**Tetrahedron Letters No.35, pp. 3115-3122, 1965. Pergamon Press Ltd.
Printed in Great Britain.**

A TRACER STUDY OF THE ACID-CATALYZED CONDENSATION OF 2-BENZOYL-1,2-DIHYDROISOQUINALDONITRILE WITH 1,1-DIPHENYLETHYLENE

Tucker T. Yee

Departments of Chemistry, University of Massachusetts, Amherst, Massachusetts
and Brookhaven National Laboratory, Upton, Long Island, New York

William E. McEwen

Department of Chemistry, University of Massachusetts, Amherst, Massachusetts

and

Alfred P. Wolf

Department of Chemistry, Brookhaven National Laboratory, Upton, Long
Island, New York

(Received 25 June 1965)

In a previous communication (1), which was concerned mainly with the benzoylation of the benzhydryl cation by the reaction of 2-benzoyl-1,2-dihydroisoquinaldonitrile (I) with benzhydrol in concentrated sulfuric acid, mention was also made of the acid-catalyzed condensation of I with 1,1-diphenylethylene (II). Two isomeric products of molecular formula $C_{31}H_{22}N_2$ were obtained. One of these, a colorless compound of m.p. 194.0-194.5°, could be converted to the other, a yellow compound of m.p. 262.5-263.5°, either by treatment with 12 N sulfuric acid or by potassium hydroxide fusion. Also, prolonged hydrolysis of the colorless compound in 3.6 N sulfuric acid gave both the yellow compound and an equimolar mixture of 1-hydroxyisoquinoline (V) and 2,3,5-triphenylpyrrole (VI) (2).

A tracer study has now been completed in which carbonyl-C^{14} labeled I and cyano-C^{14} labeled I were condensed with unlabeled II and unlabeled I was condensed with methylene-C^{14} labeled II, each of the three reactions being carried out in sulfuric acid-dioxane medium. A pure product of molecular formula $C_{31}H_{22}N_2$ was isolated in each case. The colorless compounds of m.p. 194.0-194.5° were subjected to hydrolytic cleavage in hot, dilute sulfuric acid. Subsequent degradations of the labeled 2,3,5-triphenylpyrroles by the scheme outlined in Fig. 1 gave the carbon-14 distributions summarized in Table I.

TABLE I

Carbon-14 Distribution in the Hydrolytic Cleavage Products

Specifically Labeled	Label in Products	
Precursor	1-Hydroxyisoquinoline	2,3,5-Triphenylpyrrole
2-Benzoyl-1,2-dihydro-isoquinaldonitrile-carbonyl-C^{14}	Inactive	100 ± 2% in 5-position
2-Benzoyl-1,2-dihydro-isoquinaldonitrile-cyano-C^{14}	Inactive	100 ± 2% in 2-position
1,1-Diphenylethylene-2-C^{14}	Inactive	100 ± 2% in 4-position

Of the 24 theoretical structures which may be written for a triphenyl-(1-isoquinolyl)-pyrrolenine *only one* is consistent with the observed carbon-14 distribution of the cleavage products (3). Thus, the colorless product of m.p. 194.0-194.5° is now known to be 2-(1-isoquinolyl)-3,35-triphenylpyrrolenine (III), and the isomer of m.p. 262.5-263.5° is 2-(1-isoquinolyl)-3,4,5-triphenylpyrrole (IV).

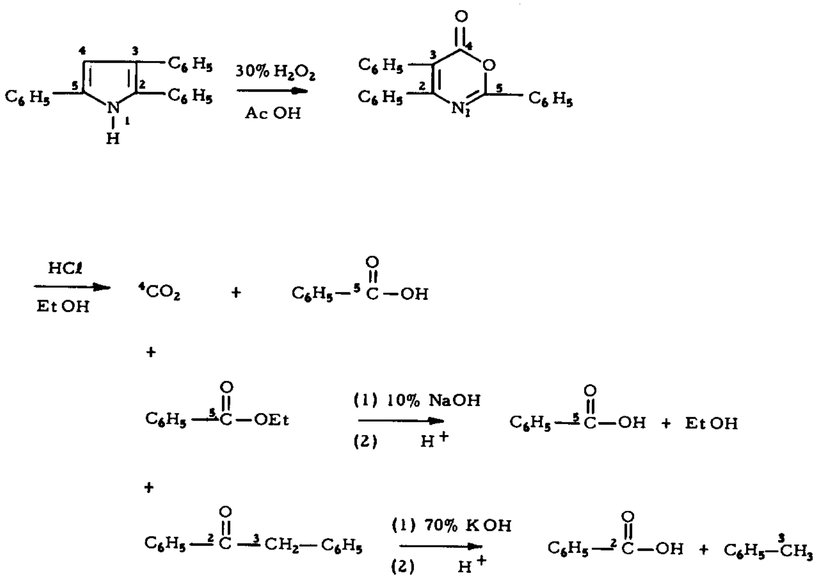


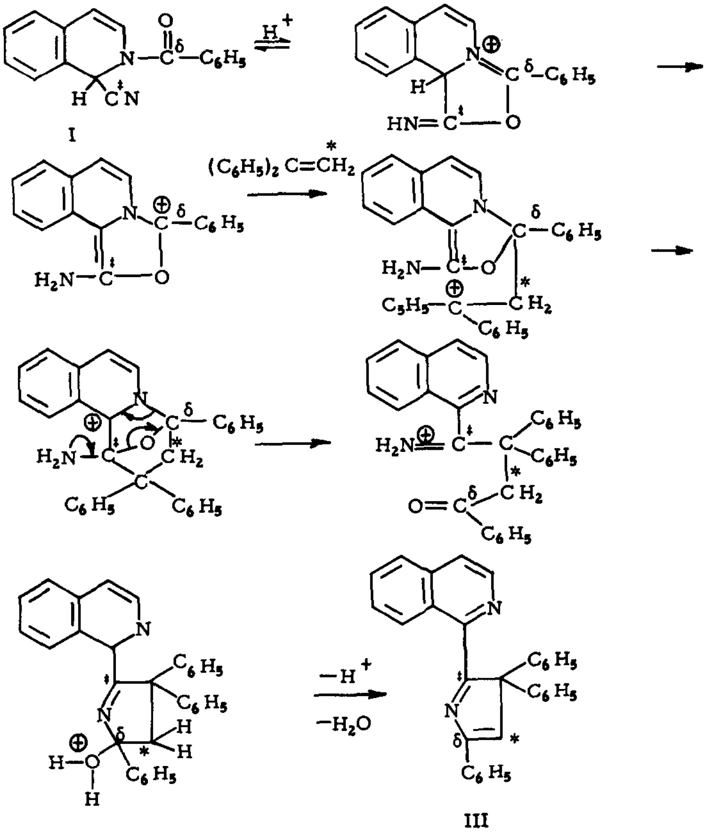
FIG. 1

Degradation of 2,3,5-Triphenylpyrrole

A mechanism for the formation of III, consistent with all of the available data, is shown in Fig. 2. Suggested mechanisms for the conversion of III to IV plus the cleavage products, V and VI, by the action of acid are shown in Fig. 3. Finally, a logical mechanism for the isomerization of III to IV by potassium hydroxide fusion is shown in Fig. 4 (4).

Complete and satisfactory analyses, both elemental and isotopic, have been obtained for all of the compounds mentioned in this communication. Authentic 2,3,5-triphenylpyrrole (VI) was prepared by the method of Smith (5). 2,3,5-Triphenylpyrrole-5-C^{14} was prepared from 1,2,4-triphenyl-1,4-butanedione by the same method, and a specifically labeled 2,3,5-triphenylpyrrole, in a control experiment, was found to undergo the degradation, outlined in Fig. 1, in an uncomplicated manner. Authentic 1-hydroxyisoquinoline (V) was prepared by the method of Tschitschibabin and Kurasanova (6). 1,1-Diphenylethylene-1-C^{14} was prepared from benzophenone and methyl-C^{14}-triphenylphosphonium bromide by the Wittig reaction (7), while 1,2,4-triphenyl-1,4-butanedione-4-C^{14} was obtained by reaction of acetophenone-carbonyl-C^{14} with benzoin in the presence of potassium cyanide (5).

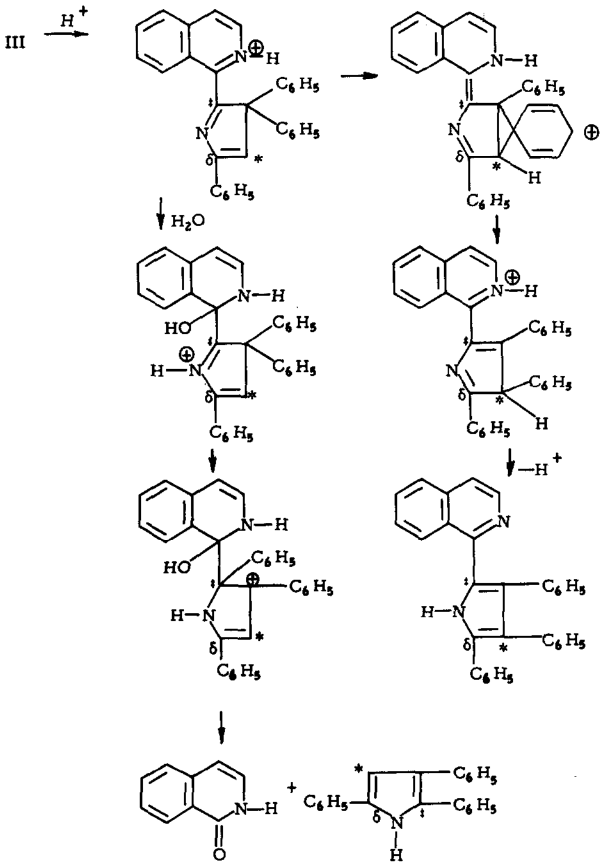
In a subsequent, detailed paper, arguments in addition to those based on the results of the tracer experiments will be advanced to show that III is the only pyrrolenine condensation product of the 24 theoretical triphenyl-(1-isoquinolyl)-pyrrolenines which accommodates the following facts: (1) the formation of 1-hydroxyisoquinoline (V) and 2,3,5-triphenylpyrrole (VI) on acid-catalyzed hydrolytic cleavage, (2) the concomitant formation of a triphenyl-(1-isoquinolyl)-pyrrole, and (3) the observation that the latter product does not undergo hydrolytic cleavage to give V and VI on prolonged refluxing in dilute sulfuric acid.



Note: original carbonyl C^{14} = δ; original cyano C^{14} = ‡ ; original methylene C^{14} = * ; labels used in three separate experiments.

FIG. 2

Proposed Mechanism of Condensation Reaction



V VI

FIG. 3

Mechanisms of Acid-catalyzed Isomerization and Cleavage

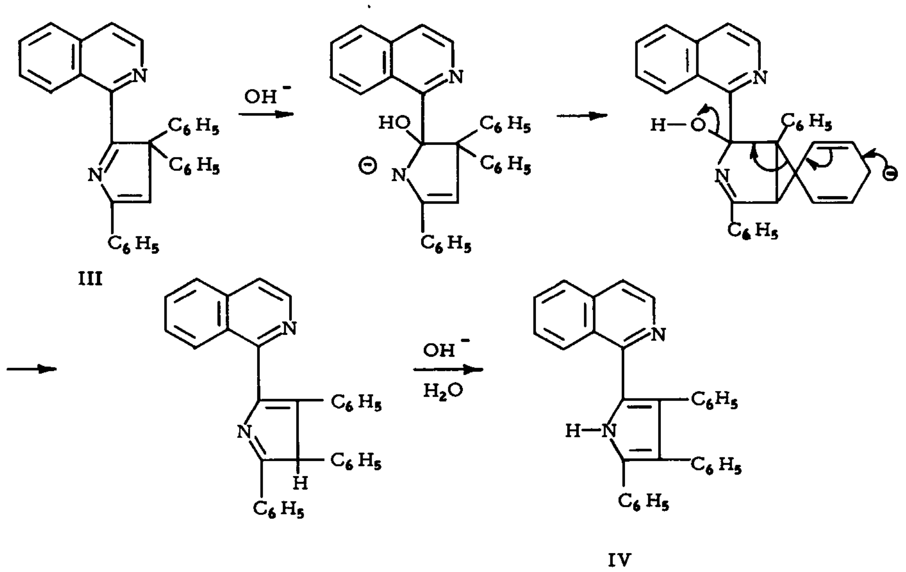


FIG. 4

Mechanism of Isomerization Catalyzed by Potassium Hydroxide

Acknowledgment.—This investigation was supported in part by a research grant, CA-06620, from the National Cancer Institute of the National Institutes of Health, Public Health Service and in part by the U. S. Atomic Energy Commission.

REFERENCES

1. T. K. Liao and W. E. McEwen, J. Org. Chem. 26, 5257 (1961).

2. On the basis of spectral data and the information cited above, the colorless compound of m.p. 194.0-194.5° was tentatively assigned the structure of 2,2,5-triphenyl-4-(1-isoquinolyl)-pyrrolenine and the yellow compound of m.p. 262.5-263.5° the structure of 2,3,5-triphenyl-4-(1-isoquinolyl)-pyrrole. It was also inferred that the latter compound was the precursor of 1-hydroxyisoquinoline and 2,3,5-triphenylpyrrole. These tentative conclusions now must be modified in the light of the new data described in this communication.

3. Details are given in the Ph.D. Dissertation of Tucker T. Yee, University of Massachusetts, Amherst, Massachusetts, September, 1964.

4. It is significant that the pyrrolenine, analogous to III, obtained by the acid-catalyzed condensation of 2-benzoyl-1,2-dihydroisoquinaldonitrile (I) with 1-phenyl-1-p-anisylethylene, gives two isomeric pyrroles, analogous to IV, one predominating in the acid-catalyzed isomerization and the other in the potassium hydroxide fusion (T. K. Liao, Ph.D. Disseration, University of Kansas, 1961). It is clear that a p-anisyl group would undergo a 1,2-shift more rapidly than a phenyl group in an acid-catalyzed isomerization of the type shown in Fig. 3, while a phenyl group would undergo a 1,2-shift more rapidly than a p-anisyl group in the type of rearrangement reaction depicted in Fig. 4.

5. A. Smith, J. Chem. Soc. 57, 643 (1890).

6. A. E. Tschitschabine and A. I. Kurasanova, J. Russ. Phys. Chem. Soc. 62, 1211 (1930); Chem. Abstr. 25, 2727 (1931).

7. G. Wittig and M. Rieher, Ann. 562, 177 (1949).