solidified on standing overnight. The solid was filtered and crystallized from 15 cc. of ethanol to give 7.73 g. of the pyridindene (XI), m.p. 245–248°. After recrystallization, it melted at 246–248 .

Anal. Calcd. for $C_{26}H_{22}NBr$: C, 67.41; H, 6.22. Found: C, 67.15; H, 6.29.

Acknowledgment. We are indebted to Dr. Al Steyermark for the microanalyses, to Mr. A. Motchane for the ultraviolet spectra, and to Mr. Pat Bevilacqua for technical assistance.

NUTLEY, N. J.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, CARNEGIE INSTITUTE OF TECHNOLOGY]

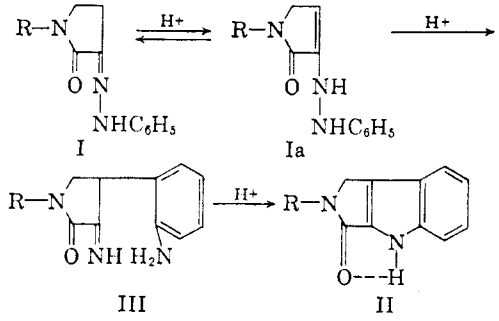
Synthesis of Compounds in the Pyrrolo[3,4-b]indole Series[1]

PHILIP L. SOUTHWICK AND RICHARD J. OWELLEN[2]

Received December 29, 1959

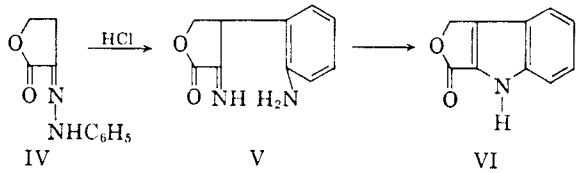
The previously unknown pyrrolo[3,4-b]indole ring system is represented in a series of compounds which were produced when the Fischer indole synthesis was conducted with phenylhydrazones of 1-substituted 2,3-dioxopyrrolidines (I). Seven 2-substituted 1,4-dihydropyrrolo[3,4-b]indol-3(2H)ones (II) have been prepared in this manner; the 2-substituents were *n*-propyl, *n*-butyl, cyclohexyl, phenyl, β-phenylethyl, β-phenylisopropyl, and homoveratryl. The three compounds containing the cyclohexyl, β-phenylethyl, and β-phenylisopropyl groups have been reduced with lithium aluminum hydride and converted into corresponding 2-substituted 1,2,3,4-tetrahydropyrrolo[3,4-b]indoles (VII).

Apparently no compounds containing the relatively simple fused-ring heterocyclic system of pyrrolo[3,4-b]indole have been described in the literature. The report of the preparation of two such compounds by Heller and Wunderlich[3] has been shown by Taylor and Kalenda[4] to be in error. The fact that other compounds containing the indole nucleus have been known to display a variety of interesting types of physiological activity provided the incentive for an attempt to prepare compounds of this class. It seemed possible that the ring system could be created by conducting the



Fischer indole synthesis using phenylhydrazones of 2,3-dioxopyrrolidines (I), a number of which had been prepared in this laboratory.[5]

The result of subjecting the phenylhydrazones I to the conditions of the Fischer indole synthesis was, however, considered subject to uncertainty because of reports in the literature regarding the course of acid-catalyzed reactions of certain similar compounds. Meyer and Vaughan[6] had shown that the phenylhydrazone of 1,5-diphenyl-2,3-dioxopyrrolidine rearranges to 1,5-diphenyl-Δ^2-pyrrazoline-3-carboxanilide when treated with hydrochloric acid, and this type of behavior might have proved general for phenylhydrazones of 2,3-dioxopyrrolidines. On the other hand, the work of Plieninger[7] with the phenylhydrazone of α-keto-γ-butyrolactone (IV) suggested that another interesting departure from the normal course of the Fischer indole synthesis might well be encountered. Compound IV, when treated with hydrogen chloride in acetic acid at 90°,



had yielded the hydrochloride of α-imino-β-*o*-aminophenyl-γ-butyrolactone (V). Compound V required treatment with a boiling mixture of concentrated hydrochloric and glacial acetic acids to undergo cyclization to the indole derivative VI. Whether the failure of compound V to undergo rapid spontaneous ring-closure to VI is the result of a steric or an electronic effect, the close resemblance

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(1) Supported principally by a research grant (RG-4371) from the National Institutes of Health, U. S. Public Health Service.

(2) National Science Foundation Cooperative Predoctoral Fellow, 1959–1960.

(3) G. Heller and P. Wunderlich, *Ber.*, **47**, 1617 (1914).

(4) E. C. Taylor, Jr., and N. W. Kalenda, *J. Org. Chem.* **18**, 1755 (1953).

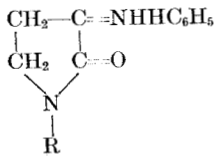
(5) (a) P. L. Southwick, E. P. Previc, Joseph Casanova, Jr., and E. Herbert Carlson, *J. Org. Chem.* **21**, 1087 (1956); (b) P. L. Southwick and R. T. Crouch, *J. Am. Chem. Soc.* **75**, 3413 (1953); (c) P. L. Southwick and L. L. Seivard, *J. Am. Chem. Soc.*, **71**, 2532 (1949). The concern expressed in ref. 5a over the possibility that the phenylhydrazine derivatives of the 2,3-dioxopyrrolidines might not represent the expected phenylhydrazone structure (or the related enhydrazine tautomeric form Ia) was evidently unwarranted. *Cf.* discussion by Meyer and Vaughan, ref. 6.

(6) W. L. Meyer and W. R. Vaughan, *J. Org. Chem.* **22**, 1565 (1957).

(7)(a) H. Plieninger, *Ber.* **83**, 273 (1950); (b) H. Plieninger and I. Nógrádi, *Ber.*, **88**, 1965 (1955).

TABLE I

1-SUBSTITUTED 2,3-DIOXOPYRROLIDINE PHENYLHYDRAZONES,



R	M.P., °	Yield,[b] %	Starting Material,[b] g.	Hydrolysis Mixture Volume,[b] ml.	Hydrolysis Mixture HCl concn., %	Heating Period, min.	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found[c]
n-C_3H_7—	205–207	9(A)	15(A)	600	10	90	67.50	67.18	7.41	7.29	18.17	19.70 17.54
n-C_4H_9—	193–194[a]	56(B)	20(B)	400	20	60						
cyclo-C_6H_{11}—	213–214[a]	47(A) 63(B)	30(A) 30(B)	170	37	50						
C_6H_5—	218–219	19(A)	10(A)	500	10	240	72.40	72.42	5.70	5.39	15.84	14.78
$C_6H_5CH_2CH_2$—	213–214[a]	60(A) 37(B)	50(A) 50(B)	1000	20	60						
$C_6H_5CH_2CH(CH_3)$—	178–179	50(A) 42(B)	15(A) 25(B)	240(A)[d] 400(B)[e]	25	90	74.24	74.56	6.89	6.94	13.67	14.17 13.30
3,4-$(CH_3O)_2C_6H_3(CH_2)_2$—	206–207	48(A) 38(B)	20(A) 15(B)	500	20	60	67.97	68.48	6.56	6.42	11.89	11.6

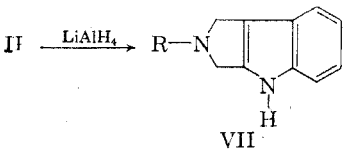
[a] Characterization of these compounds is described in ref. 5a. [b] The letters in parentheses following the figures in these columns indicate the procedure (A or B) for which the value is given. [c] Nitrogen analyses on these phenylhydrazones have been erratic, but no explanation of the difficulty is apparent. [d] Ethanol (15 ml.) was added to increase the solubility of the starting material. [e] Ethanol (25 ml.) was added.

in structure of V to the expected intermediate III in the conversion of I to II suggested that III might also prove stable. Such a result could have complicated the synthesis of the pyrrolo[3,4-b]indole derivatives II but would have been of interest as another of the rare instances in which an intermediate could be isolated in the Fischer indole synthesis.

The phenylhydrazones of seven 1-substituted 2,3-dioxopyrrolidines (I) (see Table I) have been prepared and subjected to treatment in acetic acid solution with dry hydrogen chloride (Plieninger's procedure for preparing Compound V) or with concentrated aqueous hydrochloric acid at the boiling point. Under either set of conditions a rapid reaction occurred. It was apparent from the composition of the products obtained in this way that they were not simply rearrangement products, either of the type III or of the type encountered by Meyer and Vaughan; the elimination of one nitrogen (as ammonium chloride) from the molecule indicated that the reaction which had occurred was the Fischer indole synthesis. The yields of 2-substituted 1,4-dihydropyrrolo[3,4-b]indol-3(2H)ones (II) produced (see Table II) were good enough (59–86%) to make the reaction of preparative value. It was not possible to isolate an intermediate of the type III; cyclization occurred even at 30° in glacial acetic acid containing hydrogen chloride. Data concerning the preparation and characterization of the seven compounds of type II which were prepared are given in Table II.

The assignment of structure II to these products was supported not only by their composition and method of preparation, but also by their properties. All were stable, high-melting compounds of insufficient basicity to yield salts with aqueous acids. The infrared spectra of the compounds (measured in Nujol mulls) showed broad N–H bands at the relatively long wave length of 3.19 μ (overlapping, on the long wave-length side, the aromatic C–H bands), and the band for the lactam carbonyl was displaced to 6.01–6.03 μ from its position at 5.86 μ in the parent 2,3-dioxopyrrolidines. Conjugation with a carbon to carbon double bond has probably shifted the carbonyl band, and it seems reasonable to assume that the positions of both carbonyl and N–H absorptions may have been influenced by the opportunity for intramolecular hydrogen bonding as pictured in formula II.

To obtain compounds in the series with basic properties and some likelihood of showing physiological activity, reduction of the lactam carbonyl of the compounds II with lithium aluminum hydride was undertaken. Attempts to bring about the reduction according to the usual procedures were unsuccessful. In order to secure higher reaction temperatures a procedure was adopted in which the reaction mixtures were prepared in the usual way with ether as the solvent, then were diluted with dry toluene and distilled until the ether was removed and the reflux temperature had reached 110°. Under these conditions reduction was accomplished during a heating period of 1 to 3.5 hours. The yields of 2-substituted 1,2,3,4-tetrahydropyrrolo[3,4-b]indoles (VII), however, were only fair (47–52%). The data relating to the preparation and characterization of the compounds VII are given in Table III. When treated with aqueous hydrochloric acid, these substances formed sparingly soluble hydrochlorides and were characterized in this form. The free bases darkened when exposed to the air. The hydrochlorides appeared to be quite stable but were not easily freed of colored impurities developed during manipulation of the compounds in the basic form. Susceptibility to air oxidation has been observed in other compounds in which the carbon atoms of the 2- and 3-positions of the indole nucleus are incorporated into a fused ring which is not aromatic.[8]



VII

The assigned structure (VII) for these compounds is supported by ultraviolet spectroscopic data. The spectrum of the member of the group in which R is β-phenylethyl was measured in 95% ethanol. (The compound was dissolved as the hydrochloride and the free base was liberated with sodium hydroxide.) Comparison with a similarly determined spectrum of 1,2,3,4-tetrahydrocarbazole revealed a striking similarity. Structure VII showed maxima at 225 mμ (ϵ 38,100) and 277 mμ (ϵ 7500) with an inflection at *ca.* 289 mμ (ϵ 5750). The minimum was at 245 mμ (ϵ 2450). Tetrahydrocarbazole showed maxima at 228 mμ (ϵ 33,400) and 283 mμ (ϵ 7100) with a marked inflection almost amounting to another maximum at 291 mμ (ϵ 6100). There was a minimum at 250 mμ (ϵ 2000).

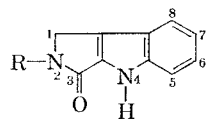
The infrared spectrum in chloroform of the same new compound (VII. R = β-phenylethyl) in the hydrochloride form showed no carbonyl band, and an N–H band (sharp) was observed at 2.87 μ, as was expected for an indole N–H. (The N–H band for 1,2,3,4-tetrahydrocarbazole was found at 2.89 μ in chloroform.) There should be no reason to doubt that the desired compounds of the structure VII have been obtained.

The 2,3-dioxopyrrolidines from which the phenylhydrazones (I) were obtained were themselves prepared by the acid hydrolysis of 4-carbethoxy-2,3-dioxopyrrolidines.[5] In most cases the 2,3-dioxo-

(8) See (a) B. Witkop and J. B. Patrick, *J. Am. Chem. Soc.* **73**, 2188, 2196 (1951); (b) B. Witkop, J. B. Patrick, and M. Rosenblum, *J. Am. Chem. Soc.* **73**, 2641 (1951); (c) R. B. Carlin and M. S. Moores, *J. Am. Chem. Soc.*, **81**, 1259 (1959). References to earlier literature on autoxidation of indoles are cited in these papers.

TABLE II

2-SUBSTITUTED 1,4-DIHYDROPYRROLO[3,4-b]INDOL-3(2H)ONES

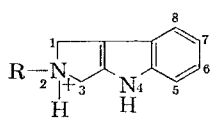


R	M.P., °	Yield,[a] %	Starting Material,[a] g.	Reaction Mixture: Volume[a] of HCl soln., ml.	Reaction Mixture: Volume[a] of HOAc, ml.	Heating[a] Period, min.	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen Calcd.	Nitrogen Found
n-C_3H_7—	207–208	68(B)	0.8(B)	—	8(B)	5(B)	72.87	72.44	6.59	6.19	—	
n-C_4H_9—	216–218	76(A)	12(A)	15(A)	50(A)	20(A)	73.65	73.59	7.06	6.94	12.27	12.18
cyclo-C_6H_{11}—	251–253	59(A)	20(A)	70(A)	100(A)	10(A)	75.56	75.73	7.31	7.24	11.02	10.9
C_6H_5	303–305	71(A)	1.5(A)	7(A)	20(A)	15(A)	77.40	77.80	4.87	4.68	11.28	11.25
$C_6H_5CH_2CH_2$—	253–254	85(A)	20(A)	50(A)	200(A)	30(A)	78.23	77.77	5.84	5.79	10.14	10.22
		69(B)	20(B)	—	200(B)	15(B)		78.05		5.83		
$C_6H_5CH_2CH(CH_3)$—	159–160[b]	80(A)	8(A)	15(A)	50(A)	15(A)	78.59	78.21	6.25	6.23	9.65	9.95
3,4-$(CH_3O)_2C_6H_3(CH_2)_2$—	216–217	68(B)	17(B)	—	300(B)	15(B)	71.41	71.46	5.99	6.08	8.33	8.24

[a] The letters in parentheses following the figures in these columns indicate the procedure (A or B) for which the value is given. [b] Recrystallized from a 1:1 isopropyl alcohol-acetone mixture. $[\alpha]_D = +168°$ (c 1.5, acetone).

TABLE III

HYDROCHLORIDES OF 2-SUBSTITUTED 1,2,3,4-TETRAHYDROPYRROLO[3,4-b]INDOLES,



Cl⁻

R	M.P.,[a]	Yield, %	Starting Material, g.	Weight of $LiAlH_4$, g.	Heating Period, hr.	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
cyclo-C_6H_{11}—	206–207[b]	50	15	13.5	3.5	69.42	68.90	7.65	7.49	10.12	10.0
$C_6H_5CH_2CH_2$—	207–208	52	18	21	2.5	72.35	72.19	6.41	6.39	9.38	9.28
$C_6H_5CH_2CH(CH_3)$—	219–220[c]	47	7	7	1	72.94	72.44	6.77	6.59	8.96	8.82

[a] These compounds melted with decomposition. [b] A picrate, m.p. 175–177° dec. was obtained by treating the hydrochloride with picric acid in ethanol. *Anal.* Calcd. for $C_{22}H_{23}N_5O_7$: C, 56.28, H, 4.94. Found: C, 56.53, H, 4.89. [c] $[\alpha]_D$ +88.2° (c 0.4, 95% ethanol).

pyrrolidines were isolated in the crude form but were not purified prior to conversion to the phenylhydrazones. In other cases it was desirable to prepare the phenylhydrazone in the hydrolysis mixture without isolating the 2,3-dioxopyrrolidine at all. This could be done by reducing the acidity of the solutions to *p*H 4–5 by addition of sodium acetate, then adding the requisite amount of phenylhydrazine. Both procedures are described in the Experimental. Also described are two new 1-substituted 4-carbethoxy-2,3-dioxopyrrolidines which were prepared during the present investigation. One, in which the 1-substituent was β-(3,4-dimethoxyphenyl)ethyl, was obtained from homoveratrylamine. The second, in which the 1-substituent was β-phenylisopropyl, was an optically active compound obtained from *d*-β-phenylisopropylamine, and led to a series of optically active products.

Three of the compounds (II. R = β-phenylethyl and III. R = phenylethyl or cyclohexyl) have been tested in the screening program of the Cancer Chemotherapy National Service Center, but did not show significant antitumor activity. Other tests of possible physiological activity are in progress.

EXPERIMENTAL[9]

1-Substituted 2,3-dioxopyrrolidine phenylhydrazones (I). *Procedure A.* 1-Substituted 4-carbethoxy-2,3-dioxopyrrolidines were hydrolyzed and decarboxylated by treating the compounds with refluxing hydrochloric acid solutions.[5] The quantities of materials used and other details of the individual experiments are recorded in Table I. The crude 2,3-dioxopyrrolidines were taken up in chloroform by three extractions of the hydrolysis mixtures. The chloroform solutions were dried over magnesium sulfate, filtered, and evaporated under reduced pressure on a steam cone. The resulting residues were dissolved in 95% ethanol (5 ml. per g. of 2,3-dioxopyrrolidine) and a few drops of glacial acetic acid were added, followed by the calculated amount of phenylhydrazine (calculated on the basis of the amount of 4-carbethoxy-2,3-dioxopyrrolidine hydrolyzed). The mixtures were heated to boiling on a steam bath, then allowed to cool. After further cooling in an ice bath, the crystalline products were removed by filtration and recrystallized from 95% ethanol. Yields in Table I are for recrystallized products.

Procedure B. In procedure B the 1-substituted 4-carbethoxy-2,3-dioxopyrrolidines were hydrolyzed and decarboxylated as in procedure A. At the end of the reflux period the aqueous acid solution was cooled and filtered. Sodium acetate was then added until the *p*H of the solution became 4 to 5. The calculated amount of phenylhydrazine for the quantity of 4-carbethoxy-2,3-dioxopyrrolidine hydrolyzed was then added while the mixture was vigorously stirred. Separation of the phenylhydrazone usually began at once and appeared to be complete after a few minutes. The product was collected by filtration and recrystallized from 95% ethanol. The amounts of materials used and other details of individual experiments are recorded in Table I.

2-Substituted 1,4-dihydropyrrolo[3,4-b]indol-3(2H)ones (II). *Procedure A.* The 1-substituted 2,3-dioxopyrrolidine phenylhydrazones (I) were treated with refluxing mixtures of concd. hydrochloric acid and glacial acetic acid. Heating was continued until the phenylhydrazones dissolved and for approximately 10 min. thereafter. (The total reaction times ranged from 15 to 30 min.) Several of the products separated as crystalline precipitates when the reaction mixtures were cooled, and were then collected by filtration. In other cases the cooled reaction mixture was diluted with an equal volume of water and cooled in an ice bath to induce separation of the product. The compounds were purified by crystallization from 95% ethanol. Details of individual experiments are recorded in Table II.

Procedure B. The 1-substituted 2,3-dioxopyrrolidine phenylhydrazones (I) were suspended in glacial acetic acid which was kept at the boiling point under a reflux condenser. A slow stream of dry hydrogen chloride was passed into the mixture while refluxing was continued and the phenylhydrazones dissolved. After a reflux period of 5 to 15 min. the solution was cooled and filtered, either directly or after dilution with water, to collect the products, which were then recrystallized from 95% ethanol. Details of these experiments are also included in Table II.

2-Substituted 1,2,3,4-tetrahydropyrrolo[3,4-b]indole hydrochlorides (VII). The 1,4-dihydropyrrolo[3,4-b]indol-3(2H)-ones (II) were added in solid form in small portions to vigorously stirred solutions or suspensions of excess lithium aluminum hydride in ether (7 to 21 g. of lithium aluminum hydride in 100 ml. of dry ether). After about 10 min. of stirring, 300 ml. of dry toluene was added. The ether was then removed from the reaction mixture by distillation through a short packed column. After the temperature of the distilling vapors reached 110°, the distilling column was replaced by a reflux condenser, and heating and stirring under reflux were continued for an additional period of time to complete the reduction.

The mixture was cooled and the excess lithium aluminum hydride was destroyed by cautious addition of water while the mixture was kept in an ice bath. The cold mixture was then acidified by addition of a considerable excess of 20% hydrochloric acid while ice bath cooling was maintained. Stirring was continued for an additional 30 min. to dissolve all of the inorganic reaction products. The hydrochlorides of the tetrahydropyrrolo[3,4-b]indoles (VII), which were not soluble in either the aqueous or the organic phase of the mixtures, were then collected by filtration of the mixtures through a pad of glass wool. The products were purified by crystallization from 95% ethanol. (Yields quoted are for products obtained after one recrystallization.) The characterization of individual compounds and details of their preparation are given in Table III.

1-Homoveratryl-4-carbethoxy-2,3-dioxopyrrolidine. The previously recommended one-step procedure[5a] for similar compounds was modified by using excess sodium ethoxide and slightly simplifying the method of isolating the product. A solution of 78 g. (0.42 mole) of homoveratrylamine and 42 g. (0.42 mole) of ethyl acrylate in 200 ml. of absolute ethanol was allowed to stand overnight. Ethyl oxalate (61.3 g.; 0.42 mole) was added and the mixture was stirred while a solution of sodium ethoxide prepared from 15 g. (0.695 g.-atom) of sodium and 250 ml. of absolute ethanol was added slowly. The mixture was heated under reflux and stirred for 2 hr., then cooled in an ice bath. Water (100 ml.) was added and the mixture was acidified to a *p*H of less than 2 by careful addition of 20% aqueous hydrochloric acid while cooling and stirring were continued. The crude product which precipitated was removed by filtration and dried. The yield was 123 g. (88%) of a light-tan product melting at 127–128°. Recrystallization from 95% ethanol did not change the melting point.

(9) Melting points are uncorrected. Microanalyses by Drs. G. Weiler and F. B. Strauss, Oxford, England, and Geller Microanalytical Laboratories, Bardonia, N. Y. Infrared spectra were determined with a Perkin-Elmer model 21 spectrophotometer, ultraviolet spectra with a Cary recording spectrophotometer.

Anal. Calcd. for $C_{17}H_{21}NO_6$: C, 60.88; H, 6.31; N, 4.18. Found: C, 60.53; H, 6.17; N, 4.23.

d-1-(β-Phenylisopropyl)-4-carbethoxy-2,3-dioxopyrrolidine. The compound was prepared by the one-step procedure previously described.[5a] From 78 g. (0.58 mole) of *d*-β-phenylisopropylamine, 90 g. (59% yield) of the 4-carbethoxy-2,3-dioxopyrrolidine was obtained. After recrystallization from an ethanol-water mixture white needles were obtained, m.p. 115–116°, $[\alpha]_D = +75.48°$ (c 4.0, 95% ethanol).

Anal. Calcd. for $C_{16}H_{19}NO_4$: C, 66.42; H, 6.62. Found: C, 66.55; H, 6.81.

PITTSBURGH 13, PA.

[CONTRIBUTION FROM THE WILLIAM H. CHANDLER CHEMISTRY LABORATORY LEHIGH UNIVERSITY]

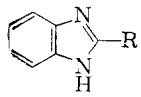
Study of the Synthesis and Chemistry of the 5,6-Dihydroimidazo[ij]quinoline Series[1]

ALFRED RICHARDSON, JR.,[2] AND E. D. AMSTUTZ

Received September 23, 1959

A series of 2-substituted 5,6-dihydroimidazo[ij]quinolines has been synthesized by the condensation of 8-amino-1,2,3,4-tetrahydroquinoline with carboxylic acids or their derivatives. These condensations may lead directly to the final product or to amides which may be subsequently cyclized. In general, the amino-amides are obtained and isolated in the case of substituted or unsubstituted aromatic acid chlorides. Attempts to form 2-substituted imidazo[ij]quinolines from 8-amino-1,2-dihydroquinoline led only to 8-amidoquinolines. Certain pyridoquinoxalines were synthesized from 8-amino-1,2,3,4-tetrahydroquinoline and benzoin-type compounds. The spectra of the dihydroimidazo[ij]quinolines are similar to those of the benzimidazoles.

In view of the fairly wide range of physiological activities shown by benzimidazole (I.R = H) and its derivatives, it was of interest to prepare a series of derivatives of the related 5,6-dihydroimidazo-[ij]quinolines (II). This paper describes the synthetic methods employed in the preparation of a variety of new members of this virtually unexplored group.



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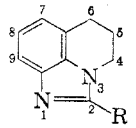

II

The first synthesis of a 5,6-dihydroimidazo-[ij]quinoline was realized by Kunckell,[3] who condensed 8-amino-6-bromo-1,2,3,4-tetrahydroquinoline with acetic acid. The product he obtained was 8-bromo-2-methyl-5,6-dihydroimidazo[ij]quinoline. Other earlier workers[4–12] synthesized compounds in this series where the 2-substituent was an alkyl group sometimes containing hydroxyl groups or aromatic residues. The diamine usually was 8-amino-1,2,3,4-tetrahydroquinoline, although at times, an 8-amino-1,2,3,4-tetrahydroquinoline was employed which contained substituents on the aromatic ring.[6–9] In most cases, the appropriate diamine was heated with the corresponding acid in the absence of solvent,[4–9] although a few members of the series were synthesized by condensing an 8-amino-1,2,3,4-tetrahydroquinoline with aliphatic aldehydes and ketones.[10–12]

Although simple amidines are readily hydrolysed in aqueous acid,[13] the dihydroimidazoquinolines, which are essentially cyclic amidines, are stable in a refluxing 4*N* hydrochloric acid medium and many can be prepared by its use. This inertness toward acid hydrolysis is apparently due to a resonance stabilization of the benzimidazole system.

Tables I and II list the dihydroimidazo[ij]-quinolines and benzimidazoles synthesized during this research, while the condensation procedures are discussed in detail in the paragraphs which follow.

Condensations with carboxylic acids.[16] The methods used in condensing 8-amino-1,2,3,4-tetrahydroquinoline with carboxylic acids were either to reflux in 4*N* hydrochloric acid or to heat the reactants without a solvent. Other methods which were attempted without success were heating in

(1) Abstracted from a thesis submitted by A. Richardson, Jr., in partial fulfillment of the requirements for the Ph.D. degree.

(2) Present address: The Wm. S. Merrell Company, Cincinnati 15, Ohio.

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