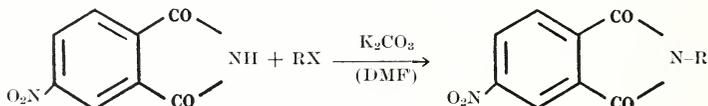


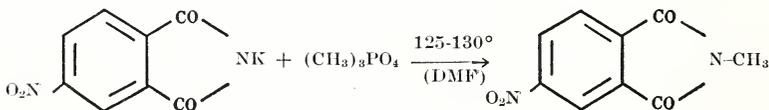
4-Nitrophthalimide III. Methylation with Trimethyl Phosphate and Hydroxymethylation with Formaldehyde¹

JOHN H. BILLMAN and R. VINCENT CASH, Indiana University

In an earlier paper (2) we reported that 4-nitrophthalimide can be alkylated to give solid derivatives of alkyl halides and that these derivatives afford a satisfactory saponification equivalent. Dimethylformamide was employed as a reaction medium for these alkylations (1).

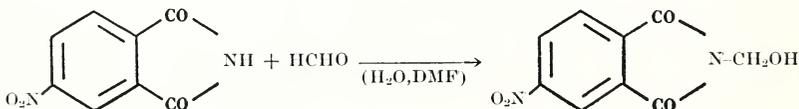


We now wish to describe two related reactions of 4-nitrophthalimide. Methyl phosphate in the presence of dimethylformamide can be used to methylate potassium 4-nitrophthalimide in good yield, giving a product identical with that obtainable from methyl iodide.



The high-boiling trimethyl phosphate is more convenient as a reagent than the low-boiling methyl iodide. This reaction shows similarity to that involving the use of alkyl esters of *p*-toluenesulfonic acid to introduce an alkyl group into phthalimide as reported by Sakellarios (6) and by Clemo and Walton (4).

The second reaction which we carried out involves the addition of formaldehyde to 4-nitrophthalimide to form *N*-dihydroxymethyl-4-nitrophthalimide. This condensation is easily brought about by brief refluxing in a mixture of dimethylformamide and water.



The analogous condensation between phthalimide and formalin to yield *N*-hydroxymethylphthalimide has been recorded by Sachs (5) and by Buc (3).

Experimental

N-Methyl-4-nitrophthalimide. In a 250-ml. round-bottomed flask were placed 4.8 grams (0.021 mole) of potassium 4-nitrophthalimide, 2.0 grams (0.014 mole) of trimethyl phosphate, and 30 ml. of dimethylformamide. Under a reflux condenser bearing a drying tube, the mixture was heated

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at 125-130° for one and one-half hours. The cooled reaction mixture was poured into 100 ml. of cold water, using another 50 ml. of water to wash out the flask. The solid material which separated was collected, washed with water, and dried. This crude product weighed 4.5 grams and gave a melting point of 175.5-177.0°. After recrystallization from aqueous ethyl alcohol, the yield of colorless product was 3.5 grams (81.4% of theory). The melting point of this product, 177.5-178.0° was not depressed by mixing with an authentic sample of N-methyl-4-nitrophthalimide prepared from methyl iodide (2).

N-Hydroxymethyl-4-nitrophthalimide. A mixture of 19.2 grams (0.10 mole) of 4-nitrophthalimide, 8.3 ml. of 40% formalin (3.3 grams or 0.11 mole of formaldehyde), 75 ml. of water, and 25 ml. of dimethylformamide was heated under reflux until all the solid dissolved, and then five minutes longer. When the reaction mixture had been cooled overnight in a refrigerator, the crystalline material which formed was collected by filtration and washed with ice-cold water. After drying in air, the colorless product amounted to 18.2 grams. This was recrystallized from a mixture (4:1 by volume) of water and dimethylformamide, yielding 16.4 grams (74.0% of theory) of product of melting point, 156-157° cor.

Anal. Calc'd for $C_9H_8O_5N_2$: N, 12.60%. Found: N, 12.83%.

Summary

The methylation of potassium 4-nitrophthalimide by treatment with trimethyl phosphate in dimethylformamide is described as a novel and convenient preparation of N-methyl-4-nitrophthalimide. It is also shown that 4-nitrophthalimide can be condensed with formaldehyde to yield N-hydroxymethyl-4-nitrophthalimide.

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