[CONTRIBUTION FROM THE STERLING CHEMISTRY LABORATORY, YALE UNIVERSITY]

A MODIFICATION OF THE CURTIUS SYNTHESIS OF PRIMARY AMINES

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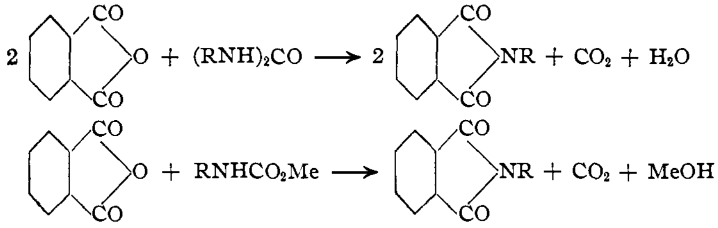
The usefulness of the Curtius reaction for the synthesis of primary amines is considerably decreased because of the difficulty frequently encountered in hydrolyzing the intermediate alkylureas and urethans. Di-β-phenylethylurea is hydrolyzed completely only after prolonged heating in a sealed tube with concentrated hydrochloric acid at high temperatures.[2] Such a procedure is likely to result in dealkylation when alkoxyl groups are present. The author observed that di-β-(3-indolylethyl)-urea was completely resinified on heating with hydrochloric acid even for a short time, while boiling with saturated alcoholic potassium hydroxide for twenty-four hours resulted in no change. Distillation with soda lime is generally to be avoided and is obviously too drastic in this case. The high temperature is conducive to decomposition and the yield of impure product is frequently very low.

When alkylureas are heated with phthalic anhydride, alkyl phthalimides are formed in excellent yield,[3] and the same reaction has now been applied to alkyl urethans. The reactions are represented as follows



and bring the methods of Gabriel and of Curtius into a common field. The subsequent hydrolysis of the alkylphthalimides may be quantitatively accomplished by the reaction of Ing and Manske.[4]

The examples described in the experimental section suffice to illustrate the generality of the reaction here discussed.

Experimental

1,8-Diphthalimido-octane.—A mixture of octamethylene-1,8-dimethylurethan[5] (4 g.) and phthalic anhydride (8 g.) was heated in an oil-bath at 230° until evolution of gases ceased (*ca.* thirty minutes). The reaction mixture which contained a small

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[1] Eli Lilly Research Fellow, Yale University, 1927–1928–1929.

[2] Thiele and Pickard, *Ann.*, **309,** 200 (1899).

[3] Tingle and Brenton, THIS JOURNAL, **32,** 116 (1910).

[4] Ing and Manske, *J. Chem. Soc.*, 2348 (1926).

[5] Steller, *J. prakt. Chem.*, [2] **62,** (a) 224, (b) 226 (1900).

amount of phthalic anhydride was cooled to 100°, treated with a small volume of alcohol and then neutralized with an excess of aqueous sodium bicarbonate. The precipitated diphthalimide compound crystallized almost at once. It was filtered off, thoroughly washed with water, dried and recrystallized from a small volume of alcohol, in which it is moderately soluble; yield, 7.4 g. It consists of colorless, glistening needles melting at 138°.[6]

Anal. Calcd. for $C_{24}H_{24}O_4N_2$: N, 6.93. Found: N, 6.43, 6.71.

In order to confirm the identity of this product a small amount was hydrolyzed with hydrazine hydrate.[4] The hydrochloride of the resulting base was identical in all respects with an authentic specimen of octamethylenediamine hydrochloride (mixed m. p. 277°).[5b]

Di-γ-phenoxypropylurea.—γ-Phenoxybutyric hydrazide, $C_6H_5OCH_2CH_2CONH$-NH_2, was prepared by heating a mixture of 70 g. of ethyl γ-phenoxybutyrate, 20 g. of hydrazine hydrate (90%) and 50 cc. of ethyl alcohol under a reflux for ninety minutes. The greater portion of the alcohol was removed by distillation and the residue was heated under reflux for sixty minutes more. The cooled mixture yielded 55 g. of hydrazide which after two recrystallizations from alcohol had a melting point of 81–82°.

The crude hydrazide was converted into the azide by treating an iced solution of 19.4 g. in 200 cc. of water and 10 cc. of concentrated hydrochloric acid with 6.9 g. of sodium nitrite. The precipitated azide was thoroughly washed with iced water (it melted at room temperature to a pale yellow liquid) and decomposed by gradually heating it in 50 cc. of acetic acid and 300 cc. of water. The urea crystallized even while the liquid was boiling. It was filtered off, washed with water and recrystallized from alcohol, in which it is only sparingly soluble. The yield of purified product was 10 g. After another recrystallization from alcohol (charcoal) it melted sharply at 150°.

Anal. Calcd. for $C_{19}H_{24}O_3N_2$: N, 8.54. Found: N, 8.47.

γ-Phenoxypropylphthalimide.—Di-γ-phenoxypropylurea (16.4 g.) was heated with phthalic anhydride (16 g.) at 225° in an oil-bath until evolution of gases ceased (fifteen minutes). The excess phthalic acid was removed with aqueous sodium bicarbonate and the alkyl phthalimide recrystallized from alcohol; yield of pure product, 24 g. It melted alone or admixed with an authentic specimen at 91°.[7] Hydrolysis with hydrazine hydrate[4] yielded γ-phenoxypropylamine hydrochloride melting at 168° (alone or admixed with an authentic specimen).[7]

β-(3-Indolylethyl)-phthalimide, $(C_8H_6N)CH_2CH_2N(CO)_2C_6H_4$.—In the course of some experiments with the azide of indolylpropionic acid,[8,9] a small yield of di-β-(3-indolylethyl)-urea was frequently encountered. The exact conditions for obtaining this urea in good yield have not been investigated sufficiently and this subject together with some further work on indolylpropionic and indolylbutyric acids will form the substance of an early communication.

When the urea was heated at 225° with an excess of phthalic anhydride and the mixture worked up in the usual way, the phthalimide was obtained in excellent yield. After two recrystallizations from alcohol (charcoal) it consisted of pale yellow needles (readily soluble in hot alcohol) melting at 164–165°.

Anal. Calcd. for $C_{18}H_{14}O_2N_2$: C, 74.48; H, 4.83. Found: C, 74.32; H, 4.96.

On hydrolysis with hydrazine hydrate it produced tryptamine (β-3-indolylethyl-

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[6] Melting points are corrected.

[7] Lohmann, *Ber.*, **24**, 2634 (1891).

[8] Manske and Robinson, *J. Chem. Soc.*, 240 (1927).

[9] Kalb, Schweizer and Schimpf, *Ber.*, **59**, 1858 (1926).

amine) in quantitative yield. The hydrochloride consisted of colorless needles melting at 248°. The picrate had a melting point of 243°.[10]

Summary

1. It is suggested that the hydrolysis of alkylureas and urethans, when acid or alkali hydrolysis is impracticable, be accomplished by means of phthalic anhydride and subsequently with hydrazine hydrate.
2. This procedure has been utilized in the synthesis of tryptamine.

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[CONTRIBUTION FROM THE DYE LABORATORY OF THE CHEMISTRY DIVISION OF THE BUREAU OF STANDARDS, U. S. DEPARTMENT OF COMMERCE]

THE RELATION BETWEEN THE ABSORPTION SPECTRA AND CHEMICAL CONSTITUTION OF CERTAIN AZO DYES. I. THE EFFECT OF POSITION ISOMERISM ON THE ABSORPTION SPECTRA OF METHYL DERIVATIVES OF BENZENE-AZOPHENOL[1,2]

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The effect of position isomerism on the absorption spectra of similarly constituted aromatic compounds has been studied by Baly,[3] Purvis,[4] Klingstedt[5] and Henri[6] together with their co-workers in this field. In general it has been shown that substitution in the para position produces a stronger absorption band than substitution of the same group in either the ortho or meta position in the benzene ring. This effect, although not always mentioned, can be noted in the data of other observers. Recent work by Henri on the absorption spectra of isomeric xylenes and dihalogenated benzene compounds in the vapor phase has shown considerable variation in the fine structure of the absorption bands with a change in the position of substitution. The unstable nature of azo dyes, however, does not permit the study of their absorption spectra in a vapor state, so that data by this method are unobtainable on the compounds studied in this paper.

The object of this investigation is a fundamental quantitative study

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[10] Ewins, *J. Chem. Soc.*, **99**, 270 (1911).

[1] Publication approved by the Director of the National Bureau of Standards, Department of Commerce.

[2] Presented in part at the Philadelphia meeting of the American Chemical Society in September, 1926.

[3] Baly, *J. Chem. Soc.*, **107**, 1058 (1915).

[4] Purvis, *ibid.*, **103**, 1088 (1913).

[5] Klingstedt, *Compt. rend.*, **175**, 365 (1922).

[6] Henri, "Structure des Molécules," Herman, Paris, **1925**, and unpublished data communicated to the author.