

The Leuckart Reaction: A Study of the Mechanism

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J. Am. Chem. Soc., **1948**, 70 (4), 1422-1424 • DOI: 10.1021/ja01184a038

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and ammonia protects the formamide from the air, and no trouble is encountered unless the heating is interrupted, or unless the heating is continued after the evolution of gases has ceased.

Standard Method of Carrying Out the Reaction.—Eighty-five grams of benzophenone (0.467 mole) and 110 cc. of 99% formamide (6×0.467 mole) (obtained from the Eastman Kodak Co.) together with any substances to be tested for catalytic effect, and a chip of porous plate were placed in a 200-cc. balloon flask equipped with an air-reflux-condenser. The air was displaced with nitrogen, and the flask immersed in an oil-bath kept at 190–200°. After boiling had started, the temperature in the flask was at 180–190°. A small quantity of ammonium carbonate sublimed into the reflux condenser, and ammonia and carbon dioxide were evolved. At exactly four hours after boiling started, the flask was removed from the oil-bath, allowed to cool to about 140°, and cautiously poured into about 200 cc. of cold water. (If it was cooled much below 130°, the formyl derivative crystallized, and removal from the flask was difficult.) The flask was washed out with a little water, and the mixture of benzophenone, N-benzhydryl formamide, and water soluble substances was cooled, seeded with a crystal of benzophenone, and the mixture of solids collected on a Buchner funnel, washed with a little water, and dried. The amount of benzophenone and of N-benzhydryl formamide in the mixture of solids was determined by distillation *in vacuo* without a column. Benzophenone boils at 114° at 1.2 mm., but was collected at 120–130° in order to speed up the distillation. When the benzophenone was all gone, the boiling point rose rapidly; at 160° the receiver was changed, and the remaining formyl derivative was distilled with strong enough heating to prevent crystallization in the side arm of the flask.

The amide boils at 173° at 1.2 mm., but as before, it saved time to collect it at 185–190°. A small amount of tar (about a gram) remained in the Claisen flask. The amount of benzophenone determined by this method may be too great by one to two grams (estimated), as a small amount of formamide remains with the solids, and distills over with the first few drops of benzophenone.

All of the reaction mixtures were homogeneous, with the exception of 3-C; the ammonium sulfate added is not completely soluble in the reaction mixture. The results are shown in Table I. The melting point determined by Fischer block method was higher when the reaction was more complete. The value for the pure substance in the literature and in our hands is 132°.² In order to judge the purity of the amide, a solution of 2% benzophenone in molten N-benzhydryl formamide was made up and allowed to cool. This material melted at 126.5–130.5°, from which it is concluded that the maximum impurity in the amide samples in Table I is about 2 or 3%.

Summary

1. The Leuckart reaction with benzophenone and formamide has been run under various conditions; with pure formamide (99%) the yield is low unless a large amount of the reagent is used.
2. Ammonium formate, ammonium sulfate, and magnesium chloride have been shown to be effective catalysts for the reaction.
3. A partial mechanism is advanced for the reaction.

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RECEIVED AUGUST 20, 1947

[CONTRIBUTION FROM THE CONVERSE MEMORIAL LABORATORY OF HARVARD UNIVERSITY]

Gelsemine

BY BERNHARD WITKOP¹

Several recent papers^{1a,2,3} deal with the structure of gelsemine, $C_{20}H_{22}O_2N_2$, the principal crystalline alkaloid of *Gelsemium sempervirens*, the American "yellow jasmine." Marion² isolated an indole derivative as the product of soda-lime or selenium treatment of gelsemine. This is the first major degradation product reported, and relates gelsemine to the indole alkaloids. Indole itself occurs in the oils from the enfleurage of jasmine flowers, where it is present in the form of an unknown complex.⁴ Marion and other investigators,^{1a,2} studying the degradation of gelsemine, report the presence of bases that were difficult to purify and obtainable only in very small yield.

By the use of a modified mild zinc dust distillation three degradation products have been obtained from gelsemine. Two of basic nature were separated by the difference in basicities. The stronger base is an oil with quinoline or isoquinoline odor, and yields a well-crystallized picrate. Analysis of the latter corresponds to an ethyl- or

dimethyl- quinoline or -isoquinoline. It is clear from the data of Table I that gelsemine is such a strong tertiary base that the basic nitrogen atom can neither be attached to a benzene nucleus nor form part of an unreduced pyridine ring, as has been suggested already by Forsyth, Marrian and Stevens.^{1a} A more weakly basic product, probably $C_{14}H_{11}N$, was obtained in the form of a picrate. According to the analytical data it might be a methylbenzquinoline (or -isoquinoline). Skatole was isolated as the main non-basic product of indolic nature in the form of the picrate.

TABLE I

pKa (negative logarithms of acidity constants of the hydrochlorides)

Quinoline	4.89 ⁵
Isoquinoline	5.36
Py-tetrahydroquinoline	5.03
Py-tetrahydroisoquinoline	9.41
Gelsemine	9.37 ^{1a}

The dimethylindole reported by Marion² has not been observed in the present investigation. It should be pointed out, however, that the identification of alkyl indoles is often rendered difficult

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