

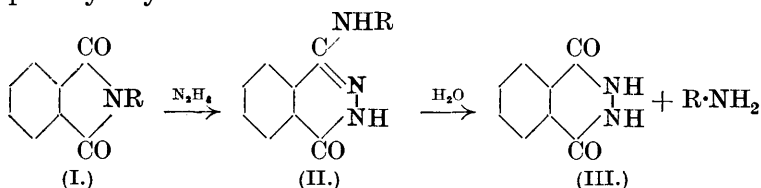
CCCXII.—*A Modification of the Gabriel Synthesis of Amines.*

By HARRY RAYMOND ING and RICHARD HELMUTH FRED MANSKE.

Two modifications of the well-known synthesis of primary amines due to Gabriel have been encountered and constitute distinct improvements where applicable :

(i) It is possible to prepare some alkylphthalimides by heating the alkyl halide with a mixture of phthalimide and potassium carbonate, a method which avoids the troublesome preparation of potassium phthalimide. An excess of the halide is used and is recovered by steam-distillation.

(ii) It is well known that alkylphthalimides are often difficult to hydrolyse. It has now been found that this can easily be achieved indirectly, the condensation product with hydrazine hydrate being readily hydrolysed. Alkylphthalimides (I) react with hydrazine hydrate, in most cases exothermally, to form an intermediate product, probably represented by (II), which is easily decomposed by acids with the formation of phthalylhydrazide (III) and the primary alkylamine.



This reaction has been applied to the preparation of benzylamine, the three nitrobenzylamines, β -phenylethylamine, ethylenediamine, and trimethylenediamine, the yields in all cases being nearly theoretical. A further application in the synthesis of harmaline will be described in an early communication. Attention may also be directed to a point of some theoretical interest: the attempted preparation of *cyclohexylphthalimide*, by heating a large excess of *cyclohexyl* bromide with potassium phthalimide, yielded only *cyclohexene* and phthalimide. On the other hand, no styrene could be detected as a by-product of the preparation of β -phenylethylphthalimide from β -phenylethyl bromide and potassium phthalimide.

EXPERIMENTAL.

Benzylphthalimide.—An intimate mixture of phthalimide (300 g.) and anhydrous potassium carbonate (150 g.) is treated with benzyl chloride (300 g., 20% excess) and the whole is heated in an oil-bath under reflux for about 3 hours. The excess of benzyl chloride is distilled in a current of steam, and the residual solid benzylphthalimide is filtered and washed with water; yield 360–375 g. One recrystallisation from acetic acid gives the pure product, m. p. 116° (compare Gabriel, *Ber.*, 1887, 20, 2227).

γ -Bromopropylphthalimide.—In this preparation phthalimide (300 g.), potassium carbonate (150 g.), and trimethylene dibromide (1000 g.) are intimately mixed in a 2-litre Pyrex flask and gradually

heated until reaction begins. It is essential to attach two efficient reflux condensers to prevent loss of alkyl bromide during the subsequent vigorous reaction. At first, the mixture becomes almost solid but as reaction proceeds it becomes mobile again. It is finally heated under reflux for 2 hours in an oil-bath and the excess of trimethylene dibromide distilled in a rapid current of steam (570—590 g. is recovered). The oily residue in the flask solidifies to a pale brown solid which, after filtering, washing, and drying, weighs 480—520 g. It contains as chief impurity $\alpha\gamma$ -diphthalimidopropane. After one crystallisation from 400 c.c. of alcohol and drying, the mixture is separated into its constituents by extraction in a continuous apparatus with petroleum ether (b. p. 40—60°), only the bromo-compound dissolving. The yield of pure product, m. p. 72°, is 275—300 g.

The residue, insoluble in petroleum ether, yields, after one recrystallisation from acetic acid, 100—120 g. of pure $\alpha\gamma$ -diphthalimidopropane, m. p. 197° (compare Gabriel and Weiner, *Ber.*, 1888, **21**, 2671).

β -Phenylethylphthalimide.—Phenylethyl bromide (20 g.) was heated with potassium phthalimide (25 g.) for 2—3 hours at 180—200°. The product was distilled in steam to remove unchanged bromide, the solid filtered, washed with cold alcohol, and recrystallised from acetic acid. *β -Phenylethylphthalimide* is sparingly soluble in cold alcohol and acetic acid, readily in the hot solvents. It melts at 131—132° (Found: N, 5.9. $C_{16}H_{14}O_2N$ requires N, 5.5%).

Benzylamine.—Finely-powdered benzylphthalimide (1 mol.) was warmed in alcoholic suspension with hydrazine hydrate (1 mol.). A white, gelatinous precipitate was rapidly produced which was decomposed by warming with excess of hydrochloric acid. The insoluble phthalylhydrazide was filtered and washed with water. The filtrate was concentrated to remove alcohol and the cooled solution, after filtration from the small amount of precipitated phthalylhydrazide, made alkaline and extracted with ether. The ether solution was dried with solid caustic potash and evaporated and the benzylamine distilled, b. p. 185—187°. Acetylation yielded benzylacetamide, m. p. 60° (Amsel and Hofmann, *Ber.*, 1886, **19**, 1286). The yield of benzylamine was 90—95% of the theoretical.

The following bases (or their salts) were prepared in an exactly similar manner from the corresponding phthalimides: β -Phenylethylamine, b. p. 200—205°, yield 95%; *o*-nitrobenzylamine hydrochloride, m. p. 248°, yield 90%; *m*-nitrobenzylamine hydrochloride, m. p. 220°, yield 90%, nitrate, m. p. 181—182° [Holmes and Ingold (*J.*, 1925, **127**, 1812) give the m. p.'s of these salts as 250° and 214° respectively]; *p*-nitrobenzylamine hydrochloride, m. p. 250°,

yield 80%, nitrate, m. p. 218° [Holmes and Ingold (*loc. cit.*) give the m. p.'s of these salts as 224° and 180—181° respectively]; ethylenediamine, diacetyl derivative, m. p. 172°, yield 90%; trimethylenediamine, b. p. 134—136°, yield 96%.

We wish to thank the Ramsay Memorial Fellowship Trust for a Fellowship awarded to one of us (H. R. I.) and the Commissioners of the Exhibition of 1851 for a Scholarship awarded to the other (R. H. F. M.).

THE UNIVERSITY, MANCHESTER.

[Received, June 29th, 1926.]
