

The Alkylation Reaction of the Gabriel Synthesis¹

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Although the usual procedure for the alkylation of phthalimide by the Gabriel (4) method has been to heat the organic halide with potassium phthalimide (or phthalimide plus potassium carbonate) to 170-200° for several hours, some attention has been given to the use of a solvent or liquid medium for the reaction. The use of such a reaction medium permits a lower reaction temperature and a shorter heating period, prevents overheating and browning of the product, and avoids caking of the reaction mixture in the vessel on cooling. Among the liquids employed as reaction media have been ethanol (1), methanol (8), acetone (2), toluene (6), xylene (5), and nitrobenzene (3)—the usual conditions being heating under reflux for periods as long as fifty hours. The best solvent seems to be dimethylformamide, suggested by Sheehan and Bolhofer (10), in which several N-substituted phthalimides were prepared in high yield by warming potassium phthalimide and the organic halide together for a short period.

We have found that dimethylformamide may likewise be employed for the reaction between phthalimide, anhydrous potassium carbonate, and the appropriate organic halide, according to the modified reaction of Ing and Manske (7). Thus we have prepared N-benzylphthalimide in higher yield and of greater purity than previously reported (9). In a similar manner we have obtained the new compound, N-hexylphthalimide, which completes the series of N-alkylphthalimides of ten or less carbons in the normal alkyl-group. Although unnecessary in the case of benzyl chloride, it was found advantageous to add a small amount of potassium iodide when the alkyl halide was a less-reactive bromide or chloride.

Experimental

N-Benzylphthalimide.—With provision for the exclusion of atmospheric moisture, a mixture of 14.7 g. (0.10 mole) of phthalimide, 7.6 g. (0.055 mole) of anhydrous potassium carbonate, and 19.0 g. (0.15 mole) of dry benzyl chloride in 40 ml. of dimethylformamide was heated at 140-145° for two and one-fourth hours. Little or no refluxing occurred, but carbon dioxide was evolved rapidly. The mixture was agitated occasionally.

After cooling, the reaction mixture was poured into 200 ml. of water. The solid which formed was collected upon a Büchner funnel and washed with successive 40-ml. portions of water, 2% sodium hydroxide solution, water again, and 50% ethyl alcohol. The air-dried, crude product weighed 20.4 g. (86.3%), m.p. 109-112°. Recrystallization from 95% ethyl alcohol provided 17.5 g. (73.8%) of colorless crystals, m.p. 115-116° (corr.).

N-Hexylphthalimide.—This preparation was similar to that above, substituting 24.8 g. (0.15 mole) of *n*-hexyl bromide for the benzyl chloride, and adding a few small crystals of potassium iodide. The material

¹ Contribution No. 577 from the Department of Chemistry of Indiana University.

which separated upon pouring the reaction mixture into water was semi-solid and oily in appearance, but could be collected after ice had been added to the water. Ice-cold washing solutions were used. Recrystallization was from ethyl alcohol, with the addition of water to the hot solution since the product is readily soluble in alcohol. After drying over calcium chloride in a small desiccator placed in the refrigerator, the yield of colorless crystals was 8.0 g. (34.7%), m.p. 37.5-38.5° (corr.). Further recrystallization did not alter this melting point value.

Anal. Calcd. for $C_{14}H_{17}NO_2$: N, 6.07. Found: N, 6.08.

Summary

A new procedure has been developed for the preparation of N-alkyl-phthalimides.

N-Hexylphthalimide has been prepared for the first time.

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