

Fig. 4.—(A) 8.5 mg. of ascorbic acid in 2 ml. of formaldehyde (1.41 *M* in *M* acetate buffer, *pH* 5.4), 40° (B) same except 0.71 *M* formaldehyde; (C) same except 0.18 *M* formaldehyde.

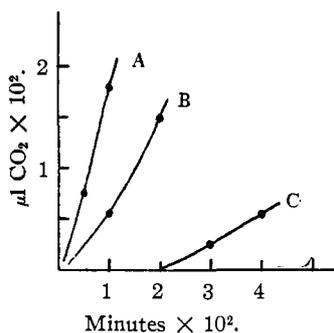


Fig. 5.—(A) 8.5 mg. of ascorbic acid in 2 ml. of formaldehyde (5.85% in *M* acetate buffer, *pH* 5.4), 40°; (B) same except 32°; (C) same except 25°.

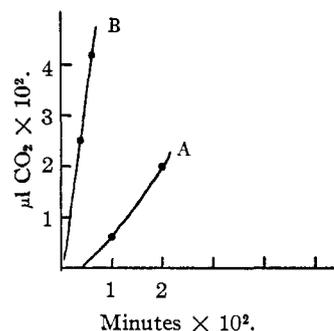


Fig. 6.—(A) 8.5 mg. of  $\alpha$ -hydroxytetrone acid in 2 ml. of formaldehyde (5.85% in *M* acetate buffer, *pH* 5.4): 25.8° (B) same except 40°.

the phenomena described in this paper may lead to a quantitative method for determining ascorbic acid which is more specific than any yet devised.

### Summary

1. It has been shown that ascorbic acid and  $\alpha$ -hydroxytetrone acid react with formaldehyde and that under certain conditions one of the products of the reaction is carbon dioxide.

2. The rate of carbon dioxide formation in re-

action mixtures of ascorbic acid and formaldehyde has been studied in relation to *pH*, temperature and concentration of reactants.

3. A similar study has been made on an  $\alpha$ -hydroxytetrone acid-formaldehyde system.

4. The present work has been discussed in relation to previous studies which employed diminution of the reducing action of enediols as a criterion of reaction.

EUGENE, OREGON

RECEIVED MAY 31, 1947

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF PARKE, DAVIS & Co.]

## The Synthesis of 1-R-5-R'-5-Phenylhydantoin

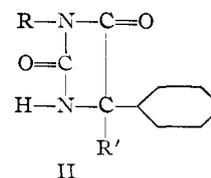
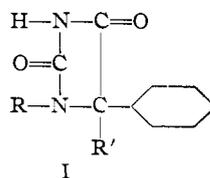
BY LOREN M. LONG, C. A. MILLER AND H. D. TROUTMAN

The discovery by Putnam and Merritt<sup>1</sup> of the efficacy of Dilantin<sup>2</sup> in the treatment of epilepsy has resulted in the synthesis and subsequent testing of a large number of related compounds. The activity of many of these against electrically induced convulsions has been reported by Merritt and Putnam.<sup>3</sup> On examining this report one notes that the majority of the hydantoins which have been studied are those substituted in the 5-position only. It was logical, then, to extend the types of hydantoins studied to include those containing an N-substituent.

Since a search of the literature revealed that an appreciable number of 3,5-substituted hydantoins have been prepared,<sup>4</sup> it seemed that the synthesis of hydantoins substituted in the 1- and 5-positions offered a better opportunity of finding new and useful anticonvulsants. Indeed, in reference

to 3-substituted hydantoins, a derivative of 5-ethyl-5-phenylhydantoin (nirvanol) has been introduced recently<sup>5</sup> as being effective in reducing the number of convulsions exhibited by epileptic patients. However, the use of this drug, 3-methyl-5-ethyl-5-phenylhydantoin, may result in rash formation similar to that caused by nirvanol.

Another possible advantage of compounds unsubstituted in the 3-position, as in structure (I), was thought to be the retention of dilute alkali solubility in contrast to the dilute alkali insolubility of compounds of structure (II). Thus, in many



cases the sodium salts of cyclic ureides are preferred over the free compounds, *i. e.*, Dilantin<sup>2</sup> and phenobarbital.

A few derivatives of type (I) have been prepared

(5) Lascalzo. *J. Nerv. Ment. Dis.*, **101**, 537 (1945).

(1) Putnam and Merritt, *Science*, **85**, 525 (1937).

(2) Dilantin—registered trade-mark of Parke, Davis & Co. for 5,5-diphenylhydantoin.

(3) Merritt and Putnam, *Epilepsia*, **3**, 51 (1945).

(4) British Patents 430,255, 430,282, 430,283, 430,473; French Patent 769,667; German Patent 611,057; Swiss Patents 166,004, 168,947, 168,948, 169,509, 171,982, 176,827, 177,411, 179,255, 179,690, 179,692.

TABLE I  
 1-R-5-R'-5-PHENYLHYDANTOINS

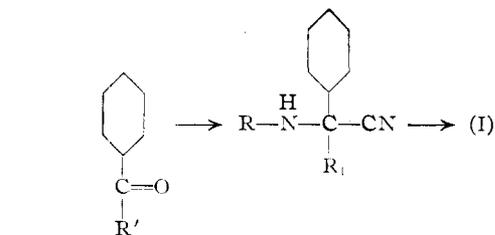
R	R'	M. p., °C.	Yield, % <sup>a</sup>	Formula	Analyses, % <sup>b</sup>			
					Carbon		Hydrogen	
					Calcd.	Found	Calcd.	Found
Methyl <sup>c</sup>	H	177-179	59	C <sub>10</sub> H <sub>10</sub> N <sub>2</sub> O <sub>2</sub>	63.14	63.23	5.30	5.36
Methyl <sup>d</sup>	Methyl	186-188	53	C <sub>11</sub> H <sub>12</sub> N <sub>2</sub> O <sub>2</sub>	64.69	64.78	5.93	6.00
Methyl <sup>e</sup>	Ethyl	210	47	C <sub>12</sub> H <sub>14</sub> N <sub>2</sub> O <sub>2</sub>	66.03	66.13	6.47	6.14
Methyl	<i>n</i> -Propyl	235	49	C <sub>13</sub> H <sub>16</sub> N <sub>2</sub> O <sub>2</sub>	67.21	67.15	6.94	6.74
Methyl	Phenyl	224-226	14	C <sub>16</sub> H <sub>14</sub> N <sub>2</sub> O <sub>2</sub>	72.16	72.27	5.30	5.29
Ethyl	H	109-111	61	C <sub>11</sub> H <sub>12</sub> N <sub>2</sub> O <sub>2</sub>	64.69	64.78	5.93	5.81
Ethyl	Methyl	176-177	43	C <sub>12</sub> H <sub>14</sub> N <sub>2</sub> O <sub>2</sub>	66.03	66.08	6.47	6.40
Ethyl	Ethyl	164-166	45	C <sub>13</sub> H <sub>16</sub> N <sub>2</sub> O <sub>2</sub>	67.21	67.44	6.94	6.83
Ethyl	<i>n</i> -Propyl	210	37	C <sub>14</sub> H <sub>18</sub> N <sub>2</sub> O <sub>2</sub>	68.27	68.85	7.37	7.10
Ethyl	Phenyl	185-187	20	C <sub>17</sub> H <sub>16</sub> N <sub>2</sub> O <sub>2</sub>	72.84	72.60	5.75	5.70
<i>n</i> -Propyl	H	108-110	62	C <sub>12</sub> H <sub>14</sub> N <sub>2</sub> O <sub>2</sub>	66.03	66.19	6.47	6.44
<i>n</i> -Propyl	Methyl	133-135	57	C <sub>13</sub> H <sub>16</sub> N <sub>2</sub> O <sub>2</sub>	67.21	67.27	6.94	6.93
<i>n</i> -Propyl	Ethyl	127	52	C <sub>14</sub> H <sub>18</sub> N <sub>2</sub> O <sub>2</sub>	68.27	68.49	7.37	7.05
<i>n</i> -Propyl	<i>n</i> -Propyl	135	45	C <sub>15</sub> H <sub>20</sub> N <sub>2</sub> O <sub>2</sub>	69.20	69.23	7.74	7.77
<i>i</i> -Propyl	H	173-174	35	C <sub>12</sub> H <sub>14</sub> N <sub>2</sub> O <sub>2</sub>	66.03	66.33	6.47	6.55
Allyl	H	94-96	65	C <sub>12</sub> H <sub>12</sub> N <sub>2</sub> O <sub>2</sub>	66.65	66.95	5.60	5.35
Allyl	Methyl	98-99	40	C <sub>13</sub> H <sub>14</sub> N <sub>2</sub> O <sub>2</sub>	67.80	67.56	6.13	6.16
Allyl	Ethyl	117-119	48	C <sub>14</sub> H <sub>16</sub> N <sub>2</sub> O <sub>2</sub>	68.83	68.94	6.60	6.66
Allyl	<i>n</i> -Propyl	137	42	C <sub>15</sub> H <sub>18</sub> N <sub>2</sub> O <sub>2</sub>	69.74	69.91	7.02	6.80
<i>n</i> -Butyl	H	141-142	67	C <sub>13</sub> H <sub>16</sub> N <sub>2</sub> O <sub>2</sub>	67.21	67.63	6.94	6.96
<i>n</i> -Butyl	Methyl	100-101	50	C <sub>14</sub> H <sub>18</sub> N <sub>2</sub> O <sub>2</sub>	68.27	68.39	7.37	7.32
<i>n</i> -Butyl	Ethyl	149-152	45	C <sub>15</sub> H <sub>20</sub> N <sub>2</sub> O <sub>2</sub>	69.20	69.02	7.74	7.70
<i>n</i> -Butyl	<i>n</i> -Propyl	98-100	51	C <sub>16</sub> H <sub>22</sub> N <sub>2</sub> O <sub>2</sub>	70.04	70.37	8.08	8.06
Cyclohexyl	H	190-193	32	C <sub>13</sub> H <sub>18</sub> N <sub>2</sub> O <sub>2</sub>	69.74	69.85	7.02	6.95
<i>n</i> -Heptyl	H	103-105	51	C <sub>16</sub> H <sub>22</sub> N <sub>2</sub> O <sub>2</sub>	70.04	70.35	8.08	8.01
<i>n</i> -Heptyl	Methyl	94-95	43	C <sub>17</sub> H <sub>24</sub> N <sub>2</sub> O <sub>2</sub>	70.80	70.57	8.39	8.42
<i>n</i> -Heptyl	Ethyl	118-119	45	C <sub>18</sub> H <sub>26</sub> N <sub>2</sub> O <sub>2</sub>	71.46	71.53	8.70	8.78
$\beta$ -Phenethyl	H	173-175	65	C <sub>17</sub> H <sub>16</sub> N <sub>2</sub> O <sub>2</sub>	72.84	72.84	5.75	5.89
$\alpha$ -Methyl- $\beta$ -phenethyl	H	149-152	64	C <sub>19</sub> H <sub>18</sub> N <sub>2</sub> O <sub>2</sub>	73.45	73.34	6.16	5.86
$\beta$ -Hydroxyethyl	H	155-157	52	C <sub>11</sub> H <sub>12</sub> N <sub>2</sub> O <sub>3</sub>	59.99	60.00	5.49	5.40
$\beta$ -Hydroxyethyl	Methyl	115	43	C <sub>12</sub> H <sub>14</sub> N <sub>2</sub> O <sub>3</sub>	61.52	61.43	6.02	6.07
$\beta$ -Hydroxyethyl	Ethyl	102	44	C <sub>13</sub> H <sub>16</sub> N <sub>2</sub> O <sub>3</sub>	62.88	62.61	6.50	6.57
$\alpha$ -Dimethyl- $\beta$ -hydroxyethyl	H	229	33	C <sub>13</sub> H <sub>16</sub> N <sub>2</sub> O <sub>3</sub>	62.88	62.51	6.50	6.43
$\beta$ -Bromoethyl	H	131-133	70	C <sub>11</sub> H <sub>11</sub> BrN <sub>2</sub> O <sub>2</sub>	46.66	46.81	3.92	3.78

<sup>a</sup> Based on the amount of aldehyde or ketone employed. by Arthur W. Spang. <sup>c</sup> Gabriel, *Ann.*, **350**, 124 (1906). Patent 769,667; Swiss Patent 169,509.

<sup>b</sup> The analytical data reported in this paper were determined by Arthur W. Spang. <sup>d</sup> Swiss Patent 179,692. <sup>e</sup> German Patent 611,057; French Patent 769,667; Swiss Patent 169,509.

previously. The emphasis, however, has been on those representing 1-substituted nirvanol,<sup>4</sup> although an attempt was made to produce effective germicides by synthesizing 1,5-dihydroxyphenylhydantoin.<sup>6</sup>

Although the details of the procedure employed in the synthesis of the compounds listed in Table I were varied to improve yields, the general method was essentially the same throughout and may be represented by the following scheme.



(6) Coghill, *THIS JOURNAL*, **47**, 216 (1925).

This procedure is similar to that employed by other investigators<sup>4,6</sup> and is necessary since on alkylating 5,5-substituted hydantoin the first group entering the ring does so at the 3-position as in (II).

Since with primary amines benzaldehyde readily forms benzyldienimines which in turn react with hydrogen cyanide to form aminonitriles, such a procedure was utilized in preparing the 1-substituted-5-phenylhydantoin. It was found unnecessary to isolate any of the compounds intermediate between the imine and the hydantoin. In general the best method of synthesis consisted of mixing benzaldehyde with the appropriate amine. The resulting mixture was then added to cold 70-80% acetic acid containing about one-half of the required sodium or potassium cyanide. The remainder of the cyanide was then added and was followed shortly by the portion-wise addition of a slight excess of potassium cyanate. The resulting mixture, when treated with concentrated

hydrochloric acid, gave yields of 35–70% of the expected hydantoin.

The procedure with ketones such as acetophenone and propiophenone was changed in that the ketone was first treated with liquid hydrogen cyanide. When the cyanohydrin thus formed reacted with an amine, water split out and the resulting aminonitrile was treated with potassium cyanate. In several reactions of this type results indicated that the presence of a strong mineral acid, either with or without acetic acid, offers some advantage over acetic acid alone.

The problem of preparing 1-alkyl derivatives of 5,5-diphenylhydantoin differs somewhat from that involved in either of the above types. Although it has been shown that diaryl ketones such as benzophenone, contrary to the findings of Bucherer and Lieb,<sup>7</sup> do in fact form hydantoins,<sup>8</sup> it is true that benzophenone exhibits very little tendency toward cyanohydrin formation with hydrogen cyanide.<sup>9</sup> In confirmation of this fact, all attempts to prepare aminonitriles from benzophenone itself ended in failure. However, this difficulty was overcome by treating dichlorodiphenylmethane with an amine as in the method used by Moore<sup>10</sup> in preparing benzophenone imine from dibromodiphenylmethane and ammonia. The substituted benzophenone imine thus produced reacted readily with hydrogen cyanide and the resulting amino-nitrile was converted to 1-alkyl-5,5-diphenylhydantoin by the use of cyanic acid.

**Pharmacology.**—The results of preliminary studies by Merritt and Putnam, part of which have been published,<sup>3</sup> and especially by Chen<sup>11</sup> of this Laboratory indicate that although many of the compounds in Table I exhibit anticonvulsant activity, the maximum inhibition of variously induced convulsions is attained with the 1-R-5-phenylhydantoins, where R represents a hydrocarbon radical of from two to four carbon atoms inclusive. Like other types of derivatives of 5,5-diphenylhydantoin,<sup>8</sup> the 1-alkyl-5,5-diphenylhydantoins have no inhibitory effect on electrically induced convulsions.

### Experimental

**1-Propyl-5-phenylhydantoin.**—Two hundred and sixty-five grams (2.5 moles) of benzaldehyde was placed in a 1-liter flask fitted with a stirrer, a reflux condenser and a dropping funnel. The flask was cooled in a cold water-bath and 154 g. (2.6 moles) of *n*-propylamine (Sharples) was added with stirring. The addition, which was completed in twenty minutes, was made at such a rate as to cause the mixture to reach a temperature of 60°. Stirring was continued for one-half hour after the last of the amine had been added. The mixture was then cooled in an ice-bath.

One liter of 75% aqueous acetic acid was placed in an open 3-liter flask fitted with a stirrer and a thermometer

(7) Bucherer and Lieb, *J. prakt. Chem.*, [2] **141**, 5 (1934).

(8) Henze and Long, *THIS JOURNAL*, **63**, 1941 (1941); Henze, U. S. Patents 2,409,754, 2,409,755, 2,409,756.

(9) Lapworth and Manske, *J. Chem. Soc.*, 2533 (1928).

(10) Moore, *Ber.*, **43**, 563 (1910).

(11) Private communication.

and cooled to 0° in an ice-salt-bath. The acid was stirred slowly while 71 g. of sodium cyanide was added so that the temperature remained below 5°. The benzylidene-propylamine-water mixture was then added dropwise, keeping the temperature below 10°. The remainder of the sodium cyanide (70 g.) was added in 10-g. portions.

Stirring was continued, and when the aminonitrile solution had again cooled to 0°, a total of 212 g. of potassium cyanate was added over a period of one-half hour. The temperature increased to 5°. After one hour the slowly stirred mixture was heated to 70° for fifteen minutes on a steam-bath.

Concentrated hydrochloric acid (750 ml.) was added cautiously to the warm solution. After the acidified mixture had been heated on the steam-bath for an hour, it was diluted to 3 liters with cold water and thoroughly cooled in an ice-bath. The oily layer on top solidified slowly. The resulting mixture was filtered and the solid product washed with cold water and dried. Purification was accomplished by solution in 5% aqueous alkali, charcoaling and reprecipitation with Dry Ice. The final product was a white, crystalline solid weighing 337 g.

**1-Allyl-5-phenylhydantoin.**—Four hundred and twenty-four grams (4.0 moles) of benzaldehyde was mixed with 500 ml. of water in a 2-liter flask fitted with a stirrer, reflux condenser and a dropping funnel. The mixture was stirred and 234 g. (4.1 moles) of allylamine was added at a moderate rate. The temperature increased to about 65°. After refluxing for one-half hour, the mixture was cooled and extracted twice with 300-ml. portions of ether. The combined ether extracts were dried over magnesium sulfate, concentrated on a steam bath and the residue distilled at reduced pressure. The product, 517 g. or 89%, distilled at 96–99° (20 mm.).<sup>12</sup>

One hundred and forty-five grams (1.0 mole) of benzylidene allylamine was placed in a 500-ml. flask fitted with a stirrer, reflux condenser and a dropping funnel and cooled in an ice-salt mixture. While the imine was stirred slowly, 27 g. (1.0 mole) of liquid hydrogen cyanide was added dropwise. The resulting aminonitrile was allowed to warm up to room temperature.

The aminonitrile was dissolved in 350 ml. of 80% aqueous acetic acid cooled to 0°. To the cold solution was added in small portions with slow stirring 89 g. (1.1 mole) of potassium cyanate. The remainder of the process was carried out as in the preparation of 1-propyl-5-phenylhydantoin. The yield of white, crystalline product based on the benzylidene allylamine was 73%.

**1-Methyl-5-methyl-5-phenylhydantoin.**—One hundred and twenty grams (1.0 mole) of acetophenone was mixed with 29.7 g. (1.1 mole) of liquid hydrogen cyanide in a pressure bottle. A few drops of saturated sodium carbonate solution were added, and the bottle closed and allowed to stand at room temperature for twenty-four hours. The solution was then cooled and methylamine was passed in until one mole had been absorbed. On standing at 25° for twenty hours, an appreciable quantity of water separated.

The crude aminonitrile was added slowly to 1 liter of dilute hydrochloric acid cooled to 0°. A large part of the nitrile dissolved. The mixture was stirred slowly while 89 g. (1.1 mole) of potassium cyanate was added in small portions. After twenty minutes a white solid precipitated. The mixture was kept in the ice-bath for an additional hour. It was then heated on a steam-bath and 100 ml. of concentrated hydrochloric acid was added. After an hour the mixture was thoroughly cooled and filtered. The product was dissolved in an excess of 5% aqueous sodium hydroxide and the resulting mixture extracted twice with small portions of ether to remove unreacted ketone. The solution was then charcoaled, filtered and the product reprecipitated with Dry Ice. The purified product was a white crystalline solid.

**1-Ethyl-5-diphenylhydantoin.**—To a solution of 23.6 g. (0.1 mole) of benzophenone chloride<sup>13</sup> in 50 ml. of toluene

(12) Borsche and John, *Ber.*, **57**, 664 (1924).

(13) Norris, Thomas and Brown, *ibid.*, **43**, 2958 (1910).

in a small metal bomb was added 22.5 g. (0.5 mole) of anhydrous ethylamine. The bomb was closed and heated to 100–105° for twenty hours. It was then cooled, opened and the contents filtered. The solid consisted of ethylamine hydrochloride (16.1 g.). The yellow filtrate was concentrated *in vacuo*. The cooled residue was mixed with 2.7 g. (0.1 mole) of liquid hydrogen cyanide. The solution became warm. It was cooled and mixed with 500 ml. of cold, dilute hydrochloric acid. Treatment with 8.9 g. (0.11 mole) of potassium cyanate and purification of the product as previously described in the preparation of 1-methyl-5-methyl-5-phenylhydantoin yielded a crystalline product.

**1- $\beta$ -Hydroxyethyl-5-phenylhydantoin.**—Fifty-three grams (0.5 mole) of benzaldehyde and 14.9 g. (0.55 mole) of liquid hydrogen cyanide were mixed together in a small pressure bottle (ice-bath) and allowed to stand at 25° for two hours. The product was cooled and 30.5 g. (0.5 mole) of ethylamine was added. Heat was evolved. The resulting mixture was cooled and added to a cold solution of 50 ml. of concentrated hydrochloric acid and 200 ml. of water. After the solution had cooled to 0°, 44.6 g. (0.55 mole) of potassium cyanate was added. Within a few minutes a yellow, semi-solid material precipitated. The mixture was left in the ice-bath for an hour before

being heated on the steam-bath with an additional 100 ml. of concentrated hydrochloric acid. After the mixture was thoroughly chilled, it was filtered. The yellow solid was purified by dissolving in 800 ml. of boiling water, charcoaling and cooling to reprecipitate the product.

**1- $\beta$ -Bromoethyl-5-phenylhydantoin.**—Twenty-two grams (0.1 mole) of 1- $\beta$ -hydroxyethyl-5-phenylhydantoin was mixed with 50 ml. of dry chloroform and cooled in an ice-bath. Ten grams of phosphorus tribromide in 50 ml. of chloroform was added with stirring. After one-half hour the mixture was placed on a steam-bath and warmed for an hour. The resulting solution was poured with stirring into an excess of chipped ice. The solid product was filtered off and recrystallized from ethanol and water.

### Summary

A series of 1-R-5-R'-5-phenylhydantoins, most of which are new compounds, has been prepared and tested for anticonvulsant activity.

Maximum activity is exhibited by those derivatives having a lower hydrocarbon group in the 1-position and only a phenyl group in the 5-position.

DETROIT, MICHIGAN

RECEIVED OCTOBER 4, 1947

[CONTRIBUTION FROM THE VENABLE CHEMICAL LABORATORY OF THE UNIVERSITY OF NORTH CAROLINA]

## The Preparation of Some Substituted Quinoxalines

By R. W. BOST AND E. E. TOWELL<sup>1,2</sup>

The reaction between aromatic ortho-diamines and alpha-diketones to form quinoxalines has been utilized to prepare a series of 2,3-disubstituted quinoxalines and 2,3-disubstituted-6-methoxyquinoxalines, with the purpose of studying their pharmacological properties.

The two diamines used were *o*-phenylenediamine and 3,4-diaminoanisole in the form of its hydrochloride, which was prepared in the laboratory from 4-amino-3-nitroanisole. The 4-amino-3-nitroanisole was prepared from commercial *p*-anisidine by the method of Reverdin,<sup>3</sup> with minor modifications. The diacetyl was obtained from the Forest Products Company. 3,5-Dicarboethoxycyclopentanedione-1,2 was prepared by the condensation of ethyl oxalate and ethyl glutarate in the presence of sodium ethoxide.<sup>4</sup> The following benzoinz were prepared from the corresponding aldehydes by the "benzoin" condensation in the presence of alcoholic potassium cyanide: 4,4'-dimethoxybenzoin, *p*-dimethylaminobenzoin, 3,3',4,4'-bis-(methylenedioxy)-benzoin, 2,2',3,3'-tetramethoxybenzoin, 4-methoxy-3',4'-methylenedioxybenzoin, and *p*-diethylaminobenzoin. *alpha*-Furoin and benzil were available in the laboratory.

(1) This paper is a portion of a dissertation presented by E. E. Towell in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the Graduate School of the University of North Carolina, June, 1944.

(2) New York Community Trust Fund Fellow, 1942–1943; Wm. S. Merrell Co. Fellow, 1943–1944. Present address: Department of Chemistry, College of Charleston, Charleston, S. C.

(3) Reverdin, *Ber.*, **29**, 2595 ff. (1896).

(4) Adams, *et al.*, "Organic Reactions," Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1942, p. 284.

The following diketones were prepared by oxidation of the corresponding hydroxyketone with copper sulfate in pyridine<sup>5</sup>: 4,4'-dimethoxybenzil, *p*-dimethylaminobenzil, 3,3',4,4'-bis-(methylenedioxy)-benzil, 2,2',3,3'-tetramethoxybenzil<sup>6</sup>; 4-methoxy-3',4'-methylenedioxybenzil, *alpha*-fural, and *p*-diethylaminobenzil (not obtained in crystalline form; alcoholic solution used to prepare the quinoxaline).

Attempts to prepare the quinoxaline from 2,3,2'-3'-tetramethoxybenzil and *o*-phenylenediamine were unsuccessful. An explanation of this anomalous behavior of an alpha-diketone toward an aromatic ortho-diamine has been offered by Schönberg and co-workers.<sup>7</sup>

Bennett and Willis<sup>8</sup> have shown that the methyl groups in 2,3-dimethylquinoxaline react with certain aromatic aldehydes in an excess of boiling acetic anhydride to form mono- and di-styrylquinoxalines. Attempts were made by us to bring about a similar reaction between 2,3-dimethylquinoxaline and formaldehyde, acetaldehyde and *n*-butyraldehyde, respectively, using the method of Bennett and Willis. Since no identifiable products could be isolated from the reaction mixtures, the experimental details are not given in this paper. An unsuccessful attempt was made to carry out a

(5) "Organic Syntheses," Coll. Vol. I, 2nd ed., John Wiley and Sons, Inc., New York, N. Y., 1941, p. 87; Kinney, *THIS JOURNAL*, **51**, 1595 (1929); Hartmann and Dickey, *ibid.*, **55**, 1228 (1933).

(6) Hartwell and Kornberg, *ibid.*, **67**, 1607 (1945).

(7) Schönberg and co-workers, *Ber.*, **55B**, 1174 ff., 3746 ff., 3755 (1922).

(8) Bennett and Willis, *J. Chem. Soc.*, 1960 (1928); 256 (1929).