The residues from fractions 22–27 were combined and recrystallized once from benzene (Darco), affording 0.22 g. (23%) of crystalline product, m.p. 225–226°, with slight sintering at 223°. Two more recrystallizations from benzene gave white needles of 2-chloro-6-methoxy-*p*-phenylenedibenzamide, m.p. 225–226.5°.

Anal. Calcd. for $C_{21}H_{17}ClN_2O_3$: C, 66.23; H, 4.50; N, 7.36. Found: C, 66.24; H, 4.51; N, 7.23.

The melting point of a mixture of this product and the previously described authentic 2-chloro-6-methoxy-*p*-phenylenedibenzamide was not depressed. The infrared spectra of the two samples were identical.

The total yield of chloro-methoxy-*p*-phenylenedibenzamide isomers from the addition of hydrogen chloride to 2-methoxy-*p*-quinonedibenzimide was thus 0.44 g. (46%), based on the quantity of 2-methoxy-*p*-phenylenedibenzamide employed.

Although the two isomers melted at essentially the same point, the melting point of a mixture was depressed. The infrared spectra of the compound were different. The 2,5-isomer was more soluble in benzene than the 2,6-isomer.

5'-Chloro-2'-methoxy-4'-nitrobenzanilide.—To a solution of 0.72 g. of 2-amino-4-chloro-5-nitroanisole[11] in 10 ml. of pyridine was added 1.00 g. of benzoyl chloride. The reaction mixture was allowed to stand for 12 minutes and then boiled for 2 minutes, cooled to room temperature, and poured into 100 ml. of 10% hydrochloric acid containing 50 g. of ice. An oil precipitated which rapidly solidified. The solid was collected by filtration, washed with water, and recrystallized once from carbon tetrachloride, after which it weighed 0.79 g. (73%). A subsequent recrystallization from an acetic acid–water solvent pair (Darco) gave pinkish-yellow needles, m.p. 138–143° (lit.[12] m.p. 142°). Further recrystallization improved the melting point only very slowly.

4'-Amino-5'-chloro-2'-methoxybenzanilide.—To a boiling solution of 0.58 g. of 5'-chloro-2'-methoxy-4'-nitrobenzanilide in 35 ml. of ethanol, water was added until the cloud point was attained. To the still boiling solution was slowly added 1.01 g. of sodium hydrosulfite, followed by water until the cloud point was again attained. The solution was cooled, caused the crystallization of 0.28 g. of the product, m.p. 151.5–153°, which was collected by filtration. By dilution of the filtrate with water, followed by heating and recooling, an additional 0.02 g. of crystals was obtained, thus bringing the total yield to 0.30 g. (58%). The product was recrystallized once from an ethanol–water solvent pair, giving lustrous creamish needles, m.p. 152–154° (lit.[12] m.p. 152.5°).

2-Chloro-5-methoxy-*p*-phenylenedibenzamide. Method B.—To a solution of 0.11 g. of 4'-amino-5'-chloro-2'-methoxybenzanilide in 1.0 ml. of pyridine, cooled in an ice-bath, was added a solution of 0.07 g. of benzoyl chloride in 1.0 ml. of pyridine. The solution was allowed to stand at room temperature for 10 minutes, then boiled for 2 minutes, and finally cooled and allowed to stand at room temperature for another 5 minutes. The solution was poured into 20 ml. of 10% hydrochloric acid containing 5 g. of ice, causing the precipitation of 0.14 g. (93%) of the product, which was collected by filtration and washed with water. Two recrystallizations from benzene gave small lustrous white prisms, m.p. 225.5–226.5°.

Anal. Calcd. for $C_{21}H_{17}ClN_2O_3$: C, 66.23; H, 4.50; N, 7.36. Found: C, 66.24; H, 4.58; N, 7.31.

(11) Aktien-Gesellschaft für Anilin-Fabrikation, German Patent 137,956 (December 1, 1902); *Chem. Zentr.*, **74**, I, 112 (1903); T. E. Young, Thesis Doctor of Philosophy, University of Illinois, 1952.

(12) N. Kizhner and V. Krasnova, *Anilinokrasochnaya Prom.*, **3**, 179 (1933); *Chem. Zentr.*, **105**, I, 2354 (1934); *C. A.*, **27**, 5319 (1933).

URBANA, ILLINOIS

CONTRIBUTION FROM THE THOMPSON CHEMICAL LABORATORY, WILLIAMS COLLEGE, AND THE FRICK CHEMICAL LABORATORY, PRINCETON UNIVERSITY]

The Synthesis and Antibiotic Activity of Analogs of Citrinin and Dihydrocitrinin

BY HAROLD H. WARREN,[1] GREGG DOUGHERTY AND EVERETT S. WALLIS

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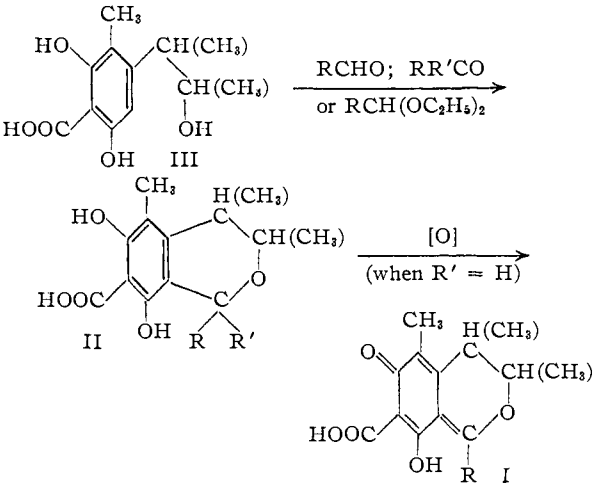
A method has been developed for the preparation of 1-substituted dihydrocitrinin derivatives (II) by the cyclization of the carboxylic acid derivative of Compound A (III) with acetals, aldehydes and ketones, and the conversion of the dihydro derivatives to the corresponding 1-substituted citrinin derivatives (I) by oxidation. Assay of the antibiotic activity of the compounds prepared indicated that the 1-methyl-, 1-ethyl- and 1-phenylcitrinin derivatives possess considerably less activity than the parent compound. The 1-methyl-, 1-ethyl-, 1-phenyl- and 1,1-dimethyldihydrocitrinin derivatives are inactive as is dihydrocitrinin, while the 1-benzyl derivative shows moderate activity.

In a previous article[2] we reported a partial synthesis of citrinin[3] (I, R = H) involving the cyclization of the carboxylic acid derivative of Raistrick's Compound A[4] (III) with methylal to give dihydrocitrinin[5] (II, R = H; R' = H) and the oxidation of the latter with bromine to citrinin. The purpose of the present work was to extend this synthesis to the preparation of dihydrocitrinin and citrinin derivatives bearing alkyl and aryl substituents at the 1-position and to determine the effect of such structural variation on their antibiotic activity.

It has been found that aldehydes, acetals and ketones will condense with the carboxylic acid derivative of Compound A in a fashion analogous to that of methylal. The reactants used and the products obtained are summarized in Table I.



(1) Thompson Chemical Laboratory, Williams College, Williamstown, Mass.

(2) H. H. Warren, G. Dougherty and E. S. Wallis, THIS JOURNAL, **71**, 3422 (1949).

(3) 4,6-Dihydro-8-hydroxy-3,4,5-trimethyl-6-oxo-3H-2-benzopyran-7-carboxylic acid.

(4) 4-(2-Hydroxy-1-methylpropyl)-3-methyl-γ-resorcylic acid.

(5) 6,8-Dihydroxy-3,4,5-trimethyl-7-isochromancarboxylic acid.

The cyclization occurs readily at room temperature with zinc chloride or anhydrous hydrogen chloride as the catalyst. In the case of acetone and phenylacetaldehyde, both reagents are required to give a reasonably rapid reaction. Although the carboxylic acid derivative is only slightly soluble in benzene, the reaction occurs readily in that solvent, and its progress can be followed easily by observing the disappearance of the suspended material.

TABLE I

CONDENSATION PRODUCTS OF CARBONYL COMPOUNDS WITH THE CARBOXYLIC ACID DERIVATIVE OF COMPOUND A

Reactant	Product	Yield, %	M.p., °C.[a]
Acetal	1-Methyldihydrocitrinin (II, R = CH_3; R′ = H)	28	152.0–153.0
Propionaldehyde (or its acetal)	1-Ethyldihydrocitrinin (II, R = C_2H_5; R′ = H)	9	170.0–171.4
Acetone	1,1-Dimethyldihydrocitrinin (II, R = CH_3; R′ = CH_3)	31	166.5–167.5
Benzaldehyde	1-Phenyldihydrocitrinin (II, R = C_6H_5; R′ = H)	23	168.5–169.5
Phenylacetaldehyde	1-Benzyldihydrocitrinin (II, R = $CH_2C_6H_5$; R′ = H)	24	172.5–173.5

[a] Decomposition occurred at the melting point in all cases.

Purification of the products by recrystallization resulted in considerable loss and was complicated by the fact that, while the dihydrocitrinin derivatives crystallize most readily from halogenated hydrocarbon solvents or mixed solvents containing them, the products are contaminated by solvent of crystallization which cannot be removed completely by prolonged drying under vacuum at elevated temperature.

The smallness of the reported yields is due largely to the losses involved in the preparation of samples of analytical purity. Yields of crude material were ample (50–80%).

All of the dihydrocitrinin derivatives are readily soluble in dilute sodium bicarbonate and give the characteristic deep blue color with dilute alcoholic ferric chloride.

The oxidation with bromine in chloroform of the substituted dihydrocitrinins to the corresponding citrinin derivatives proved less satisfactory than in the case of dihydrocitrinin itself. Small but adequate yields of light lemon-yellow crystals of 1-methylcitrinin and orange crystals of 1-phenylcitrinin were obtained, but all attempts to oxidize 1-ethyldihydrocitrinin and 1-benzyldihydrocitrinin with this reagent produced brominated products, and in the case of the latter compound a small amount of a non-brominated lemon-yellow substance which did not possess the characteristic properties of citrinin derivatives.

1-Ethyldihydrocitrinin was oxidized successfully to 1-ethylcitrinin by means of red mercuric oxide in benzene, but this method failed when applied to the 1-benzyl derivative.

In an attempt to develop a more satisfactory method for carrying out the conversion, the catalytic dehydrogenation of dihydrocitrinin was investigated. It was found that a 50% yield of citrinin can be obtained by heating dihydrocitrinin with 30% palladium–charcoal in nitrobenzene through which oxygen is slowly passed. All attempts, however, to adapt this procedure to the dehydrogenation of 1-benzyldihydrocitrinin failed. The only product that could be isolated was a small amount of material which had all the properties of citrinin and which did not depress the melting point of an authentic sample of citrinin, indicating that under the conditions of the reaction the benzyl group is eliminated more readily than hydrogen.

All the citrinin derivatives prepared give the deep red color with dilute alcoholic ferric chloride characteristic of citrinin and are soluble in dilute sodium bicarbonate but with increasing difficulty as the size of the substituent group is increased.

The agar-streak technique of Waksman and Reilly[6] was chosen as a rapid and convenient method for comparing the antibiotic activity of the synthetic derivatives to that of citrinin and dihydrocitrinin.

At the highest concentration tested, 3000 dilution units (ml. of nutrient agar/g. of test compound), of all the synthetic derivatives only four compounds show any inhibition of growth of the test organisms used. The results are summarized in Table II. As expected, none of the compounds shows activity toward the gram-negative organisms, *E. coli*.

It is apparent that introduction of an alkyl or aryl group into citrinin greatly reduces the antibiotic activity of the compound compared to the parent compound. On the other hand, the potency of dihydrocitrinin, itself inactive at the highest concentration tested, is greatly enhanced by the presence of the benzyl group.

Work is under way to determine the effect of increasing the chain length of the alkyl substituent on the antibiotic activity of citrinin derivatives and to determine whether the effect of the benzyl group on the activity of dihydrocitrinin is due merely to its size or to a specific function of that group.

Acknowledgments.—The authors wish to express their appreciation to Merck and Co., Inc., Rahway, N. J., for providing many of the microanalyses; to Dr. John Wyllie of Queens University, Kingston, Ontario, who provided a culture of *A. candidus;* and to the E. I. du Pont de Nemours and Co., Wilmington, Del., for a grant-in-aid under which a portion of this work was carried out.

Experimental[7]

Starting Materials.—Citrinin was produced by the growing of *Aspergillus candidus* on a modified Czapek–Dox medium according to the method of Wyllie.[8] The hydrolysis of citrinin to Compound A and the preparation of the carboxylic acid derivative of compound A (III) by the carboxylation of Compound A have been described previously.[2] Ethyl acetate proved to be the most effective solvent for the purification of the carboxylic acid derivative. Dihydrocitrinin was prepared by the reduction of citrinin with Raney nickel according to the method of Schwenk, Schubert and Stahl.[9] The zinc chloride used was J. T. Baker, reagent grade.

1-Methyldihydrocitrinin (6,8-Dihydroxy-1,3,4,5-tetramethyl-7-isochromancarboxylic Acid).—To a suspension of 2.0 g. of the carboxylic acid derivative of Compound A (III) in 16 ml. of benzene was added 6.0 ml. of acetal and

(6) S. A. Waksman and H. C. Reilly, *Anal. Chem.*, **17**, 556 (1945).
(7) All melting points are corrected.
(8) J. Wyllie, *Can. J. Pub. Health*, **36**, 477 (1945).
(9) E. S. Schwenk, M. Schubert and E. Stahl, *Arch. Biochem.*, **20**, 220 (1949).

TABLE II
ANTIBIOTIC POTENCY OF CITRININ AND ITS DERIVATIVES

Compound	*S. aureus* Ml. agar/g. cpd. for Partial inhib.	*S. aureus* Ml. agar/g. cpd. for Complete inhib.	*B. mycoides* Ml. agar/g. cpd. for Partial inhib.	*B. mycoides* Ml. agar/g. cpd. for Complete inhib.	*B. subtilis* Ml. agar/g. cpd. for Partial inhib.	*B. subtilis* Ml. agar/g. cpd. for Complete inhib.
Citrinin	70,000	40,000	70,000	40,000	70,000	50,000
Dihydrocitrinin	....[a]	....	....	....	....	....
1-Methylcitrinin	3,000	....	3,000	....	6,000	....
1-Ethylcitrinin		3,000		3,000	6,000	3,000
1-Phenylcitrinin	3,000	....	3,000	....	3,000	....
1-Benzyldihydrocitrinin	10,000	6,000	10,000	6,000	10,000	6,000

[a] .... indicates no inhibition at highest concentration tested.

1.0 g. of zinc chloride. The mixture was allowed to stand at room temperature with frequent shaking for 15 minutes during which most of the suspended material dissolved. After standing for 2 hr. the clear orange solution was washed twice with dilute hydrochloric acid, once with water and dried over anhydrous sodium sulfate. Evaporation of the solvent yielded a red tar which was taken up in warm ethylene dibromide. Addition of petroleum ether and vigorous stirring initiated the formation of white crystals. After five recrystallizations from ethylene dibromide and petroleum ether followed by two from 1:10 toluene–ligroin, the product melted at 152.0–153.0° dec., yield 0.62 g. (28%).

Anal. Calcd. for $C_{14}H_{18}O_5$: C, 63.12; H, 6.81. Found: C, 63.32; H, 6.83.

1-Methylcitrinin (4,6-Dihydro-8-hydroxy-1,3,4,5-tetramethyl-6-oxo-3H-2-benzopyran-7-carboxylic Acid).—To a solution of 0.20 g. of 1-methyldihydrocitrinin in 10 ml. of chloroform was added 3.0 ml. of 0.5 *M* bromine in chloroform. The solution was allowed to stand at room temperature for 15 minutes and then was washed with 5% sodium bisulfite solution, with water, dried over anhydrous sodium sulfate and evaporated to a red tar which crystallized when stirred with a small amount of ether. The product was filtered and recrystallized twice from chloroform–petroleum ether and once from absolute ethanol. The yield of lemon-yellow crystals was 0.03 g. (15%) melting at 259.2–260.0° dec. A sample introduced into the melting point apparatus preheated to 170° melted immediately, resolidified and remelted at the higher temperature.

Anal. Calcd. for $C_{14}H_{16}O_5$: C, 63.60; H, 6.10. Found: C, 63.45; H, 6.30.

The product could be purified readily by recrystallization from absolute ethanol, but it underwent decomposition in aqueous ethanol or aqueous methanol, forming a deep green solution and a deposit of dark green tar. This was the only citrinin derivative to exhibit such behavior.

1-Ethyldihydrocitrinin (1-Ethyl-6,8-dihydroxy-3,4,5-trimethyl-7-isochromancarboxylic Acid).—Dry halogen chloride was passed for 30 seconds through a suspension of 1.0 g. of the carboxylic acid derivative of Compound A (III) in 10 ml. of benzene and 3.0 ml. of propionaldehyde. The mixture was allowed to stand at room temperature for 2 hr. during which time the suspended material rapidly dissolved followed by spontaneous crystallization of the product. The mixture was diluted with sufficient ether to dissolve the crystalline deposit and was extracted twice with 5% sodium bicarbonate. The aqueous extract was acidified with excess dilute hydrochloric acid, and the resulting insoluble oil was extracted with ether. After drying over sodium sulfate, the ethereal solution was evaporated to a yellow oil which crystallized when stirred with benzene and cooled thoroughly. Recrystallization of the product once from amyl acetate and once from acetone yielded 0.10 g. (9%) of white crystals melting at 170.6–171.4° dec.

Anal. Calcd. for $C_{15}H_{20}O_5$: C, 64.27; H, 7.19. Found: C, 63.97; H, 7.01.

The diethyl acetal of propionaldehyde was found to react in exactly the same fashion as the free aldehyde.

1-Ethylcitrinin (1-Ethyl-4,6-dihydro-8-hydroxy-3,4,5-trimethyl-6-oxo-3H-2-benzopyran-7-carboxylic Acid).—A mixture of 0.20 g. of 1-ethyldihydrocitrinin, 3.0 g. of red mercuric oxide, 1.0 g. of anhydrous magnesium sulfate in 10 ml. of benzene was refluxed for 45 minutes. After cooling, sufficient dilute hydrochloric acid was added to dissolve the sludge. The organic layer was separated, washed once with dilute hydrochloric acid, once with water and then dried over sodium sulfate. Evaporation of the solvent yielded an orange oil which crystallized readily from dilute ethanol. Two recrystallizations of the product from the same solvent yielded 10 mg. (5%) of lemon-yellow crystals melting at 139.0–139.8°, resolidifying and remelting at 263.0–267.0° dec.

Anal. Calcd. for $C_{15}H_{18}O_5$: C, 64.73; H, 6.52. Found: C, 64.86; H, 6.57.

1,1-Dimethyldihydrocitrinin (6,8-Dihydroxy-1,1,3,4,5-pentamethyl-7-isochromancarboxylic Acid).—To a suspension of 0.5 g. of the carboxylic acid derivative of Compound A (III) in 6.0 ml. of benzene and 1.5 ml. of acetone was added 0.1 g. of zinc chloride, and dry hydrogen chloride was bubbled through for 10 seconds. Within 10 minutes the suspended material had dissolved. After standing at room temperature for 4 hr. the nearly colorless solution was washed once with dilute hydrochloric acid and twice with water, dried over sodium sulfate and evaporated to a colorless oil which crystallized spontaneously. The product was recrystallized once from *p*-cymene and once from cyclohexane–carbon tetrachloride, yielding 0.18 g. (31%) of white crystals melting at 166.5–167.5° dec.

Anal. Calcd. for $C_{15}H_{20}O_5$: C, 64.27; H, 7.19. Found: C, 64.26; H, 7.03.

1-Phenyldihydrocitrinin (6,8-Dihydroxy-3,4,5-trimethyl-1-phenyl-7-isochromancarboxylic Acid).—Four-tenths of a gram of zinc chloride was added to a suspension of 1.5 g. of the carboxylic acid derivative of Compound A (III) in a solution of 3.0 ml. of benzaldehyde and 15 ml. of benzene at room temperature. The suspended material completely dissolved within 30 minutes. After standing for 4 hr. the solution was washed with dilute hydrochloric acid and with water, dried over sodium sulfate and evaporated to a yellow oil which crystallized readily from carbon tetrachloride. The product was recrystallized once by dissolving it in 2 ml. of methanol, adding 15 ml. of hot carbon tetrachloride and cooling. A second recrystallization from 1:5 methyl ethyl ketone–ligroin yielded 0.57 g. (23%) of white crystals melting at 168.5–169.5° dec.

Anal. Calcd. for $C_{19}H_{20}O_5$: C, 69.49; H, 6.14. Found: C, 69.23; H, 6.30.

1-Phenylcitrinin (4,6-Dihydro-8-hydroxy-3,4,5-trimethyl-6-oxo-1-phenyl-3H-2-benzopyran-7-carboxylic Acid).—To a solution of 0.20 g. of 1-phenyldihydrocitrinin in 5.0 ml. of chloroform at room temperature was added slowly 0.7 ml. of 1.0 *M* bromine in chloroform. After standing for five minutes the orange solution was evaporated to an oil and then vacuum desiccated. The resulting glass crystallized when dissolved in hot ethanol to which water was cautiously added. Three recrystallizations of the product from dilute ethanol yielded 10 mg. (5%) of orange crystals melting at 249.5–251.5° dec. Though no shrinkage occurred at a lower temperature, a sample introduced into the apparatus preheated to 200° melted, resolidified and remelted at the higher temperature. The color of the pure product remained orange as compared to the lemon-yellow of most citrinin derivatives.

Anal. Calcd. for $C_{19}H_{18}O_5$: C, 69.94; H, 5.56. Found: C, 69.77; H, 5.43.

1-Benzyldihydrocitrinin (1-Benzyl-6,8-dihydroxy-3,4,5-trimethyl-7-isochromancarboxylic Acid).—Dry hydrogen chloride was bubbled for 15 seconds through a suspension of 1.0 g. of the carboxylic acid derivative of Compound A

(III) and 0.2 g. of zinc chloride in a solution of 13 ml. of benzene and 2.0 ml. of freshly distilled phenylacetaldehyde. After standing at room temperature for 4 hr. the resulting yellow solution was washed with three portions of water, dried over sodium sulfate and evaporated to an oil which crystallized when stirred with petroleum ether. The product was recrystallized once from ethylene bromide and petroleum ether, once from *p*-cymene and three times from xylene yielding 0.34 g. (24%) of white crystals melting at 172.5–173.5° dec.

Anal. Calcd. for $C_{20}H_{22}O_5$: C, 70.15; H, 6.48. Found: C, 70.28; H, 6.39.

Catalytic Dehydrogenation of Dihydrocitrinin.—Oxygen was bubbled slowly through a mixture of 0.10 g. of dihydrocitrinin and 0.05 g. of 30% palladium–charcoal in 1.0 ml. of nitrobenzene. After 23 minutes the solution gave a red color with ferric chloride indicating complete conversion of the dihydro compound. The solution was cooled, diluted to a convenient volume with ether, filtered to remove the catalyst and extracted with 5% sodium bicarbonate solution. Acidification of the aqueous extract with dilute sulfuric acid produced an orange-yellow crystalline precipitate. One recrystallization from hot ethanol yielded 0.05 g. (50%) of lemon-yellow crystals melting at 171.0–171.5° dec. No depression of the melting point was noted when this product was mixed with an authentic sample of citrinin.

The reaction proceeded in the absence of oxygen, but a longer reaction time was required, and the yield was considerably less.

Attempted Catalytic Dehydrogenation of 1-Benzyldihydrocitrinin.—The reaction was carried out using the same quantities and conditions given above for dihydrocitrinin. Heating was continued for 45 minutes before the blue ferric chloride test due to the dihydro compound became negative and a brown color was obtained. No appreciable product could be isolated by extraction of the reaction mixture.

The reaction was repeated using successively higher temperatures. At 150° a reaction time of nine minutes was required. Extraction of the solution yielded 0.02 g. of a yellow crystalline material which after one recrystallization from ethanol melted at 165.0–168.0° dec. A mixture of this product with citrinin melted at 166.0–169.0° dec.

Assay for Antibiotic Activity.—The comparison of the antibiotic activity of the synthetic derivatives to that of citrinin and dihydrocitrinin was made by the agar-streak method of Waksman and Reilly[6] using four organisms, *E. coli*, *S. aureus*, *B. mycoides* and *B. subtilis*. Stock solutions of the compounds to be tested were made up by dissolving the appropriate amount of substances (usually 5.0, 10.0 or 20.0 mg.) in three drops of acetone and three drops of 5% sodium bicarbonate and diluting to a volume of 10.0 ml. In no case did the latter reagents, at a concentration equal to the maximum present in the test cultures, inhibit the growth of control cultures. The stock solutions were used immediately after preparation to avoid decomposition of the sample in the slightly basic solution. A maximum concentration of test substance corresponding to 3,000 dilution units was used. The test cultures were examined after incubation for 20 hr. at 28°. The results for all compounds showing any inhibition of bacterial growth are summarized in Table II.

WILLIAMSTOWN, MASS.

[CONTRIBUTION FROM AVERY LABORATORY, UNIVERSITY OF NEBRASKA]

Ethylenimine Ketones. XII. Stereoisomerism of 1-Cyclohexyl-2-(*o*-nitrophenyl)-3-benzoylethylenimine. Quinoline Syntheses

BY NORMAN H. CROMWELL AND GERALD D. MERCER

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A *trans* configuration has been assigned to the low melting form of 1-cyclohexyl-2-(*o*-nitrophenyl)-3-benzoylethylenimine which results from the reaction of 2-nitrochalcone with iodine and cyclohexylamine. Both the *cis* and *trans* forms are obtained in nearly equal amounts from 2,3-dibromo-3-(*o*-nitrophenyl)-propiophenone. The assignment of configuration is based upon the diagnostic phenylhydrazine reaction and absorption spectra studies. The catalytic hydrogenation of either the *cis*- or *trans*-ethylenimine ketone to 3-cyclohexylamino-2-phenylquinoline provides a new method of synthesis of such materials not readily available by conventional means. The course of this reaction is considered and the ultraviolet and infrared spectra of several 2-phenylquinolines are discussed.

Several pairs of *cis*- and *trans*-arylaroylethylenimines[1] and one pair of *cis*- and *trans*-alkylaroylethylenimines[2] have been prepared by the reaction of primary amines with α,β-dibromoketones. These isomeric pairs have been separated by fractional recrystallization or by chromatographic means and characterized by chemical and physical methods.

To study the sterical and electrical effects of the *o*-nitro group on the β-aryl ring of these ketones and to investigate certain synthetic possibilities, we have now prepared the *cis* and *trans* forms of 1-cyclohexyl-2-(*o*-nitrophenyl)-3-benzoylethylenimine. A comparable study in the epoxyketone series has been reported.[3]

The reaction of cyclohexylamine with 2,3-dibromo-3-(*o*-nitrophenyl)-propiophenone[4] in benzene solution gave an 89% yield of a nearly 50–50 mixture of the *cis* (Ia) and *trans* (Ib) forms of the ethylenimine ketone. These racemic geometrical isomers were separated by column chromatography.[2] The higher-melting *cis* isomer (Ia) in this series was the more strongly absorbed on the alumina. This appears to be a general property of the *cis* forms of the ethylenimine ketones.[2,5]

The low-melting *trans* form (Ib) also was prepared in 64% yield from 2-nitrochalcone,[4] cyclohexylamine and iodine in benzene solution, using a procedure similar to that outlined by Southwick and Christman[6] for a related reaction.

The configurations of Ia and Ib were assigned by methods which have been described previously for analogous compounds.[1-3] The high-melting ethylenimine ketone isomer (Ia) reacted with phenylhydrazine in the presence of acetic acid in an alcohol–chloroform mixture to produce an 85% yield of 1,3-diphenyl-5-(*o*-nitrophenyl)-pyrazole (II).[3] Under similar conditions the low-melting isomer (Ib) gave what appeared to be, from elemental analysis

(1) (a) N. H. Cromwell, *et al.*, THIS JOURNAL, **73**, 1044 (1951); (b) N. H. Cromwell and M. A. Graff, *J. Org. Chem.*, **17**, 414 (1952).

(2) N. H. Cromwell and R. J. Mohrbacher, THIS JOURNAL, **75**, 6252 (1953).

(3) N. H. Cromwell and R. A. Setterquist, *ibid.*, **76**, 5752 (1954).

(4) R. Sorge, *Ber.*, **35**, 1065 (1902); W. Dilthey, L. Neuhaus and W. Schommer, *J. prakt. Chem.*, **123**, 235 (1930); I. Tanasescu and A. Georgescu, *ibid.*, **139**, 189 (1934).

(5) N. H. Cromwell, R. P. Cahoy, W. E. Franklin and G. D. Mercer, THIS JOURNAL, **79**, 922 (1957).

(6) P. L. Southwick and D. R. Christman, *ibid.*, **74**, 1886 (1952).