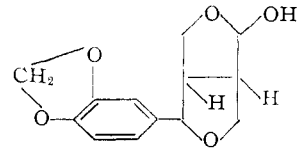


Preparation of samin from a *trans* nucleus would involve rotation about positions 1–5 followed by ring closure. Treatment of samin with excess sesamol in the presence of hydrochloric acid should regenerate sesamolin only if sesamolin existed originally in the *cis* form. Unfortunately the author thus far has been unable to prepare this compound.

Inasmuch as the isolation of the optical antipode of dilactone III had not been reported, this dilactone was isolated from asarinin, a diastereoisomer of sesamin. Its properties were identical with those of the dilactone from sesamin and sesamolin except for its optical rotation, which was negative by an approximately equal amount. Since the dilactones derived from sesamin and asarinin, like that from pinoresinol, are optically active, their nuclei also must have the *cis* configuration.

The *dl*-dilactone prepared by mixing equal weights of the optically active dilactones derived from sesamolin and asarinin melted at 137–138°. Michael and Ross, who first synthesized this compound, reported a m.p. of 138° for their product.[7]

Experimental

Permanganate Oxidation of Sesamolin.—0.92 gram of sesamolin, dissolved in 25 ml. of acetone, was heated under reflux for 8 hours while 3.3 g. of potassium permanganate was added in small portions, each portion being decolorized prior to the next addition. After standing overnight, the acetone solution was filtered from the manganese dioxide and evaporated. The manganese dioxide was not discarded. The residue was taken up in water plus some 1 *N* potassium hydroxide. The ether extract of this solution yielded 600 mg. of unchanged sesamolin after evaporation and crystallization. The extracted alkaline solution was concentrated and then acidified with hydrochloric acid. An amorphous material and a small quantity of crystals were deposited, but these products were not readily characterizable.

The manganese dioxide was washed with hot water and the alkaline filtrate acidified with hydrochloric acid. After standing overnight crystals formed. The solution and crystals were extracted several times with ether; the ether layer was extracted twice with 1 *N* potassium hydroxide and the resulting aqueous layer acidified with hydrochloric acid. After several extractions of the acidified solution with ether, the ether layer was dried over sodium sulfate and evaporated. The residue was taken up in a small amount of methanol, and water was added until a slightly turbid solution formed when the mixture was heated in hot water. After standing overnight, crystals melting at 227° were obtained. The melting point of a mixture of these crystals with authentic piperonylic acid, m.p. 228°, was not depressed; neut. equiv. 168, theory for piperonylic acid 166. The ultraviolet spectrum from 225–315 mμ agreed with that of piperonylic acid.

Dilactone from Sesamolin.—One gram of sesamolin was rubbed up in a mortar with 18 ml. of concentrated nitric acid. The sesamolin reacted rapidly with the liberation of oxides of nitrogen. The clear solution was allowed to remain overnight and then evaporated *in vacuo* (water-pump) on an 80° water-bath until the residue was a froth. After the addition of about 50 ml. of water, a precipitate formed which was filtered off and discarded. The solution was neutralized to *p*H 5–6 and again filtered. The filtrate then was extracted once with about 5 ml. of chloroform (discarded) and eight times with 60-ml. portions of chloroform. After drying over sodium sulfate, the combined chloroform extracts were completely evaporated. The residue (120 mg.) was taken up in hot benzene and after being filtered, concentrated and cooled, crystals appeared. These crystals were filtered off and washed with dry ether; yield 85 mg. (22%), $[\alpha]^{36}D$ +210° (*c* 1.01) in water, m.p. 160–161°, sapon. equiv. 73 (theory 71).

Anal. Calcd. for $C_6H_6O_4$: C, 50.7; H, 4.3. Found: C, 51.00; H, 4.33.

The melting point of the dilactone was undepressed in admixture with that obtained from dibromosesamin by following the procedure of Erdtman and Gripenberg[2] with the dimethyl ether of dibromopinoresinol.

Dilactone from Sesamin.—By following the procedure used for sesamolin, the same dilactone was obtained from sesamin.

Dilactone from Asarinin.—The procedure for sesamolin was used to obtain the dilactone from asarinin except that the reaction mixture was heated on a steam-bath for one hour after the asarinin had been rubbed up with the nitric acid. Only 17 mg. of the dilactone was obtained from 1 g. of asarinin, m.p. 160–161°, $[\alpha]^{30}D$ −204 (*c* 0.49), sapon. equiv. 73 (theory 71).

***dl*-Dilactone.**—Equal weights of the dilactones from sesamolin and asarinin were dissolved in hot benzene. After slow evaporation of the solvent the crystals melted at 137–138°.

BELTSVILLE, MD.

[CONTRIBUTION FROM THE DEPARTMENT OF PHARMACOLOGY, HARVARD MEDICAL SCHOOL]

The Synthesis of 1,3,4,5-Tetrahydrobenz[cd]indole

BY FREDERICK C. UHLE, CLIFFORD G. VERNICK AND GASTON L. SCHMIR

RECEIVED JANUARY 4, 1955

5-Nitrotetralin (I) has been treated with ethyl oxalate to yield 8-nitro-1,2,3,4-tetrahydro-1-naphthaleneglyoxylic acid (II) which, on reduction with ferrous hydroxide, has afforded 2-carboxy-1,3,4,5-tetrahydrobenz[cd]indole (III). The tricyclic derivative III lost carbon dioxide in acid solution to give 1,3,4,5-tetrahydrobenz[cd]indole (IV) which was obtained, as well, by cyclization of N-formyl-1,2,3,4-tetrahydro-5-naphthylamine in the presence of potassium *t*-butoxide.

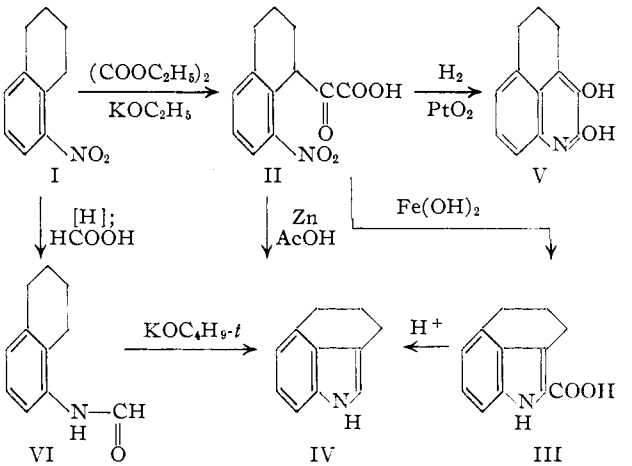
Among the natural products which fall into the classification of indole derivatives, the sole representative of a polynuclear system characterized by cyclization into the 4-position remains lysergic acid, the complex amino acid obtained by hydrolytic cleavage of the ergot alkaloids. One of the major problems encountered in attempts to construct the ergoline skeleton of lysergic acid derives from the difficulty of elaboration of this unique 3,4-trimethyleneindole mode of ring fusion for which there was no precedent in the earlier development of heterocyclic chemistry. The relatively indifferent nature of the 4-position in indole itself, as well as the frequent inaccessibility of appropriate 1,2,3-trisubstituted benzene derivatives desired as intermediates, has limited rather markedly the number of approaches practicable for extended synthetic work.

1,3,4,5-Tetrahydrobenz(cd)indole, the tricyclic substance IV, which may be regarded as the parent compound of the more complex, tetracyclic ergoline derivatives, was prepared first[1] by sodium–butanol reduction of naphthostyril, under reaction conditions which led to the production, in a quantity equal to that of the desired indole, of 8-amino-1,2,3,4-tetrahydro-1-naphthalenemethanol, the amino alcohol derived by reductive cleavage of the lactam function. A second preparation[2] of the 3,4-trimethyleneindole (IV), by Wolff–Kishner or by Clemmensen reduction of 5-keto-1,3,4,5-tetrahydrobenz(cd)indole, concerned the utilization of the substance as a reference compound in the establishment of structure of the cyclization product of β-(4-carboxy-3-indole)-propionic acid. Subsequently, the tricyclic 5-keto derivative was made available by an alternative sequence involving isomerization of 5-hydroxy-1,2-dihydrobenz(cd)indole in the presence of palladium.[3]

In the course of exploratory studies designed to evaluate projected synthetic routes to lysergic acid and related substances, two additional methods for the preparation of 1,3,4,5-tetrahydrobenz(cd)indole have been developed.

According to the first of these procedures, 5-nitro-1,2,3,4-tetrahydronaphthalene (I)[4] was allowed to react with ethyl oxalate in ether solution, in the presence of potassium ethoxide, to yield 8-nitro-1,2,3,4-tetrahydro-1-naphthaleneglyoxylic acid (II). This keto acid derivative was transformed, with ferrous hydroxide, or with sodium hydrosulfite, to 2-carboxy-1,3,4,5-tetrahydrobenz(cd)indole (III) which readily lost carbon dioxide when maintained for relatively short periods of time in ethanol solution at reflux temperature, in the presence of hydrochloric acid, to give 1,3,4,5-tetrahydrobenz(cd)indole (IV).[5] Reduction of II with zinc dust and acetic acid at 118° led to the production of a mixture of III and the decarboxylation product IV.

When the glyoxylic acid derivative II, or its ethyl ester, was submitted to hydrogenation in acetic acid solution in the presence of platinum oxide, the indolecarboxylic acid III, which was isolated in 30% yield, was accompanied by an isomeric product, formed in the amount of 50% of the theory. On the basis of solubility behavior, color tests and spectroscopic evidence, this higher melting isomer has been assigned the 2,3-dihydroxyquinoline formulation V.[6]



Condensation of I with ethyl formate proceeded less readily than did the related reaction in the case of ethyl oxalate, and, in view of the facile decarboxylation of the indolecarboxylic acid III, optimal conditions for the formylation were not determined. The oxime of the glyoxylic acid derivative II, on treatment with acetic anhydride at 140°, afforded 8-nitro-1,2,3,4-tetrahydro-1-naphthonitrile.[7]

According to a second scheme, 1,2,3,4-tetrahydro-5-naphthylamine[8] was transformed with formic acid at reflux temperature to the N-formyl derivative VI, which, when allowed to react with potassium *t*-butoxide at elevated temperature, afforded 1,3,4,5-tetrahydrobenz(cd)indole (IV).[9]

Experimental[10]

8-Nitro-1,2,3,4-tetrahydro-1-napthaleneglyoxylic Acid (II).—To a quantity of 1.56 g. (0.04 mole) of potassium covered with 40 ml. of anhydrous ether, was added, cautiously and in eight, successive, equal portions, a total of 7.35 g. (0.16 mole) of absolute ethanol. When the metal had dissolved entirely, 5.84 g. (0.04 mole) of ethyl oxalate was added, followed by a solution of 7.09 g. (0.04 mole) of 5-nitrotetralin (I)[4] in 10 ml. of ether. The mixture, which became colored red-brown within ten minutes and a deep purple after a period of one hour, was allowed to stand at ordinary temperature for 18 hours. The highly pigmented solution then was added to a well-agitated solution of 20 g. of potassium bicarbonate in a mixture of 400 ml. of methanol and 200 ml. of water. After the whole had been allowed to stand at ordinary temperature for 20 hours, the methanol was distilled under diminished pressure and the residue extracted with ether. The aqueous phase from the ether extraction was acidified with 35 ml. of 6 *N* sulfuric acid and the only slightly turbid mixture extracted with a number of successive portions of ether. The residue from the washed and dried ether solution was recrystallized from benzene.

(1) W. A. Jacobs and G. Gould, *J. Biol. Chem.*, **120**, 141 (1937).

(2) F. C. Uhle, THIS JOURNAL, **71**, 761 (1949).

(3) C. A. Grob and J. Voltz, *Helv. Chim. Acta*, **33**, 1796 (1950).

(4) G. Schroeter, *Ann.*, **426**, 39 (1922).

(5) The rather extraordinary dissimilarity in degree of stability of substituted indole-2-carboxylic acids is worthy of note. Representative examples extend from the rather labile III of the present work, through substances which evolve carbon dioxide at the melting point, *e.g.*, 6-methoxyindole-2-carboxylic acid and 3-methyl-6-methoxyindole-2-carboxylic acid (W. O. Kermack, W. H. Perkin, Jr., and R. Robinson, *J. Chem. Soc.*, 1602 (1921)), to 4-bromoindole-2-carboxylic acid which failed to decarboxylate under any of the circumstances tested (J. A. Barltrop and D. A. H. Taylor, *ibid.*, 3399 (1954)). However, the great diversity of experimental conditions selected, or, in any case, reported, by various investigators renders generalization and interpretation difficult.

(6) This finding recalls the experience of W. Madelung, *Ber.*, **45**, 3521 (1912), who observed the formation of a mixture of indole-2-carboxylic acid and 2,3-dihydroxyquinoline when *o*-methyloxanilic acid was treated with sodium ethoxide at 360°, and of W. O. Kermack, W. H. Perkin, Jr., and R. Robinson, *J. Chem. Soc.*, 1610 (1921), who obtained a 2% yield of 3-methoxy-4-methylcarbostryil, in addition to the principal product, 3-methylindole-2-carboxylic acid, on zinc–acetic acid reduction of the methylation product of ethyl *o*-nitrophenylpyruvate.

(7) *Cf.* P. L. Julian and B. M. Sturgis, THIS JOURNAL, **57**, 1126 (1935); N. Campbell and J. E. McKail, *J. Chem. Soc.*, 1251 (1948); and R. D. Haworth and T. Richardson, *ibid.*, 120 (1935), for instances of the characteristic behavior of α-oximino acids in the presence of acetic anhydride.

(8) A. G. Green and F. M. Rowe, *ibid.*, 955 (1918).

(9) This transformation was carried out independently in 5% yield, by J. A. Barltrop and D. A. H. Taylor, who record their experience in a paper, *ibid.*, 3403 (1954), which came to attention after the present manuscript had been prepared.

(10) All melting points were carried out on the micro-hot-stage and are corrected. Microanalyses by Dr. S. M. Nagy and associates of the Massachusetts Institute of Technology, Cambridge, Mass.

The substance formed large, gem-like, pale-yellow crystals which apparently contained solvent of crystallization; yield 2.0 g. (20%), m.p. 117–118°.

Anal. Calcd. for $C_{12}H_{11}NO_5$: C, 57.83; H, 4.45; N, 5.62. Found: C, 57.64; H, 4.23; N, 5.70.

The yield was not augmented when the reaction was conducted in the presence of pyridine.

The neutral fraction, obtained by concentration of the ether extract from the potassium bicarbonate hydrolysis, was dissolved in methanol, from which separated, after 24 hours at ordinary temperature, 0.70 g. (10%) of a slightly soluble substance to which has been assigned the structure 8,8'-dinitro-1,1'-bi-1,2,3,4-tetrahydronaphthyl.[11] The material was recrystallized from methanol; m.p. 177–191°.

Anal. Calcd. for $C_{20}H_{20}N_2O_4$: C, 68.16; H, 5.72; N, 7.95. Found: C, 68.44; H, 5.93; N, 7.83.

Concentration of the methanol mother liquors and maintenance at 0° for an extended period led to the crystallization of unchanged 5-nitrotetralin in good recovery.

8-Nitro-1,2,3,4-tetrahydro-1-naphthaleneglyoxylic Acid Oxime.—To a solution of 250 mg. (0.001 mole) of the acid II in 3 ml. of absolute ethanol was added 416 mg. (0.006 mole) of hydroxylamine hydrochloride and 588 mg. (0.006 mole) of anhydrous potassium acetate. After the solution had been maintained under reflux for a period of 72 hours, the ethanol was distilled under diminished pressure, water was added and the mixture clarified by filtration. The filtrate was acidified with 1 ml. of 6 *N* hydrochloric acid solution and allowed to remain at 0° for 24 hours. The crystalline precipitate then was collected by filtration and recrystallized from a mixture of ethanol and water; yield 120 mg. (46%), m.p. 160–162° with ebullition.

Anal. Calcd. for $C_{12}H_{12}N_2O_5$: C, 54.54; H, 4.58; N, 10.60. Found: C, 54.95; H, 4.88; N, 10.80.

8-Nitro-1,2,3,4-tetrahydro-1-naphthonitrile.—A solution of the oxime of the glyoxylic acid derivative II in acetic anhydride was maintained at reflux temperature for a period of 30 minutes. The residue from distillation of the acetic anhydride under diminished pressure was recrystallized from methanol and, finally, from a mixture of methanol and water; m.p. 94–96°.

Anal. Calcd. for $C_{11}H_{10}N_2O_2$: C, 65.33; H, 4.98. Found: C, 64.85; H, 5.24.

Ethyl 8-Nitro-1,2,3,4-tetrahydro-1-naphthaleneglyoxylate.—A solution of 750 mg. (0.003 mole) of the acid II in a mixture of 10 ml. of absolute ethanol and 300 mg. of concentrated sulfuric acid was allowed to remain at ordinary temperature for a period of 48 hours. A portion of the ethanol was distilled under diminished pressure, after which the residue was dissolved in ether and extracted with a dilute, aqueous solution of potassium bicarbonate. The residue from the dried ether solution was recrystallized from a mixture of benzene and petroleum ether; yield 650 mg. (78%), m.p. 61–62°.

Anal. Calcd. for $C_{14}H_{15}NO_5$: C, 60.64; H, 5.45; N, 5.05. Found: C, 60.31; H, 5.51; N, 5.56.

When a solution of the ester in absolute ether was added to an equivalent quantity of potassium ethoxide in ether, a dark, purple solution of the enolate was produced.

2-Carboxy-1,3,4,5-tetrahydrobenz(cd)indole (III).—A solution of 2.49 g. (0.01 mole) of the acid II in 3.5 ml. (0.01 mole) of 3 *N* aqueous potassium hydroxide solution was added to a suspension of ferrous hydroxide, prepared by the addition of 12 ml. of concentrated ammonium hydroxide solution to a solution of 16.70 g. (0.06 mole) of ferrous sulfate heptahydrate in 50 ml. of water. After the suspension had been maintained at 100° for 30 minutes, the ferric hydroxide was separated by filtration and the filtrate acidified with dilute hydrochloric acid solution. The crystalline precipitate was collected by filtration and recrystallized from water; yield 1.6 g. (80%), m.p. 176–177°.

Anal. Calcd. for $C_{12}H_{11}NO_2$: C, 71.62; H, 5.51; N, 6.96. Found: C, 71.57; H, 5.45; N, 7.01.

Ultraviolet absorption spectrum in 95% ethanol, λ_{max} (log ϵ): 235 (4.39), 295 (4.27); $\lambda_{min.}$ (log ϵ): 260 (3.43). Spectrum of indole-2-carboxylic acid in 95% ethanol, λ_{max} (log ϵ): 220 (4.38), 290 (4.25); $\lambda_{min.}$ (log ϵ): 250 (3.17).

The substance gave a purple color with *p*-dimethylaminobenzaldehyde and sulfuric acid.

2-Carbethoxy-1,3,4,5-tetrahydrobenz(*cd*)indole.—A solution of 100 mg. (0.0005 mole) of the acid III in 2 ml. of thionyl chloride, prepared at 0°, was allowed to remain at ordinary temperature for a period of 2 hours. The thionyl chloride was then distilled *in vacuo* with 25 ml. of benzene, the residue dissolved in 20 ml. of absolute ethanol and allowed to stand at ordinary temperature for a period of 20 hours. The ethanol was distilled under reduced pressure, the remainder dissolved in ether and extracted with dilute potassium bicarbonate solution. The residue from the washed and dried ether solution was recrystallized from ethanol; yield 100 mg. (87%), m.p. 127–128°.

Anal. Calcd. for $C_{14}H_{15}NO_2$: C, 73.44; H, 6.59; N, 6.11. Found: C, 73.43; H, 6.62; N, 6.39.

The tendency of the acid III to lose carbon dioxide in acid solution defeated attempts to prepare the ester in good yield by the Fischer procedure. The neutral fraction, derived from such experiments, consisted of a mixture of the desired ester and the indole IV which was difficult to resolve.

1,3,4,5-Tetrahydrobenz(cd)indole (IV). A (From III).—A solution of 500 mg. (0.0025 mole) of 2-carboxy-1,3,4,5-tetrahydrobenz(cd)indole (III) in 3 ml. of ethanol containing 0.33 ml. of 6 *N* hydrochloric acid solution was maintained at reflux temperature for a period of 5 hours. The solution was then brought to *p*H 8 with dilute sodium hydroxide solution, the ethanol distilled under diminished pressure and the remainder extracted with ether. The residue from the washed and dried ether solution was treated with 10 ml. of a 0.25 *N* solution of picric acid in ethanol and, after 24 hours at 0°, the dark red, crystalline deposit was collected by filtration and recrystallized from ethanol; yield 0.75 g. (78%), m.p. 164–166°.

Anal. Calcd. for $C_{17}H_{14}N_4O_7$: C, 52.85; H, 3.65; N, 14.50. Found: C, 53.07; H, 3.83; N, 14.64.

The picrate was dissolved in benzene and poured through a column of aluminum oxide prepared in benzene. The residue, after distillation under reduced pressure of the benzene elutes, was recrystallized from a mixture of ethanol and water; m.p. 55–56°.

Anal. Calcd. for $C_{11}H_{11}N$: C, 84.03; H, 7.05; N, 8.91. Found: C, 84.11; H, 6.83; N, 8.82.

In a similar experiment after a period of 30 minutes, 60 mg. of crystalline IV was obtained and 400 mg. (80%) of unchanged III was recovered.

Certain inorganic cations appeared to influence the rate of evolution of carbon dioxide. When the reaction was carried out in the presence of stannous chloride, in hydrochloric acid solution, decarboxylation was found to be essentially complete after a period of 30 minutes.

B (From II).—A solution of 250 mg. (0.001 mole) of the glyoxylic acid derivative II in 5 ml. of glacial acetic acid was maintained at reflux temperature in the presence of 2.0 g. of zinc dust for a period of 12 hours. The metal then was separated by filtration with the aid of ethanol, the filtrate concentrated under reduced pressure, the residue dissolved in ether and extracted with dilute, aqueous sodium hydroxide. The residue from the washed and dried ether solution, 65 mg. (40%), was recrystallized from petroleum ether; m.p. 55–56°. Acidification of the alkaline extract yielded 60 mg. (30%) of III, m.p. 176–177°. The ratio of III to IV in a series of experiments was dependent on the extent of reaction time.

C (From VI).—To a solution of 1.74 g. (0.045 mole) of potassium in 15 ml. of *t*-butyl alcohol which had been concentrated under diminished pressure to remove excess *t*-butyl alcohol, was added 5.25 g. (0.03 mole) of N-formyl-1,2,3,4-tetrahydro-5-naphthylamine (VI), the reagents thoroughly mixed, and the whole placed in a Woods metal-bath at 340–360° for a period of ten minutes. Fifty per cent. of the starting material was accounted for as 1,2,3,4-tetrahydro-5-naphthylamine which distilled over and was isolated as the hydrochloride. The viscous residue was extracted with ethanol under reflux in the presence of dilute, aqueous sodium hydroxide solution for 30 minutes, the total solution concentrated to a small volume and extracted with ether. The ether extract was repeatedly washed with dilute sulfuric acid solution and finally with water. The resi-

(11) The formation of carbanion coupling products under reaction conditions of this type was observed, as long ago as 1897, by A. Reissert, *Ber.*, **30**, 1032 (1897), in his classical studies on the condensation reactions of the nitrotoluenes.

due from the dried ether extract was treated with a saturated solution of picric acid in ethanol and the resultant deposit recrystallized from ethanol; yield 1.25 g. (10.8%), m.p. 164–166°. The picrate was converted, with aluminum oxide and benzene, to the indole IV, which was then recrystallized from a mixture of ethanol and water; m.p. 55–56°.

2,3-Dihydroxy-4H-5,6-dihydrobenzo(de)quinoline (V).—A solution of 554 mg. (0.002 mole) of the ethyl ester of 8-nitro-1,2,3,4-tetrahydro-1-naphthaleneglyoxylic acid (II) in 10 ml. of acetic acid was submitted to hydrogenation at 26°, at ordinary pressure, with 250 mg. of platinum oxide, prereduced with hydrogen. After 147 ml. of hydrogen had been absorbed during a period of 3 hours (theory for 0.006 mole, 149 ml.), the hydrogenation was interrupted, the catalyst removed by filtration, the acetic acid distilled under diminished pressure, and the residue maintained under reflux in ethanol solution in the presence of aqueous sodium hydroxide for a period of one hour. The ethanol was distilled *in vacuo*, water was added, and carbon dioxide was admitted into the solution until the base had been transformed completely to sodium bicarbonate. The precipitate which separated under these conditions was collected by filtration, washed with water, and recrystallized from acetone; yield 200 mg. (50%), m.p. 232–233°.

Anal. Calcd. for $C_{12}H_{11}NO_2$: C, 71.62; H, 5.51; N, 6.96. Found: C, 71.77; H, 5.72; N, 7.26.

Ultraviolet absorption spectrum in 95% ethanol, λ_{max} (log ϵ): 225 (4.57), 295 (3.96), 315 (4.00), 330 (3.90); $\lambda_{min.}$ (log ϵ): 265 (3.61), 310 (3.87), 325 (3.84).[12]

The substance was insoluble in dilute bicarbonate and ammonium hydroxide solutions, was soluble in dilute fixed alkali but formed a slightly soluble sodium salt. It gave a green color with dilute ferric chloride solution and failed to give a color with *p*-dimethylaminobenzaldehyde and sulfuric acid.[13]

The 3-acetate was formed when a solution of 100 mg. of the quinoline derivative V in 1 ml. of acetic anhydride was maintained under reflux for a period of one hour. After the reaction mixture had been kept for 24 hours at 0°, the crystalline precipitate was collected by filtration and recrystallized from ethanol. The substance gave no color with dilute ferric chloride solution; yield 90 mg. (75%), m.p. 256–259°.

Anal. Calcd. for $C_{14}H_{13}NO_3$: C, 69.12; H, 5.39; N, 5.76. Found: C, 69.26; H, 5.42; N, 5.99.

The potassium bicarbonate filtrate from the collection of V was acidified with dilute hydrochloric acid solution, the precipitate, which proved to be identical with 2-carboxy-1,3,4,5-tetrahydrobenz(cd)indole (III), collected by filtration and washed with water, yield 120 mg. (30%), m.p. 176–177°.

N-Formyl-1,2,3,4-tetrahydro-5-naphthylamine (VI).—An ether solution of 1,2,3,4-tetrahydro-5-naphthylamine,[8] prepared from 3.75 g. (0.02 mole) of the hydrochloride, was concentrated under reduced pressure and the residue maintained under reflux with 6.0 g. of formic acid for a period of 20 hours. The formic acid was distilled *in vacuo* and the residue recrystallized from ligroin; m.p. 101–102°.

Anal. Calcd. for $C_{11}H_{13}NO$: C, 75.38; H, 7.47; N, 8.06. Found: C, 75.11; H, 7.50; N, 7.97.

These studies were assisted by a grant from the National Science Foundation.

(12) *Cf.* the curves displayed by 3-hydroxyquinoline and by carbostyril; G. W. Ewing and E. A. Steck, THIS JOURNAL, **68**, 2181 (1946).

(13) *Cf.* the properties of 2,3-dihydroxyquinoline as prepared from *o*-methyloxanilic acid, W. Madelung, *Ber.*, **45**, 3521 (1912), or from isatin with diazomethane, G. Heller, *ibid.*, **52**, 741 (1919); F. Arndt, B. Eistert and W. Ender, *ibid.*, **62**, 44 (1929).

BOSTON 15, Mass.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF COLUMBIA UNIVERSITY]

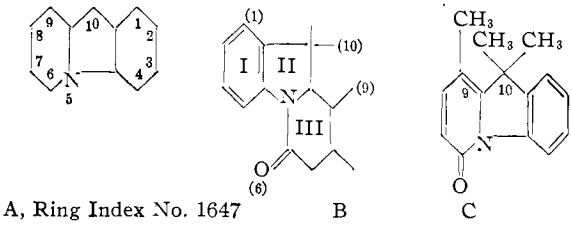
Studies on α-Pyridones. III. Ring-chain Tautomerism Involving the NH-Function. A Route to Benzo[b]pyrrocolines

BY FAUSTO RAMIREZ AND ALBERT P. PAUL[1]

RECEIVED JANUARY 17, 1955

A route to benzo[b]pyrrocolines (A), based on a hitherto unobserved ring-chain tautomerism involving the NH-function of an α-pyridone and the CO-function of a ketone, has been developed. Alkaline hydrolysis of 2-(2′-oxocyclohexyl)-methyl-6-chloronicotinic acid (I) gave an α-pyridone whose infrared spectrum was consistent with the structure of 9-carboxy-4a-hydroxy-1,2,3,4,4a,10a-hexahydro-benzo[b]pyrrocolin-6(10H)one (IIb), the ring tautomer of 2-(2′-oxocyclohexyl)-methyl-6-oxynicotinic acid (IIa). The action of 2,4-dinitrophenylhydrazine on II gave a substance whose ultraviolet spectrum (λ_{max} 341 mμ) indicates also a ring tautomer of a hydrazone III. Concentrated sulfuric acid removed one mole of water from II, quantitatively, with formation of a tetrahydrobenzo[b]pyrrocoline derivative IV. IV absorbed one mole of hydrogen (Pd–C) and yielded 9-carboxy-1,2,3,4,4a,10a-hexahydrobenzo[b]pyrrocolin-6(10H)-one (VI). The action of mineral acids directly on the chloronicotinic acid derivative I has been shown to yield 6-(4′-carboxy)-butyl-2-hydroxy-5-oxo-6,7-dihydro-1,5H-pyrindine (VIII).

The benzo[b]pyrrocoline system A constitutes the I–II–III ring sequence of the heptacyclic alkaloid strychnine (B, part formula). The parent ring system itself (A, $C_{12}H_9N$) appears to have been obtained by Braun and Nelles[2] from the pyrolysis (300°, Cu) of 2-benzylpyridine. Robinson and Saxton[3] reported recently on an ingenious method for the construction of substituted derivatives of A. Thus, the hydrogen chloride-promoted condensation of acetonylacetone with (a) skatole (3-methylindole), (b) 3-ethylindole and (c) N-acetyltryptamine was found to give (a) 6,9,10-trimethylbenzo[b]pyrrocoline, (b) 10-ethyl-6,9-dimethylbenzo[b]pyrrocoline and (c) 10-(2-acetamidoethyl)-6,9-dimethylbenzo[b]pyrrocoline, respectively. The presence of a substituent at the 3-position of indole appears necessary for the formation of A.[4] By this



A, Ring Index No. 1647 B C

(1) David W. and Ellen A. Ferguson Fellow, 1953–1954. From part of the Ph.D. Thesis of A. P. Paul.

(2) J. von Braun and J. Nelles, *Ber.*, **70B**, 1767 (1937).

(3) (a) R. Robinson and J. E. Saxton, *J. Chem. Soc.*, 3136 (1950); (b) 976 (1952).

(4) In the recently announced total synthesis of strychnine (R. B. Woodward, M. P. Cava, W. D. Ollis, A. Hunger, H. U. Daenkier and K. Schenker, THIS JOURNAL, **76**, 4501 (1954)) the establishment of an α-pyridone derivative of benzo[b]pyrrocoline is carried out as one of the last synthetic steps.