol may be identified in the presence of secondary and tertiary or a secondary in presence of tertiary. Its application is, however, not as broad as was hoped, since many of the derivatives are liquids. It serves well for the lower alcohols, methyl alcohol in particular. In fact methyl alcohol may be readily identified in presence of ethyl. Michael and Wolgast found that methyl alcohol is esterified 5.7 times as rapidly as ethyl.[1] Their action with phthalic anhydride agrees with this.

It has recently been shown[2] that *p*-nitrobenzyl bromide reacts readily, in dilute alcohol solution, with the sodium salt of an acid to form an ester which, in many cases, is crystalline and characteristic of the acid. If, now, phthalic anhydride is heated, with an alcohol, as is well known, a monoester of phthalic acid is formed. This acid ester readily forms a sodium salt which, in turn, reacts with *p*-nitrobenzyl bromide to give the ester which is relied upon for the identification.



It has been shown by Erdmann,[3] Flatau and Labbé[4] and Stephan[5] that primary alcohols combine with phthalic anhydride readily at temperatures below 100° while secondary react rapidly only above 120°. Advantage has frequently been taken of this fact for separating alcohols from non-alcohols and for separating the three classes of alcohols, but it has been customary to saponify the acid phthalic ester so obtained to

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[1] *Ber.*, **42**, 3157 (1909).

[2] THIS JOURNAL, **39**, 124, 701 (1917).

[3] *J. prakt. Chem.*, [2] **56**, 15 (1897).

[4] *Bull. soc. Chem.*, [3] **19**, 633 (1898).

[5] *J. prakt. Chem.*, [2] **60**, 248 (1899).

get the free alcohol which was then identified. In the present work the acid phthalic ester is transformed directly into its *p*-nitrobenzyl ester.

Method of Work.

A moderate excess of the alcohol is heated one hour with 1 g. phthalic anhydride. For a primary alcohol the temperature used was 100°, for a secondary 140°. For the lower alcohols 1 cc. of the alcohol is sealed up with 1 g. phthalic anhydride and the tube placed in boiling water, while with the less volatile alcohols, the mixture is placed in a test tube suspended in the water bath. A glass rod passing through the cork is used for stirring it. The product is transferred to a small separatory funnel containing 10 cc. water. About 15 cc. of ether and 5 cc. *N* caustic soda are added. The funnel is shaken five minutes and the water layer drawn off. The ether layer is shaken with a small amount of water which is added to the water solution. The water solution is again extracted with ether. This may be repeated in case much uncombined material is present. The water solution is evaporated to dryness and the sodium salt is transferred to a 100 cc. flask, with 5 cc. water and 10 cc. 95% alcohol. To this is added 1 g. of the reagent and the mixture boiled one hour on a steam bath, with return condenser. The product is worked up exactly as described in the identification of acids.

Experiment has shown that, for the alcohols used, the phthalic anhydride reacts completely so that not a trace of it remains. As 1 g. phthalic anhydride is 6.76 millimols, there will be 6.76 millimols of the acid phthalic ester formed. When an ether solution of this is shaken with 5 cc. *N* alkali, just 5 millimols of the sodium salt of the acid ester will be formed and this will remain in the water layer. The water layer has been tested with phenolphthalein paper and has always been found slightly acid, showing that the alkali has been completely neutralized. The 1 g. of the reagent is 4.63 millimols, so the sodium salt is in slight excess.

The recrystallization has been carried out as in previous work[1] and the designations of the crops are the same.

Materials.

The *p*-nitrobenzyl bromide was prepared as in previous work. The phthalic anhydride was a commercial product. The lower alcohols were dried over lime while the others were used as purchased. All alcohols in the laboratory stock were tried.

Results.

Methyl Alcohol.—This alcohol combines with phthalic anhydride even at room temperature. A mixture of 1 g. phthalic anhydride and 2 cc. anhydrous methyl alcohol was sealed up and left at room temperature. In four days all of the anhydride had gone into solution but it was heated

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[1] THIS JOURNAL, 39, 129 (1917).

to insure complete action. The *p*-nitrobenzyl ester, 1st 1st was 1.20 g. m. 105°, 1st 2nd 0.10 g. m. 80–9°, calc. 1.46 g. It was twice recrystallized, from 11 and then 17 cc. 63% alcohol giving 2nd 1st 1.15 g. m. 106°, 2nd 2nd 0.01 g. m. 101° and 3rd 1st 1.11 g. m. 105.7°, 3rd 2nd 0.01 g. m. 104°.

Ethyl Alcohol.—The reaction between this alcohol and phthalic anhydride seemed to be complete at 80° in 60 minutes. The 1st 1st was 1.23 g. m. 80.5°, 1st 2nd 0.11 g. m. 80°, calc. 1.52 g. Recrystallization from 15 cc. 63% alcohol gave 2nd 1st 1.18 g. m. 80° and 2nd 2nd 0.02 g. m. 80°.

Propyl Alcohol.—The ester separated after boiling a few minutes and 10 cc. 95% alcohol was added, which gave a clear solution. The ester separated as an oil which became crystalline on standing. The 1st 1st was 1.11 g. m. 53°, 1st 2nd 0.21 g. m. 45°, calc. 1.59 g. The 1st 1st was dissolved in 30 cc. 63% alcohol and gave 2nd 1st 0.87 g. m. 53.0° and 2nd 2nd 0.14 g. m. 53°.

Isopropyl Alcohol.—The alcohol and anhydride were heated one hour at 140–3° in a sealed tube. The *p*-nitrobenzyl ester separated during the boiling but redissolved on the addition of 10 cc. 95% alcohol. The 1st 1st was 1.01 g. m. 74° and 1st 2nd 0.39 g. m. 55–66°, calc. 1.59 g. Recrystallization from 30 cc. 63% alcohol gave 2nd 1st 0.89 g. m. 74.0° and 2nd 2nd 0.05 g. m. 74.0°. Fine white silky needles.

Allyl Alcohol.—The *p*-nitrobenzyl ester separated out during its preparation but redissolved on the addition of 5 cc. 95% alcohol. The 1st 1st was 1.15 g. m. 61.0°, 1st 2nd 0.21 g. m. 50–5°. Recrystallization from 15 cc. 63% alcohol gave 2nd 1st 1.01 g. m. 61.5° and 2nd 2nd 0.10 g. m. 61.8°. White silky needles.

***n*-Butyl Alcohol.**—The alcohol and anhydride did not react to any great extent at 80° in an hour, so the mixture was heated to 100°. During the preparation of the *p*-nitrobenzyl ester, 5 cc. 95% alcohol were added to keep it in solution. The 1st 1st was 1.20 g. m. 56°, 1st 2nd 0.10 g. m. 51°. Recrystallization from 5 cc. 69% alcohol gave 2nd 1st 0.97 g. m. 62° and 2nd 2nd 0.19 g. m. 60°. The 1st 1st was dissolved in 20 cc. 95% alcohol and remained in solution on cooling. The addition of 10 cc. water caused the separation of 3rd 1st 0.91 g. m. 62.0° and 3rd 2nd 0.04 g. m. 60°.

***n*-Octyl Alcohol.**—During the preparation of the *p*-nitrobenzyl ester, 20 cc. 95% alcohol were added to keep it in solution. The 1st 1st melted at 40° and 1st 2nd m. 40°, weights lost. The 1st 1st was dissolved in 20 cc. 95% alcohol and 7 cc. water added. This gave 2nd 1st 0.82 g. m. 41° and 2nd 2nd, only an emulsion which left nothing on the filter. It was again recrystallized yielding, 3rd 1st 0.59 g. m. 41.0° and 3rd 2nd 0.01 g. m. 40°.

Benzyl Alcohol.—The acid phthalic ester solidified on cooling. During the preparation of the *p*-nitrobenzyl ester, 30 cc. 95% alcohol were added to keep it in solution. The 1st 1st was 0.89 g. m. 83.5°, 1st 2nd 0.26 g. m. 65–71°, calc. 1.81 g. Recrystallization from 25 cc. 76% alcohol yielded 2nd 1st 0.79 g. m. 83.0°, and 2nd 2nd 0.01 g. m. 80°.

Phenyl-ethyl Alcohol.—The *p*-nitrobenzyl ester separated during the boiling and 50 cc. 95% alcohol were added, which caused all to go into solution and the addition of 10 cc. water did not cause the ester to separate while hot. The 1st 1st was 0.21 g. m. 85° and 1st 2nd 0.17 g. m. 85–90°. Recrystallization from 25 cc. 76% alcohol gave 2nd 1st 1.11 g. m. 84.3° and 2nd 2nd 0.01 g. m. 80°.

Borneol.—Three experiments have been made with borneol. In each case 1.25 g. borneol were heated one hour with 1 g. phthalic anhydride, about 0.5 cc. toluene being added to promote solution. In the second experiment the temperature went to 180°. The final product is somewhat camphoraceous and does not melt quite sharply. The results of the three preparations were essentially the same, the final results of the first two being: (A) 3rd 1st 1.02 g. m. 98–100°, (B) 2nd 1st 0.94 g. m. 98°. The third is given in detail. The 1st 1st was 1.57 g. m. 97–8°; 1st 2nd 0.12 g. m. 90–5°; 2nd 1st 1.34 g. m. 99–100°; 2nd 2nd 0.10 g. m. 87°; 3rd 1st 1.21 g. m. 99–100°; 3rd 2nd 0.06 g. m. 91°. The solvents used were 30 cc. 80% and 25 cc. 76% alcohol.

Isoborneol.—A mixture 1.25 g. isoborneol, 1 g. phthalic anhydride and 0.5 cc. toluene was heated 75 minutes at 140–50° and the product worked up as usual. The 1st 1st was 0.86 g. m. 87–117°, 1st 2nd 0.19 g. m. 60–74°. The 1st 1st was boiled with 20 cc. 95% alcohol and filtered hot. The residue was 0.08 g. m. 153° and 0.26 g. separated on cooling, m. 146°. Both of these were doubtless mainly di-*p*-nitrobenzyl phthalate and were discarded. To the mother liquor 10 cc. water were added which caused the separtion of 2nd 2nd 0.39 g. m. 84–7° and 2nd 3rd 0.01 g. m. 75–95°. The 2nd 2nd was taken to be the desired derivative and recrystallized, giving 3rd 1st 0.35 g. m. 87°, not sharp, and 3rd 2nd 0.01 g. m. 85°. This preparation is not satisfactory.

Isobutyl, Isoamyl, and Cinnamic Alcohols, Menthol and Geraniol reacted with phthalic anhydride, and the sodium salt of the acid phthalic ester reacted properly with the *p*-nitrobenzyl bromide, but the esters resulting proved to be liquids which could not be made to crystallize.

Separation of Mixtures.

Methyl and Ethyl Alcohols.—Two experiments were tried. Into each of two tubes was placed 1 cc. ethyl alcohol, 1 cc. methyl and 1 g. phthalic anhydride. The tubes were sealed off and the first kept at room temperature, with occasional shaking, while the second was heated 1 hour at 100°. At room temperature all the anhydride dissolved in seven days but the mixture was kept another week before working up. The *p*-nitrobenzyl esters were made as usual. The products were recrystallized from 20 cc.

and then three times from 30 cc. 63% alcohol. The first tube gave 1st 1st 1.10 g. m. 99°, 1st 2nd 0.08 g. m. 55–65°; 2nd 1st 103 g. m. 101°; 3rd 1st 0.94 g. m. 102°; 3rd 2nd 0.04 g. m. 85°; 4th 1st 0.86 g. m. 103°, 4th 2nd 0.05 g. m. 87°; and 5th 1st 0.78 g. m. 103° and 5th 2nd 0.04 g. m. 90°. The 3rd 1st was mixed with the pure methyl derivative (m. 105.7°) and the mixture melted at 104–5°.

The second tube gave 1st 1st 1.05 g. m. 100°, 1st 2nd 0.13 g. m. 55–65°; 2nd 1st 0.97 g. m. 102°, 2nd 2nd 0.05 g. m. 77–85°, 3rd 1st 0.91 g. m. 102.5°, 3rd 2nd 0.04 g. m. 85°; 4th 1st 0.83 g. m. 103°, 4th 2nd 0.04 g. m. 87°; and 5th 1st 0.76 g. m. 104° and 5th 2nd 0.04 g. m. 91°. The 3rd 1st gave, with the pure methyl derivative, a mixed melting point of 105°.

In both cases the product was mainly the methyl derivative which when twice recrystallized gave melting points quite near the correct value and gave mixed melting points which were entirely satisfactory. It appears that, in both cases, a small amount of the ethyl derivative was formed. Heating to 100° for an hour gave slightly better results than letting stand at room temperature. Thus methyl alcohol can be identified in the presence of ethyl.

Ethyl Alcohol and Ethyl Benzoate.—A preliminary experiment was made in which 1 g. phthalic anhydride was heated to 100° for an hour with 3 cc. ethyl benzoate and the mixture worked up as usual. The product was 0.50 g. di-*p*-nitrobenzyl phthalate, of which 0.32 g. melted at 155.5°, the correct m. p. as found by Lyman and Reid,[1] and 0.18 g. m. 154.2° and 0.20 g. was obtained from the mother liquor. This proved to be the reagent as it melted at 96° and, mixed with the reagent, melted at 98°. This shows that ethyl benzoate is entirely unaffected by this treatment with phthalic anhydride.

A mixture of 1 cc. ethyl alcohol, 2 cc. ethyl benzoate and 1 g. phthalic anhydride was heated an hour at 100°, and the product worked up as usual. The 1st 1st was 1.24 g. m. 77–8° and 1st 2nd 0.08 g. m. 68°. Recrystallization from 20 cc. 63% alcohol gave 2nd 1st 1.16 g. m. 80.0° and 2nd 2nd 0.02 g. m. 80.0°. Hence the pure ethyl derivative is obtained readily in the presence of the ester.

Ethyl Alcohol and Menthol.—A mixture of 1 cc. ethyl alcohol 1 g. menthol and 1 g. phthalic anhydride was heated an hour at 100° and the product worked up in the regular way. The 1st 1st was 1.22 g. m. 79°, 1st 2nd 0.07 g. m. 62°. Recrystallization gave 2nd 1st 1.15 g. m. 0° and 2nd 2nd 0.02 g. m. 80°. A mixed melting point with the pure ethyl derivative was 80.2°, showing their identity. This experiment shows that ethyl alcohol may be readily separated and identified when mixed with menthol, a secondary alcohol.

Borneol and Camphor.—As a preliminary experiment, 1 g. phthalic

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[1] THIS JOURNAL, 39, 701 (1917).

anhydride was heated with 2 g. camphor and 0.5 cc. toluene for 105 minutes at 140° to 180° and the product worked up as usual. The product was di-*p*-nitrobenzyl phthalate, of which 0.39 g. melted at 155.5° and 0.12 g. at 150–1°. From the mother liquor, 0.14 g. of the unchanged reagent was recovered, m. 96°, mixed m. p. 99°. This shows conclusively that camphor does not react with the anhydride.

A mixture of 1.25 g. borneol, 2 g. camphor, 1 g. phthalic anhydride, and 0.5 cc. toluene was heated 65 minutes 140–3°. The 1st 1st was 1.27 g. m. 97–8°, 1st 2nd 0.13 g. m. 70–5°. Recrystallization gave 2nd 1st 1.10 g. m. 97–8° and 2nd 2nd 0.02 g. m. 80–90°. Thus borneol is readily separated and identified in presence of camphor.

The results are brought together in tabular form, the first and second columns giving the weights of first and second crops of crystals, the fifth and sixth the first and final melting points, and the last two, the strength and amount of alcohol used for recrystallization, calculated for 1 g.

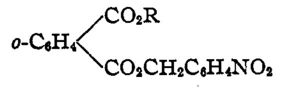
TABLE I.

Yields, Melting Points, and Approximate Solubility of Derivatives from Alcohols.

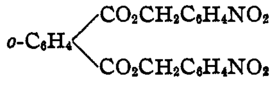
Alcohol.	1st 1st. G.	1st 2nd. G.	Total. G.	Calc. G.	First. M. p.	Final. M. p.	Alcohol. %.	Alcohol. Cc.
Methyl	1.20	0.10	1.30	1.46	105°	105.7°	63	9
Ethyl	1.23	0.11	1.34	1.52	80°	80°	63	9
Propyl	1.11	0.21	1.32	1.59	53°	53.0°	63	27
Isopropyl	1.01	0.39	1.40	1.59	74°	74.0°	63	30
Allyl	1.15	0.21	1.36	1.58	61°	61.5°	71	17
n-Butyl	1.20	0.10	1.30	1.65	56°	62.0°	76	40[1]
n-Octyl[2]	..	..	..	..	40°	41.0°	70	30
Benzyl	0.89	0.26	1.15	1.81	83°	83.0°	76	28
Phenylethyl	1.21	0.17	1.38	1.92	85°	84.3°	76	21
Borneol	1.57	0.12	1.69	2.01	95°	100°	80	20
Isoborneol	0.86	0.19	1.05	2.01	87–117°	87°	..	..

Discussion of Results.

It appears that many alcohols, particularly the lower ones, may be satisfactorily separated from mixtures and identified by the method given. Of 16 alcohols studied 11 give crystalline derivatives while 5 give liquids. The melting points of 8 of the 11 derivatives, as they were first obtained, were within 1° of their final melting points. When we compare



$$o\text{-}C_6H_4\begin{cases}CO_2R\\CO_2CH_2C_6H_4NO_2\end{cases}$$



$$o\text{-}C_6H_4\begin{cases}CO_2CH_2C_6H_4NO_2\\CO_2CH_2C_6H_4NO_2\end{cases}$$

the phthalic esters, in which one alcohol radical is a lower alcohol and the other is *p*-nitrobenzyl, with di-*p*-nitrobenzyl phthalate, we find great difference in properties, much lower melting points and far greater solubilities in hot dilute alcohol. The di-*p*-nitrobenzyl phthalate was found by

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[1] Too much solvent was used.

[2] Weights lost, but yield good.

Lyman and Reid to require 300 parts of boiling 95% alcohol for its solution, while these mixed esters dissolve in from 9 to 30 parts of alcohol containing much more water.

Since mono-menthyl phthalate melts at 110°, it is surprising that the menthyl *p*-nitrobenzyl ester is an oil.

Summary.

Alcohols may be heated with phthalic anhydride to give acid phthalic esters and the sodium salts of these heated with *p*-nitrobenzyl bromide to give mixed phthalic esters which may be used for identification of the alcohols. The following mixed esters have been made:

Methyl *p*-nitrobenzyl phthalate, $CH_3CO_2.C_6H_4.CO_2CH_2C_6H_4NO_2$, m. 105.7°;

Ethyl *p*-nitrobenzyl phthalate, $C_2H_5CO_2.C_6H_4.CO_2CH_2C_6H_4NO_2$, m. 80°;

Propyl *p*-nitrobenzyl phthalate, $C_3H_7CO_2.C_6H_4.CO_2CH_2C_6H_4NO_2$, m. 53.0°;

Isopropyl *p*-nitrobenzyl phthalate, $C_3H_7CO_2.C_6H_4.CO_2CH_2C_6H_4NO_2$, m. 74.0°;

Allyl *p*-nitrobenzyl phthalate, $C_3H_5CO_2.C_6H_4.CO_2CH_2C_6H_4NO_2$, m. 61.5°;

n-Butyl *p*-nitrobenzyl phthalate, $C_4H_9CO_2.C_6H_4.CO_2CH_2C_6H_4NO_2$, m. 62.0°;

n-Octyl *p*-nitrobenzyl phthalate, $C_8H_{17}CO_2.C_6H_4.CO_2CH_2C_6H_4NO_2$, m. 41.0°;

Benzyl *p*-nitrobenzyl phthalate, $C_6H_5CH_2CO_2.C_6H_4.CO_2CH_2C_6H_4NO_2$, m. 83.0°;

Phenylethyl *p*-nitrobenzyl phthalate, $C_6H_5CH_2CH_2CO_2.C_6H_4.CO_2CH_2C_6H_4NO_2$, m. 84.3°;

Bornyl *p*-nitrobenzyl phthalate, $C_{10}H_{17}CO_2.C_6H_4.CO_2CH_2C_6H_4NO_2$, m. 100°;

Isobornyl *p*-nitrobenzyl phthalate, $C_{10}H_{17}CO_2.C_6H_4.CO_2CH_2C_6H_4NO_2$, m. 87°.

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[CONTRIBUTION FROM THE SHEFFIELD CHEMICAL LABORATORY OF YALE UNIVERSITY, AND THE CHEMICAL LABORATORY OF MOUNT HOLYOKE COLLEGE.]

RESEARCHES ON HYDANTOINS.

XXXIX. SYNTHESIS OF THE POLYPEPTIDE-HYDANTOIN; TYROSYL-GLYCINE-HYDANTOIN.

BY TREAT B. JOHNSON AND DOROTHY A. HAHN.

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It has been shown in a previous paper from the Sheffield Laboratory[1] that the silk-protein-fibroin undergoes hydrolysis with acids with production of carbon dioxide. The amount that is evolved in this particular

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[1] Johnson, *Proc. Nat. Acad. Sci.*, 2, 69 (1916).