[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, YALE UNIVERSITY]

THE REACTION OF ALCOHOLS WITH BROMOMETHYL-PHTHALIMIDE AND ITS USE FOR THE SEPARATION AND IDENTIFICATION OF ALCOHOLS

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There is no satisfactory method for the separation and identification of a number of alcohols constituting a mixture or contained in a mixture with other substances. The procedure now generally employed is the esterification of alcohols and the separation of the resulting esters, if these are liquids, by fractional distillation, and if solids, by fractional crystallization. The esters are then identified as such, or are saponified and the resulting alcohols identified.

Fractional distillation of the esters is often difficult because the esters frequently boil at temperatures only a few degrees apart; fractional crystallization is more readily carried out, and consequently the esters of aromatic or substituted aromatic acids which are generally solids are formed, in preference to the esters of aliphatic acids which are generally liquids.

In a recent paper from this Laboratory[1] it was shown that ethyl alcohol with bromomethyl-phthalimide formed the phthalimido-methyl-ethyl ether which was crystalline. The fact that this derivative was easily prepared and purified led the author to believe that bromomethyl-phthalimide might be used to separate alcohols from aqueous or non-aqueous mixtures by fractional crystallization of its corresponding derivatives. The melting points and analyses of the pure ethers could then be used for the identification of the pure alcohols.

Methyl, ethyl, *n*-propyl and *iso*propyl alcohols, glycerol, lactic acid and pheno were condensed with bromomethyl-phthalimide. All gave well-crystallized solid derivatives. The gradual decrease in the melting point of the simple alcohol derivatives as the alkyl groups increased in molecular weight, methyl 120°, ethyl 86°, *n*-propyl 52°, indicates that the derivatives of alcohols of higher molecular weight would be very low-melting solids or oils at room temperature. The use of this reagent for the identification of alcohols was not entirely satisfactory for two reasons; first, it was absolutely necessary to have the alcohols perfectly dry in order to form the derivatives in a satisfactory way; and second, it was necessary to have an excess of the alcohol present. Furthermore, the presence of moisture immediately decomposes bromomethyl-phthalimide into the hydroxymethyl-phthalimide before it can react with the alcohols.

Tutin[2] in order to identify methyl alcohol and acetone in a mixture fractionated it many times to effect a complete separation. In a mixture

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[1] Pucher and Johnson, THIS JOURNAL, **44**, 817 (1922).

[2] Tutin, *Biochem. J.*, **15**, 496 (1920).

of acetone and methyl alcohol which was absolutely free from water, bromomethyl-phthalimide readily reacted with the methyl alcohol, giving the characteristic derivative.

Experimental Part

Bromomethyl-phthalimide, $C_6H_4(CO)_2.N.CH_2Br$.—Pucher and Johnson[1] prepared this compound.

Phthalic anhydride was treated with ammonia[3] and phthalimide thus obtained. By condensation of the phthalimide with formaldehyde and subsequent bromination of the hydroxymethyl-phthalimide with hydrobromic acid in the presence of sulfuric acid,[4] the bromomethyl-phthalimide was formed. This is an easy method, gives a very good yield and was, therefore, used in this work. From 80 g. of hydroxymethyl-phthalimide, 70 g. of the halide was obtained; m. p. 146°. This is practically the same yield as that obtained by Pucher and Johnson.

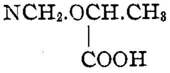
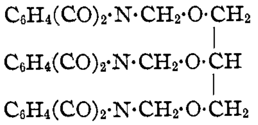
The halide is insoluble in equal parts by weight of acetone, but is partly soluble in 2 parts by weight of acetone, and is completely dissolved in 3 parts by weight of acetone; it is insoluble in benzene. After intervals of 1, 2, 3 and 4 weeks it melted at 145°, 143–4°, 141–2° and 140–1°, respectively. The halide, therefore, decomposes almost completely in about a month. During the first 2 or 3 weeks of exposure, the compound was discolored pink, but at the end of the month the decomposed product is pure white.

When the freshly prepared halide was placed on a piece of filter paper and allowed to stand in the moist air, the paper became colored a characteristic purplish-indigo where the substance had come in contact with it.

The general procedure for the production of all the ethers formed is as follows. Five g. of bromomethyl-phthalimide was digested for 10 to 15 hours with an excess of the alcohol or hydroxy compound (10 to 15 g.). Some of the alcohol was evaporated, and the compound thus precipitated

TABLE I

TABLE OF CONSTANTS OF THE ETHERS

Name Phthalimido ether	Formula derivative of $C_6H_4(CO)_2-$	M. p. °C.	Solvent for crystallization	Analysis N
Methylmethyl	$NCH_2.OCH_3$	118	abs. methyl alc.	......
Methylethyl	$NCH_2.OC_2H_5$	86	abs. ethyl alc.	......
Methyl *n*-propyl	$NCH_2.OC_3H_7$	52–53	abs. *n*-propyl alcohol	6.27 and 6.15
Methyl*iso*-propyl	$NCH_2.OCH:(CH_3)_2$	92–93	abs. *iso*-propyl alcohol	6.38 and 6.30
Methyllactic acid	 $NCH_2.O\underset{\underset{\displaystyle COOH}{\vert}}{CH}.CH_3$	185	dry acetone	5.50 (mean)
Methylphenyl	$NCH_2.OC_6H_5$	171–172	dry acetone	5.35 (mean)
Methylglycerol	 $\begin{array}{r} C_6H_4(CO)_2\cdot N\cdot CH_2\cdot O\cdot CH_2 \\ \vert\; \\ C_6H_4(CO)_2\cdot N\cdot CH_2\cdot O\cdot CH\; \\ \vert\; \\ C_6H_4(CO)_2\cdot N\cdot CH_2\cdot O\cdot CH_2 \end{array}$	174–175	dry ether	5.96

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[3] Kuhara, *Am. Chem. J.*, **3**, 27 (1881).

[4] Kamm and Adams, THIS JOURNAL, **42**, 299 (1920).

was recrystallized from the same absolute alcohol as used for the reaction, giving the ether generally in the form of a white crystalline compound possessing a sharp melting point. In the cases of the ethers formed from lactic acid, phenol and glycerol the mixtures obtained after the digestions were completed were poured into ice water, and the resulting ethers, being insoluble in cold water, were precipitated from it in the form of white crystalline compounds or, as in the case of the ether formed from the phenol, in the form of a pink crystalline compound, possessing in all three cases, after recrystallization from dry acetone, sharp melting points. It should be emphasized here that the alcohols used in the general procedure were perfectly dry.

The Separation and Identification of Methyl Alcohol in a Mixture with Anhydrous Acetone

Tutin, as mentioned above, separated methyl alcohol from acetone in a mixture of the two by several distillations, and identified the alcohol by its boiling point and analysis for carbon and hydrogen. This process can be simplified in the following manner. Equal quantities (5 cc.) of absolute methyl alcohol and dry acetone are mixed. The mixture is then warmed with 2 g. of the bromomethyl-phthalimide for 2 hours. The solution or reaction mixture is evaporated and the phthalimido-methylmethyl ether crystallized. On recrystallization from dry acetone, the ether is obtained in its characteristically white, crystalline, needle-like form; m. p. 119–120°.

The Action of Bromomethyl-phthalimide on Alcohols Containing Water

All of the above reactions were carried out in the absence of water. The solutions used were anhydrous and the presence of water vapor and liquid was continuously guarded against. To determine the effect of the presence of water vapor and liquid, on the reaction, 2 g. of the bromide was digested with 20 cc. of each of the following alcohols and hydroxy compounds for 2 hours, using 25 cc. of acetone in each case as a solvent: glycerol, *iso*propyl, *n*-propyl, amyl, benzyl and ethylene (glycol) alcohols and lactic acid. No precautions were taken to secure anhydrous materials, and they were even exposed to atmospheric moisture as much as possible. The products, when recrystallized from acetone, gave white, crystalline substances in each case resembling the hydroxymethyl-phthalimide in appearance and possessing melting points similar to it. These compounds showed no noticeable change in melting points when mixed with a little hydroxymethyl-phthalimide. The pure products when analyzed for nitrogen gave results ranging from 7.5% to 8.5%, whereas hydroxymethyl-phthalimide contains 8.00%. It was, therefore, evident that this compound was obtained in every case.

Twenty cc. of anhydrous propyl alcohol was digested for 2 hours with 2 g. of the bromide in 25 cc. of acetone as a solvent. After evaporating the solvent and recrystallizing the reaction product from pure acetone, the hydroxymethyl-phthalimide was again obtained.

TABLE II

THE SOLUBILITIES OF THE ETHERS

Solvent Required to Dissolve 0.25 g. of Ether

	Solvents				
Ether	Ethyl alc. Cc.	Methyl alc. Cc.	Benzene Cc.	Ether Cc.	Acetone Cc.
Methylmethyl	40	10	3	40	2
Methylethyl	20	2	1	2	1
Methyl *n*-propyl	10	1	1	1	1

Summary

1. It has been shown that the bromomethyl-phthalimide will react readily with certain alcohols under anhydrous conditions and can be used for their identification and separation under these conditions, but that it cannot be used in solutions where moisture is present.

2. A description of several new derivatives of methyl-phthalimide has been given.

This research was performed under the direction of Professor Treat B. Johnson.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF MICHIGAN]

THE DISSOCIATION OF N-PENTAMETHYLENE (OR N-PIPERIDYL)-S-TRIARYLMETHYL-DITHIO-URETHANES WITH THE FORMATION OF TRIARYL METHYLS[1]

BY F. F. BLICKE

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It has been shown by J. v. Braun and co-workers[2] that salts of substituted dithiocarbamic acid (such as the piperidine salt of pentamethylenedithiocarbamic acid) react very readily with acid chlorides (benzoyl chloride for example) according to the following equation:

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[1] The term *n*-piperidyl-S-triarylmethyl-dithio-urethane is a misnomer when applied to the compounds described in this paper; the above-mentioned term, when strictly applied, must refer to compounds containing two atoms of nitrogen in a molecule. However, since the misnaming of the piperidyl-dithio-urethanes has been continued throughout the literature ever since their discovery (1884) the customary name has been given to them in this paper. Correct names for the compounds described in this paper have been obtained by replacing the term "*n*-piperidyl-" by "*n*-pentamethylene."

[2] V. Braun, *Ber.*, **36**, 3520 (1903). V. Braun and Kaiser, *ibid.*, **55**, 1306 (1922).