cyanate ion (other than carbon dioxide and ammoniun ion) were identified by comparison of their infrared spectra with a series of reference spectra of the solids from hydrolyzed control solutions.

Registry No.—Bis(difluoramino)difluoromethane, 4394-93-8; bis(difluoramino)dichloromethane, 10394-50-0; 2-difluoraminoperfluoropropane, 662-23-7; difluoraminoperfluoromethane, 335-01-3; difluoraminoperfluoroethane, 354-80-3.

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Tracer Studies of the Condensation of a Reissert Compound with 1,1-Diphenylethylene

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Mainly by a series of tracer studies, but also on the basis of other evidence, it has been established that the acid-catalyzed condensation of 2-benzoyl-1,2-dihydroisoquinaldonitrile (I) with 1,1-diphenylethylene (II) affords a mixture of 2-(1-isoquinolyl)-3,3,5-triphenylpyrrolenine (III), 2-(1-isoquinolyl)-3,4,5-triphenylpyrrole (IV), and isoquinaldamide. Mechanisms are suggested for the formation of these products and also for several isomerization and cleavage reactions of III.

As mentioned in previous communications,[1,2] two isomeric products of molecular formula $C_{31}H_{22}N_2$ are produced by the acid-catalyzed condensation of 2-benzoyl-1,2-dihydroisoquinaldonitrile (I) with 1,1-diphenylethylene (II). One of these, a colorless compound of mp 194.0–194.5°, can be converted to the other, a yellow compound of mp 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 affords both the yellow compound and an equimolar mixture of 1-hydroxyisoquinoline (V)–2,3,5-triphenylpyrrole (VI).

A tracer study has now been carried out in which carbonyl-C^{14}-labeled I and cyano-C^{14}-labeled I were condensed with unlabeled II. In addition, 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 $C_{31}H_{22}N_2$ and mp 194.0–194.5° was isolated in each case, and these compounds were subjected to hydrolytic cleavage in hot, dilute sulfuric acid. Subsequent degradations of the labeled 2,3,5-triphenylpyrroles by the scheme outlined in Scheme I gave the carbon-14 distributions summarized in Table I.

TABLE I

C^{14} DISTRIBUTION IN THE HYDROLYTIC CLEAVAGE PRODUCTS

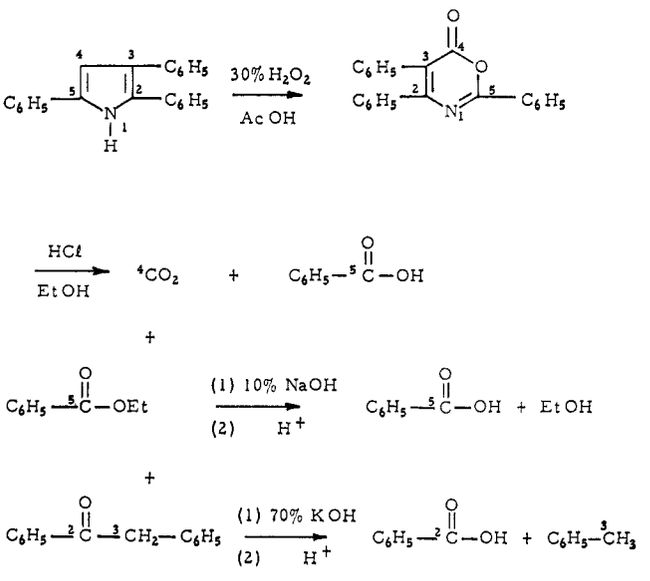
Specifically labeled precursor	Label in products: 1-Hydroxyisoquinoline	Label in products: 2,3,5-Triphenylpyrrole
2-Benzoyl-1,2-dihydroisoquinaldonitrile-carbonyl-C^{14}	Inactive	100 ± 2% in 5 position
2-Benzoyl-1,2-dihydroisoquinaldonitrile-cyano-C^{14}	Inactive	100 ± 2% in 2 position
1,1-Diphenylethylene-2-C^{14}	Inactive	100 ± 2% in 4 position

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

(2) T. T. Yee, W. E. McEwen, and A. P. Wolf, *Tetrahedron Letters*, 3115 (1965).

SCHEME I

DEGRADATION OF 2,3,5-TRIPHENYLPYRROLE



Of the 24 theoretical structures[3] which may be written for a triphenyl(1-isoquinolyl)pyrrolenine, *only one* is consistent with the observed carbon-14 distribution

(3) The names of the 24 possible compounds are hereby provided, and the numbers in parentheses refer to the criteria, listed in the main text, which have been used to eliminate all but the correct structure from further consideration: 2,5,5-triphenyl-4-(isoquinolyl)pyrrolenine (1, 3), 3,5,5-triphenyl-2-(1-isoquinolyl)pyrrolenine (1, 2), 4,5,5-triphenyl-2-(1-isoquinolyl)pyrrolenine (1, 2, 3), 4,5,5-triphenyl-3-(1-isoquinolyl)pyrrolenine (1, 2, 3), 3,5,5-triphenyl-4-(1-isoquinolyl)pyrrolenine (1, 2, 3), 2,3,3-triphenyl-4-(1-isoquinolyl)pyrrolenine (1, 2, 3), 2,3,3-triphenyl-5-(1-isoquinolyl)pyrrolenine (1, 2), 3,3,4-triphenyl-2-(1-isoquinolyl)pyrrolenine (1, 2, 3), 3,3,4-triphenyl-5-(1-isoquinolyl)pyrrolenine (1, 2), 2,4,4-triphenyl-3-(1-isoquinolyl)pyrrolenine (1, 2, 4), 2,5,5-triphenyl-3-(1-isoquinolyl)pyrrolenine (1, 2, 4), *d*- and *l*-2,3,5-triphenyl-5-(1-isoquinolyl)pyrrolenine (1), *d*- and *l*-3,4,5-triphenyl-5-(1-isoquinolyl)pyrrolenine (1, 2, 3), *d*- and *l*-3,4,5-triphenyl-3-(1-isoquinolyl)-pyrrolenine (1, 2, 4), *d*- and *l*-2,3,5-triphenyl-3-(1-isoquinolyl)pyrrolenine (1), *d*- and *l*-2,3,4-triphenyl-3-(1-isoquinolyl)pyrrolenine (1, 2, 3), *d*- and *l*-2,4,5-triphenyl-5-(1-isoquinolyl)pyrrolenine (1, 3), and 2-(1-isoquinolyl)-3,3,5-triphenylpyrrolenine (III), the correct structure.

of the cleavage products. Thus, the colorless product of mp 194.0–194.5° is now known to be 2-(1-isoquinolyl)-3,3,5-triphenylpyrrolenine (III), and the isomer of mp 262.5–263.5° is 2-(1-isoquinolyl)-3,4,5-triphenylpyrrole (IV).

In a more complete evaluation of all of the possibilities, four criteria can be considered to choose the correct structure among the 24 candidates: (1) the carbon-14 distribution in the tracer studies, (2) the formation of 1-hydroxyisoquinoline (V) and 2,3,5-triphenylpyrrole (VI) on acid-catalyzed hydrolytic cleavage of the pyrrolenine, (3) the concomitant formation of a triphenyl(1-isoquinolyl)pyrrole, and (4) the observation that the latter product does not undergo hydrolytic cleavage to give V and VI on prolonged refluxing in dilute sulfuric acid. Consideration of all four criteria serves only to emphasize the point that III is the correct structure of the pyrrolenine.[3] All of the other structures are eliminated from further consideration on the basis of the first point and usually on the basis of one or more of the other criteria also. Further details are provided in footnote 3.

A mechanism for the formation of III, consistent with all of the available data, is shown in Scheme II.[4] In this mechanism the conjugate acid of I is functioning as the electrophilic agent and II acts as the nucleophilic agent in the initial condensation step. In other acid-catalyzed reactions of I, the conjugate acid has served as the source of the nucleophilic agent.[1,5] It is evident that the electronic demands of the species which condenses with the conjugate acid of I determine in large measure the type of reactivity which it will exhibit.

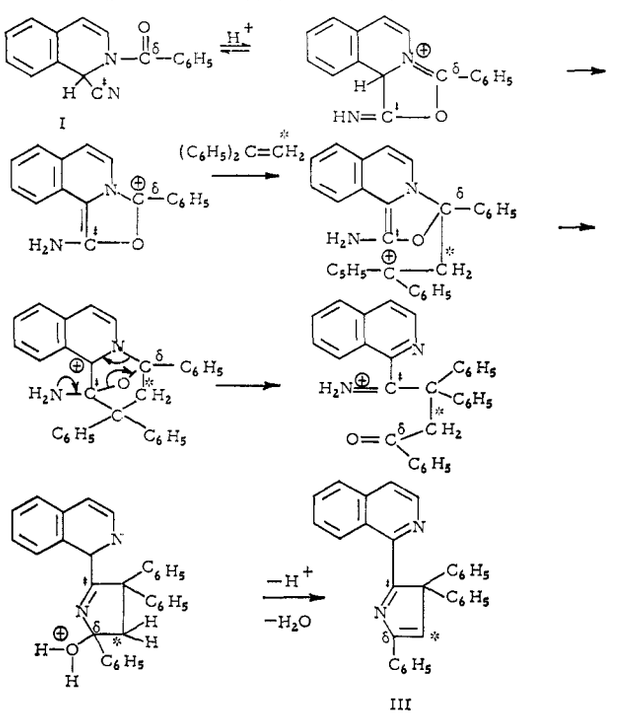
Suggested mechanisms for the conversion of III to IV plus the cleavage products V and VI by the action of acid are shown in Scheme III. Although the rearrangement of III to IV is relatively unexceptional, involving migration of a phenyl group from carbon to an adjacent cationoid center, the cleavage reaction to produce V plus VI is novel. This provides a relatively rare example of a rearrangement reaction in which the migration of an aryl group from carbon to an adjacent cationoid center is an integral part of a hydrolytic cleavage reaction.

A logical mechanism for isomerization of III to IV by potassium hydroxide fusion is shown in Scheme IV. This is of interest in that it provides a rare example of a rearrangement reaction in which the migration of an aryl group from carbon to an adjacent anionoid center is catalyzed by hydroxide ion, and in which the same product results as in the acid-catalyzed isomerization.[6]

The outline for the degradation of 2,3,5-triphenylpyrrole (VI), shown in Scheme I, requires further

Scheme II

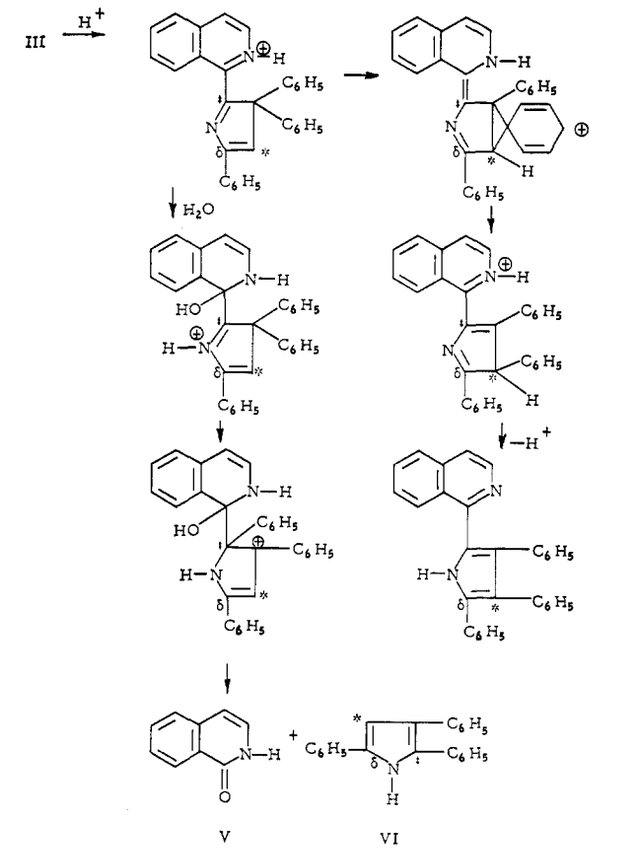
Proposed Mechanism of Condensation Reaction[a]



[a] Original carbonyl C^{14} = δ; original cyano C^{14} = ‡; original methylene C^{14} = *; labels used in three separate experiments.

Scheme III

Mechanisms of Acid-Catalyzed Isomerization and Cleavage

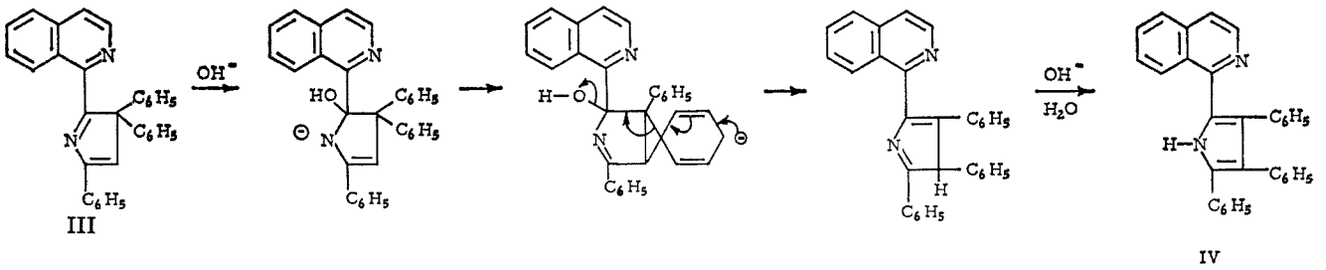


(4) Other mechanisms can be depicted to show the formation of III from I and II. However, the mechanism shown in Scheme II is more compact and probably more plausible than any of the others. Details of the other possible mechanisms are given in the Ph.D. Dissertation of T. T. Yee, University of Massachusetts, Sept 1964.

(5) R. L. Cobb and W. E. McEwen, *J. Am. Chem. Soc.*, **77**, 5042 (1955).

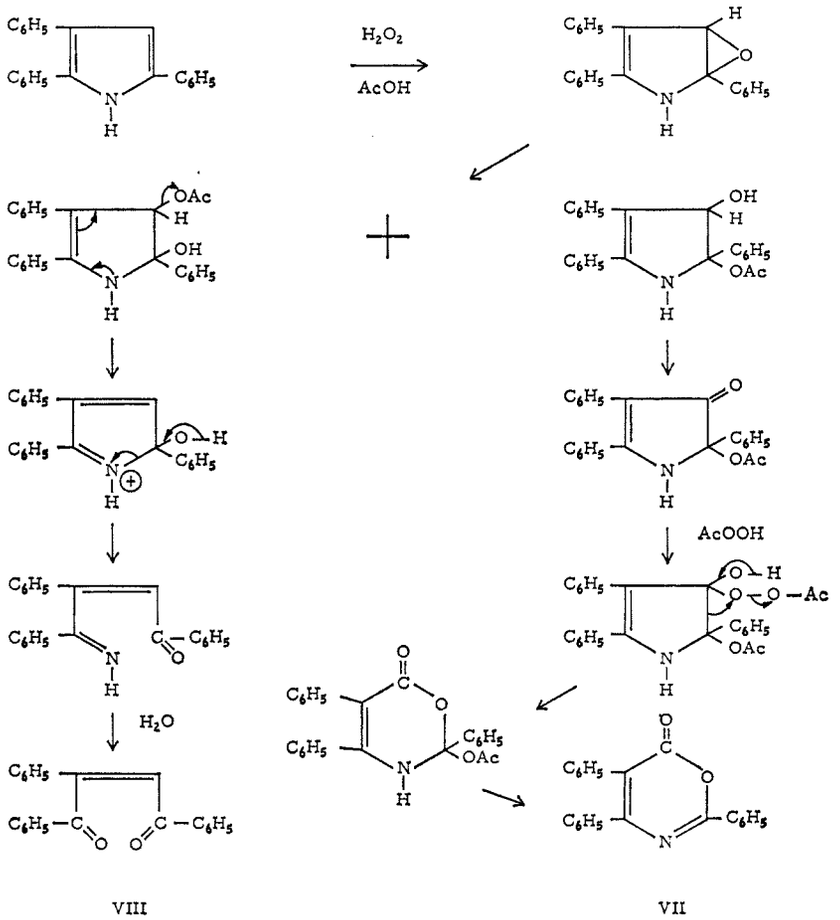
(6) It is significant that the pyrrolenine, analogous to III, obtained by the acid-catalyzed condensation of 2-benzoyl-1,2-dihydroisoquinaldonitrile (I) with 1-phenyl-1-*p*-anisylethylene, gives two isomeric pyrroles, analogous to IV, one predominating in the acid-catalyzed isomerization and the other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

SCHEME IV
MECHANISM OF ISOMERIZATION CATALYZED BY POTASSIUM HYDROXIDE



III IV

SCHEME V
MECHANISM OF DEGRADATION OF 2,3,5-TRIPHENYLPYRROLE



VIII VII

comment. According to Spiro,[7] the oxidation of 2,3,5-triphenylpyrrole (VI) with hydrogen peroxide in glacial acetic acid gives only 6-oxo-2,4,5-triphenyl-1,3-oxazine (VII), whereas the oxidation of an N-alkyl-2,3,5-triphenylpyrrole gives 1,2-dibenzoyl-1-phenylethylene (VIII) and the appropriate β-(N-alkyl-N-benzoylamine)-α,β-diphenylacrylic acid. He suggested that the oxidation of 2,3,5-triphenylpyrrole first gives the product of ring opening, β-(N-benzoylamino)-α,β-diphenylacrylic acid, which then undergoes cyclization to VII.

It has now been found that the oxidation of VI gives not only VII but also VIII. Since the conditions used for the oxidation of VI are similar to those used for the epoxidation of alkenes and in the Baeyer-Villiger reaction, it seems to us that the mechanism suggested in Scheme V is more plausible than that of Spiro. Furthermore, we suggest that the mechanism of acid-catalyzed hydrolysis of VII is that shown in Scheme VI. It should also be mentioned that a specifically labeled 2,3,5-triphenylpyrrole, in a control experiment, was found to undergo the degradation, outlined in Scheme I, in an uncomplicated manner.

(7) V. Spiro, *Gazz. Chim. Ital.*, **85**, 569 (1955).

Experimental Section[8]

2-Benzoyl-1,2-dihydroisoquinaldonitrile (I).—This compound, mp 126–127°, was prepared by the method of Weinstock and Boekelheide.[9]

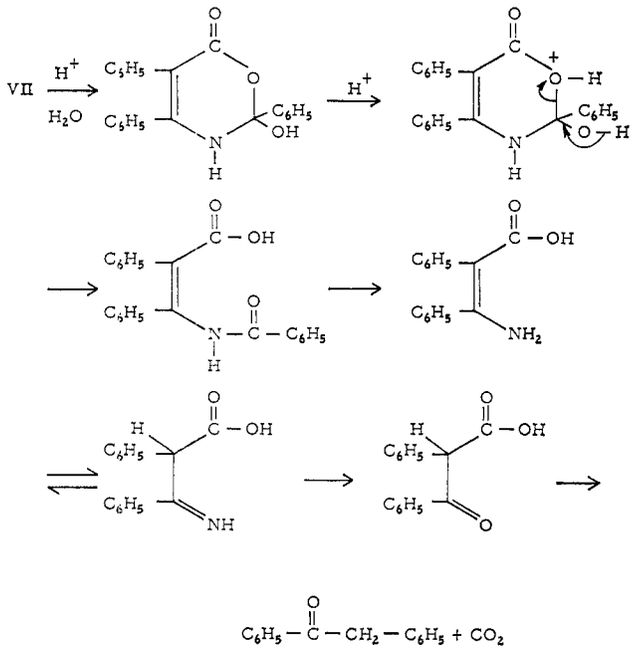
Reaction of 2-Benzoyl-1,2-dihydroisoquinaldonitrile (I) with 1,1-Diphenylethylene (II).—To a solution of 25.0 g (0.096 mole) of 2-benzoyl-1,2-dihydroisoquinaldonitrile (I) and 25.0 g (0.139

(8) Melting points were taken on a Reichert micro heating stage and are uncorrected. Nmr spectra were taken on a Varian A-60 spectrometer by Mr. T. K. Chen. Radioactivity analyses were carried out by Dr. David R. Christman and Mrs. Catherine T. Paul of Brookhaven National Laboratory. Microanalyses were carried out by Schwarzkopf Microanalytical Laboratory, Woodside, N. Y.

(9) J. Weinstock and V. Boekelheide, *Org. Syn.*, **38**, 58 (1959).

Scheme VI

Mechanism of Acid-Catalyzed Cleavage of 6-Oxo-2,4,5-triphenyl-1,3-oxazine



mole) of 1,1-diphenylethylene (II) in 500 ml of pure, anhydrous dioxane was slowly added, with vigorous stirring, 50 ml of cold, concentrated sulfuric acid, and the mixture was stirred at room temperature for 12 hr. The orange precipitate which had formed was collected by filtration, washed with a small amount of ether, and dissolved in 95% ethanol. The ethanol solution was made basic by addition of 5% sodium hydroxide solution and cooled. The precipitate which formed was collected by filtration, washed with water, and then recrystallized from 95% ethanol. There was obtained 2.3 g of isoquinaldamide, mp 168–169°, also in admixture with an authentic sample. The infrared spectrum of the compound, taken in chloroform solution, was identical with that of authentic isoquinaldamide.

The dioxane filtrate was concentrated at reduced pressure and poured into a large excess of ice and water. The orange-yellow precipitate which formed was collected by filtration and dissolved in 500 ml of absolute ethanol. A pale yellow solid slowly crystallized. It was collected by filtration and washed with a small amount of ethanol. The entire 14.0-g quantity of this material was recrystallized from hot chloroform–ethanol mixture to give 10.5 g (26%) of a colorless compound, mp 196–198°, which has been demonstrated (as follows) to be 2-(1-isoquinolyl)-3,3,5-triphenylpyrrolenine (III): ultraviolet λ_{max}^{EtOH} 220 mμ (log ε 4.974), 264 mμ (log ε 4.682); nmr ($CDCl_3$) τ 1.26 (doublet, 8.5 cps), 1.53 (doublet, 6.0 cps), 1.83 (multiplet), 2.00–3.00 (multiplet).

Anal. Calcd for $C_{31}H_{22}N_2$: C, 88.12; H, 5.25; N, 6.63; mol wt, 422.5. Found: C, 88.22; H, 5.23; N, 6.70; mol wt, 403.

When the chloroform–ethanol filtrate was cooled, 2.50 g of a colorless, crystalline compound formed and was collected. Recrystallization of this material from chloroform–ethanol gave 2.00 g of 1,1,3,5,5-pentaphenyl-1,4-pentadiene, mp 170–171°, also in admixture with an authentic sample[10] of the compound. The infrared spectrum of the compound, taken in chloroform solution, was identical with that of the authentic material. The nmr spectrum ($CDCl_3$) showed peaks at τ 2.50–3.00 (multiplet), 3.61 (doublet, 10 cps), and 5.37 (triplet, 19.5 cps). This compound arises by acid-catalyzed condensation of 1,1-diphenylethylene (II) with benzaldehyde, which, in turn, arises by the acid-catalyzed hydrolysis of 2-benzoyl-1,2-dihydroisoquinaldonitrile (I).

The absolute ethanol filtrate was made basic by addition of 5% sodium hydroxide solution and was allowed to stand overnight. A precipitate which formed was collected by filtration and was crystallized several times from chloroform–ethanol to give 10.0 g (24.7%) of a bright yellow compound, mp 264–265°, which has been deduced (see theoretical section) to be 2-(1-isoquinolyl)-3,4,5-triphenylpyrrole (IV): ultraviolet λ_{max}^{EtOH} 216 mμ (log ε 4.932); nmr ($CDCl_3$) τ 1.62 (doublet, 6.0 cps), 1.89 (doublet, 8.5 cps), 2.43 (multiplet), 2.58 (singlet), 2.68 (singlet), 2.98 (singlet).

Anal. Calcd for $C_{31}H_{22}N_2$: C, 88.12; H, 5.25; N, 6.63. Found: C, 87.79; H, 5.47; N, 5.93.

Bisulfate Salt of 2-(1-Isoquinolyl)-3,4,5-triphenylpyrrole (IV).—A mixture of 1.00 g of 2-(1-isoquinolyl)-3,4,5-triphenylpyrrole (IV) and 40 ml of 12 *N* sulfuric acid was heated under reflux for 2 hr. The mixture was cooled, and an orange precipitate which had formed was collected by filtration and washed with water. Crystallization of the material from 95% ethanol afforded 0.61 g of the bisulfate salt, mp 311–313°.

Anal. Calcd for $C_{31}H_{24}N_2O_4S$: C, 71.55; H, 4.51; N, 5.38; S, 6.13. Found: C, 72.00; H, 4.83; N, 5.39; S, 5.24.

Reaction of the Bisulfate Salt of IV with Sodium Hydroxide.—To 20 ml of a 5% solution of sodium hydroxide in 50% ethanol was added 1.00 g of the bisulfate salt of IV, and the mixture was heated until the orange color turned to yellow. The yellow solid was collected by filtration, washed with water, and crystallized from chloroform–ethanol to yield 0.66 g of IV, mp 264–265°.

Isomerization of 2-(1-Isoquinolyl)-3,3,5-triphenylpyrrolenine (III).—A mixture of 1.00 g of III and 40 ml of 12 *N* sulfuric acid was heated under reflux for 2 hr. The resultant orange precipitate was collected by filtration, washed with water, and crystallized from 95% ethanol to give 0.61 g of the bisulfate salt of IV, mp 311–313°. A mixture melting point test with the sample described above showed no depression, and the infrared spectra of the two samples, taken in chloroform solution, were identical.

1,1,3,5,5-Pentaphenyl-1,4-pentadiene.—To a solution of 5.00 g (0.028 mole) of 1,1-diphenylethylene and 1.90 g (0.018 mole) of benzaldehyde in 30 ml of anhydrous dioxane was added 2 ml of concentrated sulfuric acid. The solution turned deep blue and then brown. After the solution had been heated for 6 hr, 10 ml of glacial acetic acid was added. A precipitate which formed was collected by filtration and crystallized from glacial acetic acid to give 5.60 g (91%) of 1,1,3,5,5-pentaphenyl-1,4-pentadiene, mp 172–173°, also in admixture with an authentic[10] sample of the compound.[11]

1-Acetyl-2-(1-isoquinolyl)-3,4,5-triphenylpyrrole.—A solution of 1.50 g of the yellow compound of mp 264–265° and 0.75 g of fused sodium acetate in 40 ml of pure acetic anhydride was heated on the steam bath for several hours. The solution was poured into 200 ml of cold water, and the resulting mixture was allowed to stand at room temperature for a few hours. The precipitate which formed was collected by filtration, washed with water, and crystallized from chloroform–ethanol to give 0.40 g of 1-acetyl-2-(1-isoquinolyl)-3,4,5-triphenylpyrrole, mp 230–231°. The infrared spectrum of this compound, taken in chloroform solution, revealed that the sharp NH peak of IV at about 2.9 μ had disappeared, and a strong amide carbonyl group peak had become apparent.

Hydrolysis and Isomerization of 2-(1-Isoquinolyl)-3,3,5-triphenylpyrrolenine (III).—A suspension of 17.0 g (0.04 mole) of the colorless solid of mp 196–198° in 250 ml of 3.6 *N* sulfuric acid was refluxed for 72 hr. While the mixture was still hot, the aqueous layer was decanted from a red, oily layer and filtered through glass wool to remove the last of the red, oily matter. When the filtrate was cooled, a yellow, crystalline material formed and was collected. After two recrystallizations from 95% ethanol, 1.70 g of colorless 1-hydroxyisoquinoline (V), mp 209–210°, also in admixture with authentic[12] material, was obtained. The infrared spectrum of the compound, taken in chloroform solution, was identical with that of authentic 1-hydroxyisoquinoline.

When the aqueous layer was made basic by addition of 10% sodium hydroxide solution, the odor of ammonia became apparent.

The red, oily layer from the original reaction mixture was treated with 300 ml of 95% ethanol and filtered. There was obtained 2.00 g of a pale yellow solid. This solid was crystallized

(10) G. Wittig and H. Ksoack, *Ann.*, **529**, 167 (1937).

(11) Delbert Glover, Department of Chemistry, University of Massachusetts, independently discovered this same method of preparation of 1,1,3,5,5-pentaphenyl-1,4-pentadiene and prepared the authentic sample by the method of Wittig and Kosack for use in these studies.

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

from chloroform–ethanol and afforded 1.2 g of recovered starting material III, mp 194–196°. Further chilling of the chloroform–ethanol mother liquor gave 0.8 g of an unidentified, pale yellow, crystalline solid, mp 141–142°.

The 95% ethanol filtrate was made basic by addition of 5% sodium hydroxide solution. A bright yellow solid which precipitated was collected by filtration and crystallized from chloroform–ethanol. There was obtained 2.1 g of IV, which was identified by its melting point, a mixture melting point test, and infrared spectral comparisons.

The alkaline mother liquor was acidified once again by addition of sulfuric acid, and then addition of more water caused 6.2 g of a pale yellow solid, mp 125–130°, to precipitate. After several crystallizations by dissolution of the solid in ethanol, digestion with a small amount of sulfuric acid, and addition of water, a needlelike, colorless solid was obtained of mp 138–140°. This was identified as 2,3,5-triphenylpyrrole (VI) by a mixture melting point test with authentic[13] material and by infrared spectral comparisons of chloroform solutions of the solid from the hydrolysate and the authentic 2,3,5-triphenylpyrrole.

Benzoyl-carbonyl-C^{14} Chloride.—Benzoyl-carbonyl-C^{14} chloride was prepared from 127.8 g of benzoic-carbonyl-C^{14} acid (5.28 mμcuries/mg of C) and 192 ml of pure thionyl chloride. The yield was 131.3 g (89%), bp 196–198° (lit.[13] bp 196–198°).

2-Benzoyl-1,2-dihydroisoquinaldonitrile-carbonyl-C^{14}.—To a mixture of 60 g of freshly distilled isoquinoline, 90 g of potassium cyanide, and 600 ml of water was added slowly with stirring 131.3 g of benzoyl-carbonyl-C^{14} chloride (5.28 mμcuries/mg of C). The temperature of the reaction mixture was maintained below room temperature in a cold water bath, and the mixture was stirred for 6 hr. The solid product which formed was collected by filtration and washed successively with 100 ml of water, 150 ml of 3 *N* hydrochloric acid, and again with 100 ml of water. After four recrystallizations from absolute ethanol, 61.0 g (50.5%) of pure 2-benzoyl-1,2-dihydroisoquinaldonitrile-carbonyl-C^{14}, mp 126–127°, was obtained.

Anal. Calcd activity for $C_{17}H_{12}N_2O$: 2.17 mμcuries/mg of C. Found: 2.20 mμcuries/mg of C, 2.15 mμcuries/mg of C.

To a 10.00-g portion of this material was added 40.00 g of inactive 2-benzoyl-1,2-dihydroisoquinaldonitrile, and the recrystallized material was found to have an activity of 0.426 mμcurie/mg of C.

Reaction of 2-Benzoyl-1,2-dihydroisoquinaldonitrile-carbonyl-C^{14} with 1,1-Diphenylethylene.—To a solution of 45.6 g (0.175 mole) of 2-benzoyl-1,2-dihydroisoquinaldonitrile-carbonyl-C^{14} (activity 0.426 mμcurie/mg of C) and 45.6 g (0.253 mole) of 1,1-diphenylethylene in 912 ml of anhydrous dioxane was added dropwise 91.2 ml of concentrated sulfuric acid, with stirring. The mixture was maintained at room temperatue and stirred vigorously for 24 hr. The orange precipitate which resulted, previously identified as isoquinaldamide bisulfate, was removed by filtration. Evaporation of the solvent at reduced pressure gave a deep red, oily residue, which was poured into 1 l. of water. The precipitate which resulted was recrystallized first from absolute ethanol and then from chloroform–ethanol. There was obtained 22.0 g (27%) of 2-(1-isoquinolyl)-3,3,5-triphenylpyrrolenine-5-C^{14}, mp 196–198°.

Anal. Calcd activity for $C_{31}H_{22}N_2$: 0.239 mμcurie/mg of C. Found: 0.242 mμcurie/mg of C, 0.236 mμcurie/mg of C.

The ethanolic filtrate was made basic by addition of 10% sodium hydroxide solution. A bright yellow solid which formed was collected by filtration, washed with water, and crystallized five times from chloroform–ethanol. There was obtained 19.5 g of 2-(1-isoquinolyl)-3,4,5-triphenylpyrrole-5-C^{14}, mp 263–264°.

Anal. Calcd activity for $C_{31}H_{22}N_2$: 0.239 mμcurie/mg of C. Found: 0.242 mμcurie/mg of C.

Hydrolysis of 2-(1-Isoquinolyl)-3,3,5-triphenylpyrrolenine-5-C^{14}.—A suspension of 20.9 g of 2-(1-isoquinolyl)-3,3,5-triphenylpyrrolenine-5-C^{14} (0.239 mμcurie/mg of C) in 300 ml of 3.6 *N* sulfuric acid was refluxed for 70 hr. The hot, aqueous layer was decanted from a red, oily layer, filtered to remove the last of the red oil, and cooled. Yellow crystals which formed were collected by filtration and recrystallized from 95% ethanol to give 0.9 g of 1-hydroxyisoquinoline (V), mp 209–210°.

Anal. Calcd activity for C_9H_7NO: 0.000 mμcurie/mg of C. Found: inactive. The red, oily layer of the reaction mixture became a solid when cooled. This material was mixed with 300 ml of absolute ethanol and warmed on the steam bath. A portion of the solid was insoluble in the alcohol. When collected and crystallized several times from chloroform–ethanol, it was identified as the starting material, mp 196–198°, activity 0.239 mμcurie/mg of C (0.8 g). The chloroform–ethanol mother liquors were combined and allowed to stand in the refrigerator. A yellow solid crystallized and this was purified by chromatography on neutral Woelm alumina (activity I),[14] benzene being used as solvent and eluent. A pale yellow solid, mp 141–142° after recrystallization from absolute ethanol, was obtained (1.0 g). The structure of the compound is unknown to us at the present time.

Anal. Found: C, 90.15, 90.29; H, 5.01, 5.55; N, 5.30, 4.40; activity, 0.316 mμcurie/mg of C, 0.307 mμcurie/mg of C.

When the 300-ml portion of ethanol filtrate was made basic by addition of 5% sodium hydroxide solution, a bright yellow solid precipitated. After five recrystallizations from chloroform–ethanol, 3.1 g of pure 2-(isoquinolyl)-3,4,5-triphenylpyrrole-5-C^{14}, mp 263–264°, was obtained.

Anal. Calcd activity for $C_{31}H_{22}N_2$: 0.239 mμcurie/mg of C. Found: 0.240 mμcurie/mg of C.

The basic aqueous alcoholic filtrate was acidified by addition of a few drops of concentrated sulfuric acid, and the solution was digested for a few minutes. On addition of more water, a bright yellow solid precipitated. Further purification was achieved by dissolution of this substance in ethanol, addition of a few drops of sulfuric acid, digestion, and then addition of water. This procedure gave 6.2 g (42%) of 2,3,5-triphenylpyrrole-5-C^{14} as fine, colorless needles, mp 139–140°.

Anal. Calcd activity for $C_{22}H_{27}N$: 0.337 mμcurie/mg of C. Found: 0.346 mμcurie/mg of C, 0.345 mμcurie/mg of C.

Oxidation of 2,3,5-Triphenylpyrrole-5-C^{14}.—To a solution of 6.20 g of 2,3,5-triphenylpyrrole-5-C^{14} in 200 ml of glacial acetic acid was added slowly 9.6 ml of 30% hydrogen peroxide. The mixture was stirred overnight, and 1.0 g of yellow solid which had formed was collected by filtration. This solid was boiled with a large volume of absolute ethanol, and the hot mixture was filtered, a steam-heated Büchner funnel being used. The filtrate deposited 0.604 g of 6-oxo-2,4,5-triphenyl-1,3-oxazine-2-C^{14} as silken, yellow needles, mp 207–208° (lit.[7] mp 207–208°).

Anal. Calcd activity of $C_{22}H_{15}NO_2$: 0.337 mμcurie/mg of C. Found: 0.341 mμcurie/mg of C.

To 0.6036 g of this material was added 2.7236 g of inactive 6-oxo-2,4,5-triphenyl-1,3-oxazine. The mixture was dissolved in chloroform, the chloroform was removed *in vacuo*, and the residue was recrystallized from absolute ethanol. There was obtained 3.218 g of 6-oxo-2,4,5-triphenyl-1,3-oxazine-2-C^{14} of activity 0.0619 mμcurie/mg of C.

Hydrolysis of 6-Oxo-2,4,5-triphenyl-1,3-oxazine-2-C^{14}.—The hydrolysis of 6-oxo-2,4,5-triphenyl-1,3-oxazine-2-C^{14} was carried out in a specially designed apparatus. To 3.2172 g of the oxazine was added 12 ml of 6 *N* hydrochloric acid and 50 ml of ethanol. The mixture was degassed under vacuum and then left to sit under CO_2-free helium overnight. The mixture was then heated under reflux for 4 hr. The carbon dioxide generated during the reaction was swept through a trap cooled with an ice–salt bath followed by a trap cooled with Dry Ice–$CHCl_3$ slush, and finally collected in a liquid nitrogen cooled trap. The sweeping gas was CO_2-free helium.

Anal. Calcd activity of CO_2: 0.000 mμcurie/mg of C. Found: inactive.

The reaction mixture was concentrated and then extracted with ether. The ether solution was washed with water and dried over anhydrous sodium sulfate. Evaporation of the ether left a yellow oil which was steam distilled. The first portion of the distillate contained ethyl benzoate which was extracted into ether. The ether solution was dried over anhydrous sodium sulfate, the ether was evaporated, and the residue was distilled *in vacuo*. There was obtained 0.72 g (48.6%) of pure ethyl benzoate, which was then saponified with 5 ml of 10% sodium hydroxide solution. The alkaline solution was extracted with ether and acidified, and the precipitate of benzoic acid was collected by filtration. The acid was purified by sublimation, 0.156 g of material of mp 121–122° being collected.

Anal. Calcd activity for $C_7H_6O_2$: 0.195 mμcurie/mg of C. Found: 0.197 mμcurie/mg of C, 0.198 mμcurie/mg of C.

The second portion of steam distillate containing desoxybenzoin and benzoic acid was made alkaline by addition of a few milliliters of 2% sodium hydroxide solution and was ex-

(13) F. Wohler and J. Liebig, *Ann.*, **3**, 262 (1832).

(14) H. Brockmann and H. Schodder, *Ber.*, **74**, 73 (1941).

tracted with ether. Evaporation of the ether solution gave 1.7387 g (90%) of desoxybenzoin, mp 58–60°. The oxime derivative, when analyzed, was found to be inactive.

The alkaline, aqueous solution was concentrated to a small volume and acidified with hydrochloric acid. Extraction with ether and sublimation of the residue of the ether extract afforded 92 mg of benzoic acid, mp 121–122°.

Anal. Calcd activity for $C_7H_6O_2$: 0.195 mμcurie/mg of C. Found: 0.193 mμcurie/mg of C.

2-Benzoyl-1,2-dihydroisoquinaldonitrile-cyano-C^{14}.—This was prepared in the usual manner, but with C^{14}-labeled potassium cyanide as the source of the label. The 2-benzoyl-1,2-dihydroisoquinaldonitrile-cyano-C^{14} produced had an activity of 1.56 mμcuries/mg of C.

Reaction of 2-Benzoyl-1,2-dihydroisoquinaldonitrile-cyano-C^{14} with 1,1-Diphenylethylene.—The reaction was carried out in the manner described previously, and 2-(1-isoquinolyl)-3,3,5-triphenylpyrrolenine-2-C^{14}, mp 196–198°, was obtained in 13% yield.

Anal. Calcd activity for $C_{31}H_{22}N_2$: 0.855 mμcurie/mg of C. Found: 0.856 mμcurie/mg of C.

When the chloroform–ethanol filtrate was cooled, a second solid crystallized. Purification of this material was achieved by additional recrystallizations from chloroform–ethanol, colorless silky needles of 1,1,3,5,5-pentaphenyl-1,4-pentadiene, mp 172.0–172.5°, being obtained. A mixture melting point test with authentic 1,1,3,5,5-pentaphenyl-1,4-pentadiene[15] showed no depression.

Anal. Calcd activity for $C_{35}H_{28}$: 0.000 mμcurie/mg of C. Found: inactive.

2-(1-Isoquinolyl)-3,4,5-triphenylpyrrole-2-C^{14}, mp 264–265°, was isolated from the reaction mixture in 22% yield as described previously for a similar experiment.

Anal. Calcd activity for $C_{31}H_{22}N_2$: 0.855 mμcurie/mg of C. Found: 0.842 mμcurie/mg of C.

Hydrolysis of 2-(1-Isoquinolyl)-3,3,5-triphenylpyrrolenine-2-C^{14}.—A sample of 2-(1-isoquinolyl)-3,3,5-pyrrolenine-2-C^{14} of activity 0.290 mμcurie/mg of C was obtained by dilution of the material of activity 0.856 mμcurie/mg of C with inactive compound in chloroform solution and subsequent recrystallization of the material from chloroform–ethanol.

The acid-catalyzed hydrolysis was carried out as described previously. The aqueous layer, when cooled, afforded 1-hydroxyisoquinoline, mp 209–210°, in 48% yield.

Anal. Calcd activity for C_9H_7O: 0.000 mμcurie/mg of C. Found: inactive.

Treatment of the dark red organic material with ethanol afforded an insoluble, yellow solid. After recrystallization of the material from chloroform–ethanol there was obtained 6.4 g (from 30 g of starting material) of recovered 2-(1-isoquinolyl)-3,3,5-triphenylpyrrolenine-2-C^{14}, mp 196–198°.

Anal. Calcd activity for $C_{31}H_{22}N_2$: 0.290 mμcurie/mg of C. Found: 0.285 mμcurie/mg of C, 0.287 mμcurie/mg of C.

Concentration of the chloroform–ethanol filtrate gave 3.0 g of the compound of unknown structure, mp 141–142°, mentioned previously.

Anal. Found activity: 0.412 mμcurie/mg of C.

When the original alcohol filtrate was made basic by addition of 10% sodium hydroxide solution and then filtered, there was obtained 2-(1-isoquinolyl)-3,4,5-triphenylpyrrole-2-C^{14}, mp 264–265° after recrystallization from chloroform–ethanol.

Anal. Calcd activity for $C_{31}H_{22}N_2$: 0.290 mμcurie/mg of C. Found: 0.300 mμcurie/mg of C, 0.291 mμcurie/mg of C, 0.289 mμcurie/mg of C.

The basic alcohol solution was evaporated nearly to dryness at reduced pressure, water was added, and the mixture was extracted with ether. The ether solution was washed with water and dried over anhydrous sodium sulfate. Evaporation of the ether gave 13.2 g of crude 2,3,5-triphenylpyrrole-2-C^{14}, which, after purification by dissolution in ethanol, digestion with a few drops of sulfuric acid and then addition of water, gave 10.2 g of product, mp 137–139°.

Anal. Calcd activity for $C_{22}H_{17}N$: 0.409 mμcurie/mg of C. Found: 0.384 mμcurie/mg of C.

Degradation of 2,3,5-Triphenylpyrrole-2-C^{14}.—The oxidation of 2,3,5-triphenylpyrrole-2-C^{14} with hydrogen peroxide was carried out as described previously. 6-Oxo-2,4,5-triphenyl-1,3-oxazine-4-C^{14}, mp 207–208°, was obtained.

Anal. Calcd activity for $C_{22}H_{15}NO_2$: 0.409 mμcurie/mg of C. Found: 0.419 mμcurie/mg of C, 0.417 mμcurie/mg of C.

6-Oxo-2,4,5-triphenyl-1,3-oxazine-4-C^{14} of activity 0.148 mμcurie/mg of C was obtained by dilution of the above product with inactive material, and the compound was hydrolyzed as previously described. The ethyl benzoate and benzoic acid produced in the hydrolysis reaction were found to be inactive. A portion of the desoxybenzoin, mp 60–61°, isolated from the reaction mixture was converted to the oxime, mp 98°.

Anal. Calcd activity for $C_{14}H_{13}NO$: 0.231 mμcurie/mg of C. Found: 0.226 mμcurie/mg of C, 0.228 mμcurie/mg of C.

Desoxybenzoin of activity 0.107 mμcurie/mg of C was obtained by dilution of the sample described above with inactive material.

Cleavage of Desoxybenzoin by the Action of Alkali.[16]—A mixture of 3.2648 g (0.0125 mole) of desoxybenzoin (found activity of oxime derivative, 0.105 mμcurie/mg of C), 3.5 g of water, and 8.2 g of potassium hydroxide was refluxed for 4 hr. The toluene and water mixture was distilled and caught in a cup below the condenser. The cup, which served as a separatory funnel, sat over a two-way stopcock positioned so that the aqueous layer could be returned to the vessel used for reflux and the toluene could be passed on to the receiver after the layers had separated. The distillation was done batchwise and in this way the small amount of reaction mixture could be "recycled" until an almost quantitative yield of toluene was obtained.

The toluene was dried over phosphorus pentoxide and then distilled. There was collected a total of 1.2 ml (1.04 g, 68%) of the hydrocarbon.

Anal. Calcd activity for C_7H_8: 0.000 mμcurie/mg of C. Found: inactive.

The residual solid of the original reaction mixture was dissolved in 200 ml of water and extracted with ether to remove any unchanged desoxybenzoin. The aqueous layer was acidified with hydrochloric acid and extracted with ether. The ether solution, dried over anhydrous sodium sulfate, was concentrated to dryness. Sublimation of the residue gave 1.5741 g of benzoic acid, mp 121–122°.

Anal. Calcd activity for $C_7H_6O_2$: 0.210 mμcurie/mg of C. Found: 0.210 mμcurie/mg of C, 0.210 mμcurie/mg of C.

Methyl-C^{14}-triphenylphosphonium Bromide.[17]—A thick-walled tube, equipped with a narrow constriction and a standard taper joint, containing 30 g (0.12 mole) of triphenylphosphine and 25 ml of anhydrous benzene, was connected to a high-vacuum system and evacuated, and 16.1 g (0.17 mole) of methyl-C^{14} bromide was distilled into the tube from a storage vessel. The tube was sealed, disconnected from the vacuum system, allowed to stand at room temperature for 48 hr, and then opened. The product was collected by filtration with the aid of hot, anhydrous benzene. After the product had been dried over phosphorus pentoxide at 100° *in vacuo* there was obtained 40.8 g (98%) of methyl-C^{14}-triphenylphosphonium bromide, mp 229–231° (lit.[18] mp 229–232°).

1,1-Diphenylethylene-2-C^{14}.—A suspension of 40.8 g (0.11 mole) of methyl-C^{14}-triphenylphosphonium bromide in 250 ml of anhydrous ether was maintained under a nitrogen atmosphere while 61 ml of a 2.0 *M* solution of phenyllithium in benzene–ether was added with the aid of a syringe. The mixture turned yellow and then deep orange as the phenyllithium was added. After the mixture had been stirred for 4 hr (until all of the phosphonium bromide disappeared), there was added a solution of 20.3 g of benzophenone in 100 ml of anhydrous ether. The resulting mixture was stirred for 4 hr and refluxed overnight. A precipitate which had formed was removed by filtration, and the filtrate was washed with water. The ether solution was dried over anhydrous calcium chloride and the ether was distilled *in vacuo*. There was obtained 18.0 g (88%) of 1,1-diphenylethylene-2-C^{14}. To this material was added 75 g of nonlabeled 1,1-diphenylethylene. The liquid was stirred thoroughly, then distilled. There was obtained 93 g of 1,1-diphenylethylene-2-C^{14}: bp 82° (0.5 mm), $n^{21.5}$D 1.6070 [lit.[18] bp 98–102° (1.5 mm), n^{20}D 1.6085].

Anal. Calcd activity for $C_{14}H_{12}$: 3.36 mμcuries/mg of C. Found: 3.10 mμcuries/mg of C.

(15) This compound, which arises by an acid-catalyzed condensation of 1,1-diphenylethylene with benzaldehyde, will be discussed in more detail in a subsequent paper.

(16) E. Knoevenagel and J. Arndts, *Ber.*, **35**, 1983 (1902).

(17) G. Wittig and M. Rieber, *Ann.*, **562**, 177 (1949).

(18) G. Wittig and G. Geissler, *ibid.*, **580**, 44 (1953).

Reaction of 2-Benzoyl-1,2-dihydroisoquinaldonitrile with 1,1-Diphenylethylene-2-C^{14}.—The reaction was carried out as described previously, and 2-(1-isoquinolyl-3,3,5-triphenylpyrrolenine-4-C^{14}, mp 196–198°, was obtained in 14% yield.

Anal. Calcd activity for $C_{31}H_{22}N_2$: 1.40 mμcuries/mg of C. Found: 1.38 mμcuries/mg of C, 1.42 mμcuries/mg of C.

1,1,3,5,5-Pentaphenyl-1,4-pentadiene-2,4-C^{14}, mp 169–170°, was obtained in very low yield.

Anal. Calcd activity for $C_{35}H_{28}$: 2.48 mμcuries/mg of C. Found: 2.62 mμcuries/mg of C, 2.64 mμcuries/mg of C.

2-(1-Isoquinolyl)-3,4,5-triphenylpyrrole-4-C^{14}, mp 263–264°, was obtained in 28% yield.

Anal. Calcd activity for $C_{31}H_{22}N_2$: 1.40 mμcuries/mg of C. Found: 1.36 mμcuries/mg of C.

Degradation of 2-(1-Isoquinolyl)-3,3,5-triphenylpyrrolenine-4-C^{14}.—The labeled material described above was diluted with inactive 2-(1-isoquinolyl)-3,3,5-triphenylpyrrolenine, and the resulting material had an activity of 0.334 mμcurie/mg of C.

A 40.0-g batch of the pyrrolenine was hydrolyzed in the usual way, and 7.8 g (57%) of inactive 1-hydroxyisoquinoline, mp 209–210°, was obtained from the aqueous phase.

The usual treatment of the red, oily layer afforded 0.7 g of starting material (found activity 0.336, 0.340 mμcurie/mg of C), 2.1 g of the solid, mp 141–142°, of unknown structure (found activity 0.438 mμcurie/mg of C, 0.440 mμcurie/mg of C), 7.2 g of 2-(1-isoquinolyl)-3,4,5-triphenylpyrrole-4-C^{14} (found activity 0.320 mμcurie/mg of C), and 17.1 g (60.5%) of 2,3,5-triphenylpyrrole-4-C^{14}, mp 139–140°.

Anal. Calcd activity for $C_{22}H_{17}N$: 0.473 mμcurie/mg of C. Found: 0.477 mμcurie/mg of C.

A 17.1-g (0.058 mole) sample of the above compound was oxidized with 30 ml of 30% hydrogen peroxide in 600 ml of acetic acid as described previously, and there was obtained 1.73 g of 6-oxo-2,4,5-triphenyl-1,3-oxazine-6-C^{14}, mp 207–208°.

Anal. Calcd activity for $C_{22}H_{15}NO_2$: 0.473 mμcurie/mg of C. Found: 0.474 mμcurie/mg of C, 0.471 mμcurie/mg of C, 0.473 mμcurie/mg of C.

A 1.7312-g portion of the active compound was added to 6.1970 g of pure, inactive 6-oxo-2,4,5-triphenyl-1,3-oxazine, and the material was dissolved in hot chloroform. After removal of the chloroform by distillation at reduced pressure, a portion (about 1.2 g) of the residue was recrystallized from 1 l. of absolute ethanol. The resulting 6-oxo-2,4,5-triphenyl-1,3-oxazine-6-C^{14} had a mp of 207–208°.

Anal. Calcd activity for $C_{22}H_{15}NO_2$: 0.103 mμcurie/mg of C. Found: 0.102 mμcurie/mg of C, 0.102 mμcurie/mg of C.

A mixture of 1.0904 g of the above compound, 4 ml of 6 *N* hydrochloric acid, and 15 ml of ethanol was hydrolyzed in a manner analogous to that described under hydrolysis of 6-oxa-2,4,5-triphenyl-1,3-oxazine-2-C^{14} (*vide supra*). The CO_2 was collected and assayed.

Anal. Calcd activity for CO_2: 2.24 mμcuries/mg of C. Found: 2.23 mμcuries/mg of C, 2.22 mμcuries/mg of C,

Ethyl benzoate, benzoic acid, and desoxybenzoin were isolated as described in previous similar experiments, and all were found to be inactive.

A Control Experiment. A. 1,2,4-Triphenyl-1,4-butanedione-4-C^{14}.—A mixture of 97.9 g (0.82 mole) of acetophenone-carbonyl-C^{14}, 169 g (0.80 mole) of benzoin, 21.8 g of potassium cyanide, 436 ml of 95% ethanol, and 75 ml of water was heated under reflux for 12 hr. A heavy yellow oil which formed was collected, washed with water, and spread over a porous clay plate to dry. The resulting yellow solid was crushed and boiled with ethanol and the hot mixture was filtered to remove an insoluble substance. From the filtrate there was obtained 1,2,4-triphenyl-1,4-butanedione-4-C^{14}, mp 126–128°, 97.0 g (39%), after several recrystallizations from acetic acid and ethanol.

Anal. Calcd activity for $C_{22}H_{18}O_2$: 0.358 mμcurie/mg of C. Found: 0.352 mμcurie/mg of C.

B. 2,3,5-Triphenylpyrrole-5-C^{14}.—A mixture of 40 g (0.135 mole) of 1,2,4-triphenyl-1,4-butanedione-4-C^{14}, 100 g of ammonium acetate, and 500 ml of glacial actic acid was refluxed for 24 hr. The reaction mixture was poured into a beaker containing 500 ml of water and allowed to cool. After collection of the resulting solid by filtration and recrystallization from ethanol–water, there was obtained 37.4 g of 2,3,5-triphenylpyrrole-5-C^{14}, mp 139–140°.

Anal. Calcd acitivity for $C_{22}H_{18}N$: 0.358 mμcurie/mg of C. Found: 0.360 mμcurie/mg of C.

C. 6-Oxo-2,4,5-triphenyl-1,3-oxazine-2-C^{14}.—Oxidation of 12.0 g (0.04 mole) of 2,3,5-triphenylpyrrole-5-C^{14} with hydrogen peroxide in acetic acid as described previously for similar experiments gave 1.4 g (9%) of 6-oxo-2,4,5-triphenyl-1,3-oxazine-2-C^{14}, mp 207–208°.

Anal. Calcd activity for $C_{22}H_{15}NO_2$: 0.358 mμcurie/mg of C. Found: 0.324 mμcurie/mg of C, 0.369 mμcurie/mg of C, 0.356 mμcurie/mg of C.

D. Hydrolysis of 6-Oxo-2,4,5-triphenyl-1,2-oxazine-2-C^{14}.—This was carried out in the same manner as described previously for similar experiments. No activity was found in the carbon dioxide or desoxybenzoin (oxime derivative). The theoretical activity was found in the benzoic acid (and ethyl benzoate). The preparation of 1,2,4-triphenyl-1,4-butanedione-4-C^{14} and of 2,3,5-triphenylpyrrole-5-C^{14} was based on the work of Smith.[19] The preparation of 6-oxo-2,4,5-triphenyl-1,3-oxazine-2-C^{14} was based on the work of Spiro.[7]

Alkali Fusion of 2-(1-Isoquinolyl)-3,4,5-triphenylpyrrolenine (III).—One gram of III was added to a melt of 5 drops of water and 10 g of potassium hydroxide contained in a nickel crucible, and the mixture was heated at 250° for 10 min. The cooled mixture was treated with 100 ml of water and extracted with ether. Evaporation of the ether solution gave 0.52 g (52%) of 2-(1-isoquinolyl)-3,4,5-triphenylpyrrole (IV), mp 262.5–263.5° after several recrystallizations from chloroform–ethanol. A mixture melting point with the sample of IV described earlier showed no depression, and the infrared spectra of the two samples, taken in chloroform solution, were identical.

Perchlorate Salt of 2-Benzoyl-1,2-dihydroisoquinaldonitrile.—This salt was prepared by the method of Elliott and Leflore.[20] Its melting point was 205–206° (lit.[20] mp 204–205°).

Reaction of the Perchlorate Salt of 2-Benzoyl-1,2-dihydroisoquinaldonitrile with 1,1-Diphenylethylene.—To a suspension of 5.0 g (0.0014 mole) of the perchlorate salt of 2-benzoyl-1,2-dihydroisoquinaldonitrile in a solution of 3.5 g (0.0019 mole) of 1,1-diphenylethylene in 100 ml of dioxane was added 3 ml of concentrated sulfuric acid. After having been stirred for 4 days, the reaction mixture turned dark red. When filtered, a solid residue remained which was extracted with hot ethanol. The ethanol-insoluble material consisted of a small amount of recovered perchlorate salt of I. Addition of 5% sodium hydroxide solution to the alcohol filtrate caused 1.1 g of isoquinaldamide, mp 168–169°, to precipitate. The original dioxane filtrate gave a solid residue when the solvent was removed *in vacuo*. This was washed with water and crystallized first from ethanol and then from chloroform–ethanol to give 0.5 g (8.4%) of 2-(1-isoquinolyl)-3,3,5-triphenylpyrrolenine (III), mp 196–198°. The alcohol filtrate from the first crystallization of this compound was made basic by addition of 5% sodium hydroxide solution. A solid which formed was collected by filtration and recrystallized from chloroform–ethanol. There was obtained 0.4 g (6.7%) of 2-(1-isoquinolyl)-3,4,5-triphenylpyrrole (IV), mp 264–265°.

Registry No.—2-Benzoyl-1,2-dihydroisoquinaldonitrile-carbonyl-C^{14}, 10425-45-3; 2-benzoyl-1,2-dihydroisoquinaldonitrile-cyano-C^{14}, 4096-94-0; 1,1-diphenylethylene, 530-48-3; 1,1-diphenylethylene-2-C^{14}, 10425-47-5; III, 10425-48-6; 2-(1-isoquinolyl)-3,3,5-triphenylpyrrolenine-2-C^{14}, 10425-49-7; 2-(1-isoquinolyl)-3,3,5-triphenylpyrrolenine-5-C^{14}, 10425-51-1; IV, 10425-52-2; bisulfate salt of IV, 10425-53-3; 1-acetyl-2-(1-isoquinolyl)-3,4,5-triphenylpyrrole, 10425-54-4; 2-(1-isoquinolyl)-3,4,5-triphenylpyrrole-2-C^{14}, 10425-55-5; 2-(1-isoquinolyl)-3,4,5-triphenylpyrrole-4-C^{14}, 10425-56-6; 2-(1-isoquinolyl)-3,4,5-triphenylpyrrole-5-C^{14}, 10425-57-7; V, 491-30-5; 2,3,5-triphenylpyrrole-2-C^{14}, 10425-59-9; 2,3,5-triphenylpyrrole-4-C^{14}, 10425-60-2; 2,3,5-triphenylpyrrole-5-C^{14}, 10437-01-1; 6-oxo-2,4,5-triphenyl-1,3-oxazine-2-C^{14}, 10425-61-3; 6-oxo-2,4,5-triphenyl-1,3-oxazine-4-C^{14}, 10425-62-4; 6-oxo-2,4,5-triphenyl-1,3-oxazine-6-C^{14}, 10425-63-5; benzoic acid, 65-85-0; desoxybenzoin, 451-40-1; desoxybenzoin oxime, 952-06-7; benzoylcarbonyl-C^{14} chloride, 10425-

(19) A. Smith, *J. Chem. Soc.*, **57**, 1645 (1890).

(20) I. W. Elliott and J. O. Leflore, *J. Org. Chem.*, **28**, 3181 (1963).

64-6; methyl-C^{14}-triphenylphosphonium bromide, 1560-53-8; 1,1,3,5,5-pentaphenyl-1,4-pentadiene-2,4-C^{14}, 10425-66-8; 1,2,4-triphenyl-1,4-butanedione-4-C^{14}, 10425-679; 2-(1-isoquinolyl)-3,3,5-triphenylpyrrolenine-4-C^{14}, 10425-50-0.

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Linear Free-Energy Relations for 5- (or 6-) Substituted Benzimidazoles

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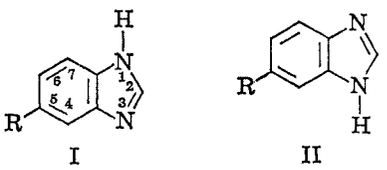
Aqueous pK_a^+ values at 25° have been measured for a series (H, CH_3, F, Cl, Br, CF_3, NO_2) of tautomeric 5- (or 6-) substituted benzimidazoles. ΔpK_a^+ values satisfy the Taft equation $\Delta pK_a^+ = (2.61 \pm 0.10)\sigma_I + (2.10 \pm 0.13)\sigma_R^0 + 0.05\ (\pm 0.04)$ with $s = 0.06$ and $r = 0.999$. Application of the 6-quinoline bicyclic substituent constants of Jaffé and Jones gives an excellent correlation. $\Delta pK_a^+ = (5.62 \pm 0.07)\sigma^{6-1} - 0.01(\pm 0.01)$ with $s = 0.02$ and $r = 1.000$. The correlations show that the relative weighing of inductive (σ_I) and polar resonance (σ_R^0) effects and their ease of transmission in 5- (or 6-) substituted benzimidazoles are nearly the same as in 6-quinolines. Substituent effects for the title compounds are found to be intermediate in composition between those which may be correlated by σ_m and σ_p^0. The excellent correlations and their insensitivity to tautomerism results from the tautomers being nearly equivalent in thermodynamic stability.

Rabiger and Joullié[2] attempted a classical Hammett correlation[3] of the acidity constants of a series of 5- (or 6-) halogenated benzimidazoles. They reported that the correlation was unsuccessful and presumed that the failure was due to tautomerism between forms I and II.



I II

In this paper we reexamine the applicability of the Hammett equation to the system in question using a wider range of compounds and a more basic and varied approach. Our major aims were to obtain increased insight into substituent effects on 5- (or 6-) substituted benzimidazoles and to clarify the role of tautomerism as it relates to linear relationships for this heterobicyclic system.

Results and Discussion

Acidity Constants.—Thermodynamic acidity constants determined spectrophotometrically in this study and that of benzimidazole determined earlier by the same method in this laboratory[4] are given in Table I. Our results are in good agreement with thermodynamic values reported for the unsubstituted and 5- (or 6-) methyl compound. The spread of the other values found in Table I indicates the desirability of obtaining a set of values from one laboratory by one method, whereby procedural or systematic errors may to some extent cancel. For 5- (or 6-) nitrobenzimidazole one finds literature values ranging from 3.5 to 4.5. Procedural or systematic errors cannot account for this large range. We judge that the high value of 4.5 involves gross error.

TABLE I

THERMODYNAMIC ACIDITY CONSTANTS OF THE CATIONS OF 5- (OR 6-) SUBSTITUTED BENZIMIDAZOLES IN WATER AT 25 ± 0.2°

Substituent	Registry no.	pK_a^+	n^a	Mean dev	Scatter[b]	Lit. pK_a^+[c]
NH_2	934-22-5		...	...	...	6.06[d]
CH_3	614-97-1	5.78	5	0.02	0.04	5.78[e]
H	51-17-2	5.55[g]	3	0.03	0.04	5.44[e]
						5.52[d,l]
						5.532[f]
F	1977-72-6	4.92	3	0.03	0.04	5.11[h]
						5.21[i]
Cl	4887-82-5	4.70	3	0.01	0.01	4.98[i]
Br	4887-88-1	4.66	3	0.01	0.02	4.89[i]
CF_3	326-55-6	4.22	6	0.01	0.05	...
NO_2	2672-29-9	3.42	3	0.02	0.02	3.48[j]
						3.80[k]
						4.50[l]

[a] Number of determinations. [b] Maximum deviation from mean value. [c] Values with superscripts *d*, *e*, and *f* are thermodynamic values obtained by extrapolation to 0 ionic strength or from the simple Debye–Hückel expression for solutions of low ionic strength, others are uncorrected. [d] By titration of hydrochloride: M. T. Davies, P. Mamalis, V. Petrow, and B. Sturgeon, *J. Pharm. Pharmacol.*, **3**, 420 (1951). [e] By titration of base; see reference in *d*. [f] G. Schwarzenbach and K. Lutz, *Helv. Chim. Acta*, **23**, 1162 (1940). [g] Reference 4. [h] In water: E. C. Fisher and M. M. Joullié, *J. Org. Chem.*, **23**, 1944 (1958). [i] Reference 2; 5:95 ethanol–water (0.1 *M* in NaCl) at 30 ± 5°. [j] J. H. Ridd and B. V. Smith, *J. Chem. Soc.*, 1363 (1960). [k] J. L. Rabinowitz and E. C. Wagner, *J. Am. Chem. Soc.*, **73**, 3030 (1951). [l] D. J. Rabiger and M. M. Joullié, *J. Org. Chem.*, **29**, 476 (1964). Same conditions as under *i*.

Data Used in Correlations.—Column 4 of Table II shows aqueous ΔpK^+ values ($\Delta pK_a^+ = pK_H - pK_R$) used in the correlations. All but the amino ΔpK^+ value were obtained in this laboratory. A reported[5] unfavorable difference between the spectra of the neutral molecule and the monocation discouraged us from obtaining the amino value. Also shown in Table II are 50:50 alcohol/water ΔpK_a^+ values for 1-methyl-

(1) Work performed as National Science Foundation Undergraduate Research Participants and in partial fulfillment of the requirements for the B.S. degree in chemistry.

(2) D. J. Rabiger and M. M. Joullié, *J. Chem. Soc.*, 915 (1964).

(3) (a) L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, p 184; (b) H. H. Jaffé, *Chem. Rev.*, **53**, 191 (1953).

(4) H. Walba and R. W. Isensee, *J. Org. Chem.*, **26**, 2789 (1961).

(5) G. Leandri, A. Mangini, F. Montanari, and R. Passerini, *Gazz. Chim. Ital.*, **85**, 769 (1955).