[Contribution from the Instituto de Química, Universidad Nacional Autónoma de México]

N-BROMOMETHYLPHTHALIMIDE AS A REAGENT FOR THE CHARACTERIZATION OF ALCOHOLS AND PHENOLS

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Although there is available already a great variety of reagents for the formation of derivatives of compounds containing hydroxyl groups, we have investigated the use of N-bromomethylphthalimide (I) for the identification of alcohols and phenols because it offers the following advantages over known reagents:

a. N-bromomethylphthalimide is easily prepared starting from phthalimide.

b. It can be stored for prolonged periods of time without taking special precautions.

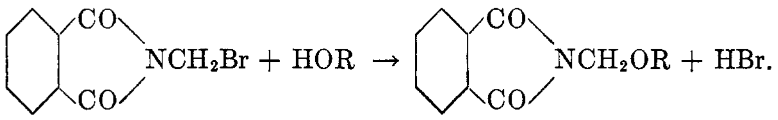
c. It forms solid derivatives even with alcohols of low molecular weight.

d. The formation of derivatives is rapid and the products are easily isolated.

e. The reaction does not require the anhydrous conditions which are necessary with many other reagents.

f. Usually there is no formation of undesirable side products during the reaction.

The bromine atom of N-bromomethylphthalimide has considerable activity, and reacts easily with substances containing hydroxyl groups to form phthalimidomethylene ethers of formula II



I II

In Table I we have summarized the results obtained in the preparation of the phthalimidomethylene ethers of a series of alcohols and phenols.

From the preparation of the derivatives mentioned in Table I we have inferred some general rules which may serve as a guide for the preparation of other similar compounds:

a. The reaction must proceed in acid medium, and it is convenient to use the crude N-bromomethylphthalimide, which always contains traces of hydrogen bromide.

b. The presence of a small amount of powdered potassium iodide seems to favor the reaction rate, probably due to the *in situ* formation of the corresponding iodo derivative.

c. The time required for the reaction depends on the nature of the alcohol. Phenols and alcohols of low molecular weight react more readily than long chain

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alcohols: for instance, ethanol reacts completely in one hour while octadecanol requires eight hours. Secondary alcohols require longer time than primary alcohols.

d. It was not possible to obtain derivatives of tertiary alcohols where a possibility of dehydration existed. On the other hand, triphenyl carbinol reacted normally in four hours. In the case of benzopinacol, with two tertiary hydroxyl groups, only one of them reacted with bromomethylphthalimide.

e. Judging from the behavior of propylene glycol, it is reasonable to assume that both hydroxyl groups will react in other glycols.

TABLE I

PHTHALIMIDOMETHYLENE ETHERS

ALCOHOL	FORMULA OF DERIVATIVE	YIELD %	M.P., °C. (UNCORR.)	N		CRYST. FROM
				Calc'd	Found[b]	
Methanol[a]	$C_{10}H_9NO_3$	—	120–121	7.3	—	Ethanol
Ethanol[a]	$C_{11}H_{11}NO_3$	92	81–83	6.8	6.8	Hexane
1-Butanol	$C_{13}H_{15}NO_3$	78	46–47	6.0	5.8	Hexane
Isobutanol	$C_{13}H_{15}NO_3$	48	58–59	6.0	5.9	Acetic acid-water
1-Tetradecanol	$C_{23}H_{35}NO_3$	83	65–66	3.7	3.3	Hexane
1-Hexadecanol	$C_{25}H_{39}NO_3$	66	70–71	3.5	3.4	Methanol
1-Octadecanol	$C_{27}H_{43}NO_3$	97	80–81	3.2	3.0	Hexane
Cyclohexanol	$C_{15}H_{17}NO_3$	94	81–83	5.4	5.5	Hexane
Phenethyl	$C_{17}H_{15}NO_3$	86	72–74	5.0	5.0	Hexane
2,2-Diphenylethanol	$C_{23}H_{19}NO_3$	65	111–112	3.9	3.8	Benzene-hexane
Thymol	$C_{19}H_{19}NO_3$	69	142–143	4.1	4.1	Benzene-hexane
Triphenyl carbinol	$C_{28}H_{21}NO_3$	50	124–125	3.3	3.1	Benzene-hexane
Benzopinacol	$C_{35}H_{27}NO_4$	95	136–138	2.7	2.4	Benzene-hexane
Propylene glycol	$C_{21}H_{18}N_2O_6$	50	136–146	7.1	7.1	Acetic acid-water
Phenol	$C_{15}H_{11}NO_3$	62	204–205	5.5	5.4	Benzene
β-Naphthol	$C_{19}H_{13}NO_3$	63	196–198	4.6	4.6	Acetic acid

[a] Previously reported by Sachs, *Ber.*, **31**, 1229 (1898).

[b] All nitrogen determinations by the macro Kjeldahl method.

f. Benzene is the most advantageous solvent for the reaction and it can be used without previous drying. When the alcohol and bromomethylphthalimide form a homogeneous mixture, the reaction can be carried out in the absence of a solvent. In one case it was necessary to use dioxane because the alcohol (propylene glycol) was insoluble in benzene and it did not dissolve the reagent.

g. The use of ethanol is not recommended for the crystallization of the derivatives due to possible transetherification. This phenomenon was observed in the case of the derivative of isobutanol, which yielded ethoxymethylenephthalimide after treatment with hot ethanol. Two other derivatives (from β-naphthol and phenethyl alcohol) could not be induced to suffer this change, even after long treatment with ethanol in alkaline or acid solution.

EXPERIMENTAL

N-bromomethylphthalimide. Phosphorus tribromide (30.6 g.) was added in small portions to a stirred suspension of 50 g. of N-hydroxymethylphthalimide (1) in 150 cc. of anhydrous benzene, and the mixture was refluxed for two hours. The clear solution was decanted while hot from the phosphorous acid which remained at the bottom of the flask, and the residue was washed with 50 cc. of hot benzene. On cooling the combined benzene solution, the bromo compound (54.1 g.) separated in crystalline form. A further amount was obtained by concentration of the mother liquor to 50 cc. and cooling. The total yield was 65.6 g. (96.5%), m.p. 149–150°.

Alternative methods for the preparation of this compound are described by Sachs (2) and Gabriel (3).

Derivatives. Two examples will suffice to illustrate the methods of preparation of the derivatives listed in Table I.

N-(β-phenylethoxymethyl)phthalimide. A mixture of 1.5 g. of bromomethylphthalimide and 1 g. of phenethyl alcohol was heated on the steam-bath for 1.5 hours. On cooling the mixture, a solid mass formed which was extracted several times with boiling hexane. The product (1.5 g., 86%) separated from the concentrated solution in the form of rosettes of colorless needles m.p. 70–72°. Recrystallization from benzene-hexane gave the pure ether, m.p. 72–74°.

N-(1-octadecyloxymethyl)phthalimide. A solution of 1 g. of bromomethylphthalimide and 1 g. of 1-octadecanol in 10 cc. of benzene containing 0.1 g. of powdered potassium iodide was refluxed for six hours. The benzene was removed and the residue was crystallized from hexane after filtering the potassium iodide. The yield of the derivative was 1.74 g. (97%), m.p. 76–78°. After three recrystallizations from benzene-hexane the pure product was obtained in the form of fine needles, m.p. 80–81°.

SUMMARY

The use of N-bromomethylphthalimide as a reagent for the characterization of alcohols and phenols has been suggested and its use exemplified by the preparation of a number of derivatives.

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REFERENCES

(1) Sachs, *Ber.*, **31**, 3230 (1898).
(2) Sachs, *Ber.*, **31**, 1229 (1898).
(3) Gabriel, *Ber.*, **41**, 242 (1908).