[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF ROCHESTER]

Curariform Activity and Chemical Structure. VIII. Lactones Derived from Quinolizidine[1,2]

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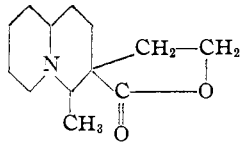
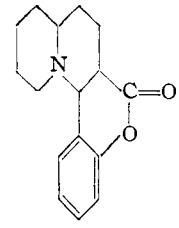
In an investigation of possible structural units which might impart curariform activity, the synthesis of a number of simple quinolizidine derivatives was recently reported.[3] Since derivatives of this type containing a lactone ring would be expected to bear some resemblance to β-erythroidine and its derivatives,[4] we have now investigated the preparation of the two lactones shown by formulas I and II.



I

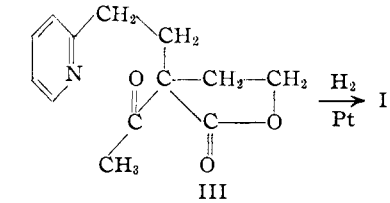


II

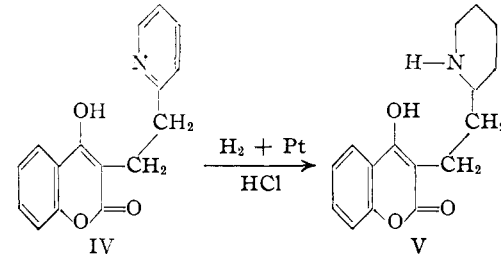
For the preparation of I the general procedure which was employed previously for the simple quinolizidine derivatives[3] proved quite successful. The addition of α-aceto-γ-butyrolactone to 2-vinylpyridine by a Michael condensation gave III in 40% yield. When III was reduced using platinum oxide as catalyst in acidic media, cyclization accompanied reduction and the product was I.

However, this approach failed when it was applied to the preparation of II. The addition of 4-hydroxycoumarin to 2-vinylpyridine occurred readily in good yield to give IV, but the desired reductive cyclization of IV to yield II did not occur. When IV was subjected to hydrogenation in acidic media using platinum oxide as catalyst, only three molar equivalents of hydrogen were absorbed and the product was V. Alteration of the conditions of reduction did not prove useful nor could V be cyclized by treatment with heat or thionyl chloride.

The failure of both IV and V to undergo reductive cyclization was somewhat surprising and the possibility that the Michael condensation had resulted in O-alkylation rather than C-alkylation was considered. However, IV gave a distinct light orange color with ferric chloride solution, was soluble in cold alkali, and showed an infrared absorption spectrum remarkably similar to that of a prepared solution containing equivalent amounts of 3-methyl-4-hydroxycoumarin and pyridine.



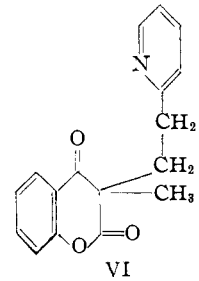
III



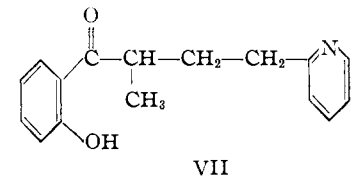
IV V

This evidence eliminates the possibility of O-alkylation and gives strong support to the structure assigned to IV.

A probable explanation for the difficulties encountered in attempts to reductively cyclize IV and V is that in these compounds the enolic form is highly stabilized by zwitterion formation with the basic amino group and that this form is not favorable for cyclization. For this reason the reaction sequence was repeated employing 3-methyl-4-hydroxycoumarin in place of 4-hydroxycoumarin. In this case the intermediate would be VI, which cannot enolize and which should therefore undergo reductive cyclization as desired. However, when 3-methyl-4-hydroxycoumarin was treated with 2-vinylpyridine, the product of the reaction proved to be VII instead of VI. Structure VII has been assigned on the basis of the phenolic character of the material, its empirical formula, its ultraviolet absorption spectrum, and its apparent reduction to 3-methyl-4-(*o*-hydroxyphenyl)-quinolizidine.[5]



VI



VII

In preliminary work directed toward an alter-

(1) Aided by a Grant from the National Foundation for Infantile Paralysis, Inc.

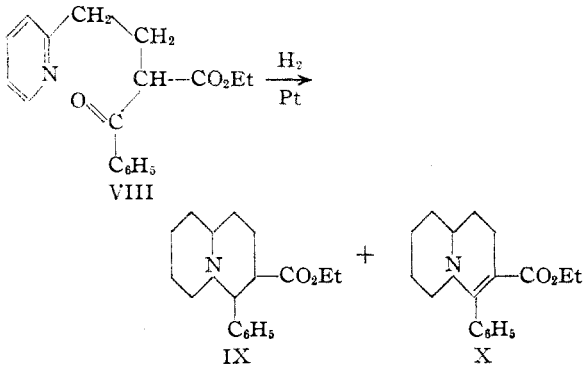
(2) For the previous paper in this series, see Boekelheide and Ainsworth, THIS JOURNAL, **72**, 2134 (1950).

(3) Boekelheide and Rothchild, *ibid.*, **71**, 879 (1949).

(4) For a summary of references to the chemistry of β-erythroidine, see Sauvage and Boekelheide, *ibid.*, **72**, 2062 (1950).

(5) The formation of VII from VI can be explained by postulating that cleavage occurs at the quaternary carbon atom by a reverse Claisen condensation and the resulting carbonate ester is subsequently hydrolyzed to yield the free phenolic group.

nate synthesis of II, the addition of ethyl benzoylacetate to 2-vinylpyridine was studied and found to give VIII in good yield. When VIII was reduced in acid with platinum oxide as catalyst, the product was a mixture of IX and X. Further reduction in neutral solution converted the mixture completely to IX. The projected transformation of IX to II proved unexpectedly difficult and was not accomplished.



The formation of X is of interest in view of the work that Glickman and Cope have done on the ultraviolet absorption spectra of β-amino-α,β-unsaturated esters,[6] and the spectrum of X is shown in Fig. 1. For comparison, the spectrum of 4-methyl-3-ene-3-carbethoxyquinolizidine[3] (X, with $-CH_3$ instead of $-C_6H_5$) is also shown. It can be seen that the nature of the group at the 4-position has little effect on the important absorption due to the conjugated vinyl amine system. The absorption maximum for X (305 mμ, log ε 4.3) is essentially identical with that recently reported by Cromwell, Miller, Johnson, Frank and Wallace for several β-amino-α,β-unsaturated ketones[7] but is at slightly longer wave lengths than that reported by Glickman and Cope for their compounds.[6]

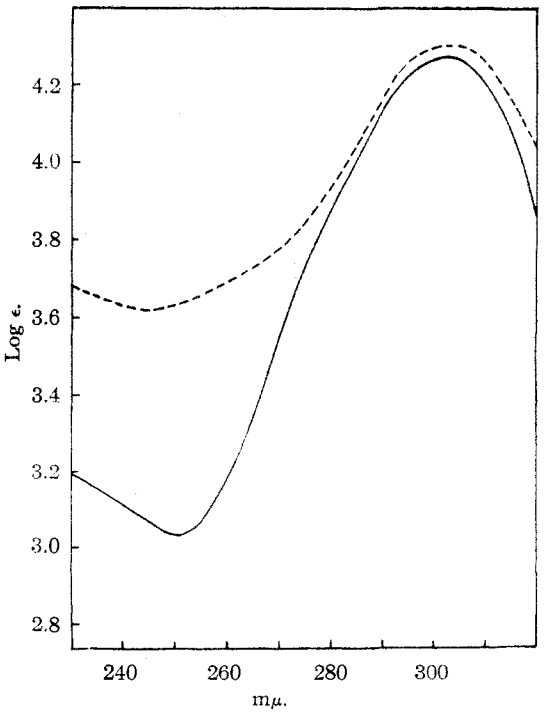


Fig. 1.—Ultraviolet absorption spectra of 4-phenyl-3-ene-3-carbethoxyquinolizidine (X, -----) and 4-methyl-3-ene-3-carbethoxyquinolizidine (——) in ethanol.

(6) Glickman and Cope, THIS JOURNAL, **67**, 1017 (1945).

Additional evidence for the structure VIII assigned to the condensation product of 2-vinylpyridine and ethyl benzoylacetate was obtained by subjecting the condensation product to acidic hydrolysis. This gave the corresponding ketone, phenyl γ-(2-pyridyl)-propyl ketone. Catalytic reduction of this ketone, as expected,[3] resulted in cyclization and yielded 4-phenylquinolizidine. For purposes of comparison the reduction of phenyl γ-(2-pyridyl)-propyl ketone was also carried out using lithium aluminum hydride and the product of this reduction was the corresponding alcohol, phenyl-γ-(2-pyridyl)-propylcarbinol.

Of the compounds described in this paper, the only one having physiological activity of interest was phenyl-γ-(2-pyridyl)-propylcarbinol. This compound was effective in causing muscular paralysis in test animals.[8] Phenyl γ-(2-pyridyl)-propyl ketone showed a similar activity of even greater intensity but the duration of its activity was exceedingly short. The site of action of phenyl-γ-(2-pyridyl)-propylcarbinol is central rather than peripheral and it thus appears to be a drug of the apo-β-erythroidine type.[9]

Experimental[10]

α-Aceto-α-(2-(2′-pyridyl)-ethyl)-γ-butyrolactone, III.—To a mixture of α-acetobutyrolactone[11] (30.0 g., 0.23 mole) and freshly-distilled 2-vinylpyridine (24.0 g., 0.23 mole), a small pea of sodium was added and the mixture was boiled under reflux for three hours. The solution was then made acidic with dilute hydrochloric acid, the aqueous layer was saturated with sodium chloride, and any neutral material present was removed by ether extraction. The aqueous layer was then made basic and extracted with ether. After this ethereal solution had been allowed to dry over anhydrous sodium sulfate, the ether was removed and the residue was distilled. There was obtained 22.0 g. (40%) of a pale orange oil; b. p. 170–180° at 1 mm.; $n^{23}D$ 1.5182.

Anal. Calcd. for $C_{13}H_{15}NO_3$: C, 66.93; H, 6.48. Found: C, 67.14; H, 6.60.

The **picrate** of III was prepared in ethanol and was obtained, after two recrystallizations from ethanol, as bright yellow crystals, m. p. 111–112°.

Anal. Calcd. for $C_{19}H_{18}N_4O_{10}$: C, 49.35; H, 3.92. Found: C, 49.31; H, 4.04.

Lactone of 3-Carboxy-3-(β-hydroxyethyl)-4-methylquinolizidine, I.—A solution of 5.3 g. of α-aceto-α-(2-(2′-

(7) Cromwell, Miller, Johnson, Frank and Wallace, *ibid.*, **71**, 3337 (1949).

(8) We are indebted to Dr. I. H. Slater of the School of Medicine and Dentistry, University of Rochester, Rochester, New York, for the physiological testing. These results will be published elsewhere.

(9) Sauvage, Berger and Boekelheide, *Science*, **109**, 627 (1949).

(10) Analyses by Mrs. G. L. Sauvage and by the Micro-Tech Laboratories.

(11) Knunyantz, Chelintzev and Osetrova, *Compt. rend. acad. sci. (U. R. S. S.)*, (N. S.), **1**, 312 (1934).

pyridyl)-ethyl)-γ-butyrolactone (III) in 8 ml. of 6 *N* hydrochloric acid was diluted with water and alcohol to yield a total volume of 50 ml. of a 50% alcoholic solution. After addition of 0.10 g. of platinum oxide catalyst the mixture was subjected to hydrogenation at room temperature and under atmospheric pressure of hydrogen. Four molar equivalents of hydrogen were absorbed in seven hours. The catalyst and most of the solvent were removed, the residue was made basic with sodium carbonate, and the oil, which separated, was extracted with ether. After the ethereal solution had been dried over *Drierite*, the ether was removed and the residue was distilled yielding 2.5 g. (50%) of a crude oil; b. p. 150–155° at 0.4 mm. To obtain purification of the oil it was found necessary to convert the product to the picrate which on crystallization from ethanol was obtained in a pure state (m. p. 210–212°). This was decomposed by treating it with dilute hydrochloric acid and the picric acid was removed by extraction with benzene. When the acidic layer was made basic and the oily product was isolated as before, there was obtained about 1.0 g. of a colorless oil, b. p. 150° at 1 mm., $n^{21}D$ 1.5125.

Anal. Calcd. for $C_{13}H_{21}NO_2$: C, 69.92; H, 9.48. Found: C, 70.04; H, 9.28.

The **picrate** of I, prepared from the crude oil as indicated above, was obtained from alcohol as granular yellow crystals, m. p. 210–212°.

Anal. Calcd. for $C_{19}H_{24}N_4O_9$: C, 50.44; H, 5.35. Found: C, 50.53; H, 5.36.

The **methiodide** of I was prepared from the crude oil and was obtained after crystallization from alcohol as white crystals, m. p. 223–225°.

Anal. Calcd. for $C_{14}H_{24}NIO_2$: C, 46.03; H, 6.62. Found: C, 45.90; H, 6.54.

Since the free base isolated from the picrate represents only one of the four possible racemates corresponding to structure I, an examination of the mother liquor from the preparation of the picrate was made and a small amount of a second picrate was isolated. This was obtained, after several crystallizations from alcohol, as yellow crystals, m. p. 225–229°. Because of the small amount of material no attempt was made to obtain the free base corresponding to this second racemate.

Anal. Calcd. for $C_{19}H_{24}N_4O_9$: C, 50.44; H, 5.35. Found: C, 50.28; H, 5.04.

3-(β-(2′-Pyridyl)-ethyl)-4-hydroxycoumarin, IV.—A solution of 4-hydroxycoumarin[12] (44.0 g., 0.27 mole), freshly-distilled 2-vinylpyridine (28.0 g., 0.27 mole), and 0.1 g. of hydroquinone in 153 g. of dry pyridine was boiled gently under reflux for twenty-six hours. The mixture was then poured into 2000 ml. of cold water and the oil, which separated, crystallized when the solution was vigorously stirred. This light pink solid was collected and, after recrystallization from alcohol, yielded 32.0 g. (44%) of white needles, m. p. 150–151°.

These crystals were soluble in cold 5% sodium hydroxide solution and gave a light orange color with ferric chloride solution. The infrared absorption spectrum of these crystals in a dioxane solution showed absorption maxima at 2.87 and 5.86 μ, and the infrared absorption spectrum of a prepared dioxane solution containing equivalent amounts of 3-methyl-4-hydroxycoumarin and pyridine was essentially identical with it in the range from 2.5 to 6.5 μ.

Anal. Calcd. for $C_{16}H_{13}NO_3$: C, 71.90; H, 4.90. Found: C, 71.94; H, 4.77.

The **hydrochloride** of IV precipitated from solution when IV was dissolved in 5% hydrochloric acid. After crystallization from dilute hydrochloric acid, the hydrochloride was obtained as white needles, m. p. 231–232° (w. dec., darkening at 220°).

Anal. Calcd. for $C_{16}H_{14}NO_3Cl$: C, 63.26; H, 4.65. Found: C, 63.04; H, 4.22.

(12) Stahmann, Wolf and Link, THIS JOURNAL, **65**, 2285 (1943).

3-(β-(2′-Piperidyl)-ethyl)-4-hydroxycoumarin, V.—A mixture consisting of 3-(β-(2′-pyridyl)-ethyl)-4-hydroxycoumarin (1.9 g., 0.007 mole) 0.1 g. of platinum oxide, 25 ml. of glacial acetic acid and five drops of concentrated sulfuric acid was shaken with hydrogen under atmospheric pressure and at room temperature until hydrogen was no longer absorbed. The catalyst was then removed and the solution was poured into 50 ml. of water. Addition of 28 g. of potassium carbonate caused the separation of a viscous oil which solidified on standing. This solid was treated with *Norite* in alcohol and then crystallized from an alcohol–water mixture to yield 1.5 g. (83%) of thick white needles, m. p. 211–212°.

Anal. Calcd. for $C_{16}H_{19}NO_3$: C, 70.30; H, 7.01. Found: C, 70.21; H, 6.95.

The **hydrochloride** of V readily separated from solution as white crystals when V was added to dilute hydrochloric acid. After recrystallization from dilute hydrochloric acid, the hydrochloride was obtained as silky white crystals, m. p. 221–222°.

Anal. Calcd. for $C_{16}H_{20}ClNO_3$: C, 62.03; H, 6.51; Cl, 11.45. Found: C, 61.95; H, 6.85; Cl, 11.60.

When 3-(β-(2′-pyridyl)-ethyl)-4-hydroxycoumarin (IV) was hydrogenated with platinum oxide in an alcohol–water mixture containing excess hydrochloric acid, the product, obtained in essentially quantitative yield, was likewise V. Several attempts were made to hydrogenate IV using Raney nickel as catalyst both in the presence and absence of added base and at both low and high pressures. Dark brown oils resulted from these attempts and they could not be characterized.

Various attempts were made to reductively cyclize V. It was subjected to hydrogenation using platinum oxide in acid, Raney nickel in weak and in strong base, and Raney nickel in dilute base at low and medium pressures. In every case either hydrogenation did not occur or was accompanied by decomposition. Treatment of V with thionyl chloride in pyridine also was unsuccessful in effecting cyclization.

1-(2′-Pyridyl)-3-(*o*-hydroxybenzoyl)-butane, VII.—A solution of freshly-distilled 2-vinylpyridine (11.5 g., 0.11 mole) and 3-methyl-4-hydroxycoumarin[13] (20.0 g., 0.11 mole) in 75 g. of dry pyridine was boiled gently under reflux for twenty-four hours with stirring. The solution was then poured into 750 ml. of water and sufficient hydrochloric acid was added to make the solution definitely acidic. The 3-methyl-4-hydroxycoumarin (5 g.), which precipitated, was removed and the solution was made basic with sodium carbonate. The basic solution was extracted with ether, the ethereal solution was dried, and the ether was removed. The crude residue weighed 18 g. (90% yield based on unrecovered coumarin). A portion of the residue was distilled, using a sublimation apparatus, to give a pale yellow oil, b. p. 60° at 0.03 mm.

Anal. Calcd. for $C_{16}H_{17}NO_2$: C, 75.26; H, 6.71. Found: C, 74.62; H, 6.61.

When VII was treated with 1% ferric chloride solution, it gave a red color. It also dissolved in cold 5% sodium hydroxide.

The ultraviolet absorption spectrum of this material in alcohol showed absorption maxima at 330 μ, (log *E*, 3.59), 256 mμ (log *E*, 4.10), and at 225 mμ (log *E*, 3.91). The corresponding values reported[14] for *o*-hydroxyacetophenone are 325 mμ (log *E*, 3.54), 251 mμ (log *E*, 3.95) and 225 mμ (log *E*, 4.00).

The **picrate** of VII was formed from ethanolic picric acid and was obtained as yellow granular crystals, m. p. 93–94.5°.

Anal. Calcd. for $C_{22}H_{20}N_4O_9$: C, 54.55; H, 4.16. Found: C, 54.62; H, 4.33.

(13) Stahmann and Link, British Patent 578,589, July 4, 1946; *C. A.*, **41**, 2443 (1947).

(14) Valyashko and Rozum, *J. Gen. Chem.* (*U. S. S. R.*), **17**, 755 (1947); *C. A.*, **42**, 2588 (1948).

3-Methyl-4-(*o*-hydroxyphenyl)-quinolizidine.—A mixture consisting of 1-(2′-pyridyl)-3-(*o*-hydroxybenzoyl)-butane (5.0 g., 0.02 mole), 4 ml. of concd. hydrochloric acid, 0.2 g. of platinum oxide, and 100 ml. of 50% aqueous ethanol was shaken at 55° under 3 atm. pressure of hydrogen for two hours. The catalyst was separated and most of the solvent was removed *in vacuo*. Potassium carbonate solution was added until a *p*H of 8 was reached and the light-colored solid, which separated, was removed. The solid, on recrystallization from ethanol, yielded 2.5 g. (52%) of crystals, m. p. 70–72°. Treatment of the crude product with Norite followed by an additional crystallization from ethanol gave pure white crystals, m. p. 81–82°.

Anal. Calcd. for $C_{16}H_{23}NO$: C, 78.32; H, 9.45. Found: C, 78.52; H, 9.06.

The crystals gave an orange color with ferric chloride solution but were not readily soluble in cold base.

Ethyl α-Benzoyl-γ-(2-pyridyl)-butyrate, VIII.—To a solution of freshly-distilled ethyl benzoylacetate (246 g., 1.3 mole) and freshly-distilled 2-vinylpyridine (68 g., 0.65 mole) there was added 1 g. of sodium and the mixture was boiled under reflux for five hours. The cold solution was then made acidic and neutral material was removed by ether extraction. The aqueous layer was then made basic; the oil, which separated, was extracted with ether; and the ethereal solution was dried over *Drierite*. After removal of the ether and 2-vinylpyridine *in vacuo*, the residue was distilled yielding 135 g. (70%) of a pale orange oil; b. p. 170–175° at 0.3 mm.; $n^{23}D$ 1.5526.

Anal. Calcd. for $C_{18}H_{19}NO_3$: C, 72.72; H, 6.44. Found: C, 73.00; H, 6.33.

The **picrolonate** of VIII was prepared in ethanol and, after four recrystallizations from ethanol, was obtained as flocculent yellow crystals, m. p. 143.5–145°.

Anal. Calcd. for $C_{28}H_{27}N_5O_8$: C, 59.89; H, 4.85. Found: C, 60.26; H, 4.81.

Reduction of Ethyl α-Benzoyl-γ-(2-pyridyl)-butyrate.—A mixture of ethyl α-benzoyl-γ-(2-pyridyl)-butyrate (25.0 g., 0.08 mole), 0.3 g. of platinum oxide, and 16 ml. of concd. hydrochloric acid in 200 ml. of 50% aqueous ethanol was shaken at room temperature under three atmospheres pressure of hydrogen until four molar equivalents of hydrogen had been absorbed (14 hr.). The catalyst was separated, most of the alcohol was removed under reduced pressure, and the residue was made basic with dilute sodium hydroxide. The oil, which separated, was taken up in ether, dried, and the ether was removed. Careful distillation of the residue yielded two fractions: a pale yellow oil, b. p. 110–130° at 0.5 mm.; and a pale orange oil, b. p. 135–145° at 0.3 mm.

The lower boiling fraction, **3-carbethoxy-4-phenylquinolizidine** (IX), was redistilled and gave 4.7 g. (20%) of a yellow oil; b. p. 138–143° at 1.2 mm.; $n^{20}D$ 1.5312.

Anal. Calcd. for $C_{18}H_{25}NO_2$: C, 75.22; H, 8.77. Found: C, 74.99; H, 8.52.

The **picrate** of IX formed slowly in ethanol and was obtained, after two recrystallizations from ethanol, as large yellow crystals, m. p. 139–141°. There was no evidence for the presence of other racemates.

Anal. Calcd. for $C_{24}H_{28}N_4O_9$: C, 55.81; H, 5.46. Found: C, 55.97; H, 5.42.

The higher boiling fraction, **3-carbethoxy-3-ene-4-phenylquinolizidine** (X), on distillation gave 5.0 g. (22%) of a yellow oil; b. p. 141–149° at 0.3 mm.; $n^{20}D$ 1.5707. The ultraviolet absorption spectrum of X is shown in Fig. 1.

Anal. Calcd. for $C_{18}H_{23}NO_2$: C, 75.76; H, 8.12. Found: C, 75.33; H, 8.15.

When the lower and higher boiling fractions from the first crude distillation were combined and again subjected to hydrogenation with platinum oxide in neutral alcoholic solution, it was found that hydrogen was absorbed and the entire product corresponded to the lower boiling fraction, 3-carbethoxy-4-phenylquinolizidine (IX). This behavior was not unexpected in view of the results obtained previously on the reduction of ethyl β-(2-pyridyl)-ethylacetoacetate.[3]

It was anticipated that IX, after hydrolysis to the free amino acid, could be cyclized to give the corresponding indanone derivative. However, in the present work these steps were not realized. A more general study on the cyclization of aryl amino acids is now under investigation.

Phenyl γ-(2-Pyridyl)-propyl Ketone.—A solution of 50 g. of ethyl α-benzoyl-γ-(2-pyridyl)-butyrate in 50 ml. of dilute hydrochloric acid was boiled gently under reflux for three hours. The solution was then made basic and extracted with ether. The ether extract was washed with water, dried over *Drierite*, and the ether was removed. The residue, on distillation, gave 34.0 g. (90%) of a yellow oil; b. p. 165–170° at 2 mm.; $n^{20}D$ 1.5730.

Anal. Calcd. for $C_{15}H_{15}NO$; C, 79.97; H, 6.71. Found: C, 79.50; H, 6.83.

The **semicarbazone of phenyl γ-(2-pyridyl)-propyl ketone** was obtained after four recrystallizations from ethanol as white needles, m. p. 163–165°.

Anal. Calcd. for $C_{16}H_{18}N_4O$: C, 68.06; H, 6.42. Found: C, 68.01; H, 6.39.

The **picrolonate of phenyl γ-(2-pyridyl)-propyl ketone** was prepared from ethanol and was obtained after several recrystallizations from ethanol as yellow platelets, m. p. 181–184°.

Anal. Calcd. for $C_{25}H_{23}N_5O_6$: C, 61.34; H, 4.74. Found: C, 61.58; H, 5.02.

4-Phenylquinolizidine.—A mixture of phenyl γ-(2-pyridyl)-propyl ketone (16.9 g., 0.07 mole), 0.3 g. of platinum oxide catalyst, and 15 ml. of concd. hydrochloric acid in 200 ml. of 50% aqueous ethanol was shaken at room temperature under three atmospheres pressure of hydrogen until four molar equivalents of hydrogen were absorbed (ten hours). After the catalyst had been separated and most of the solvent removed *in vacuo*, the aqueous residue was made basic with dilute sodium hydroxide and extracted with ether. The ethereal solution was washed with water, dried over potassium carbonate, and the ether was removed. Distillation of the residue gave two fractions: 8.0 g. of a yellow oil boiling at 105–110° at 1.5 mm. and 3.0 g. of a yellow oil boiling at 140–150° at 1.0 mm.

Since it was found that the lower-boiling fraction (4-phenylquinolizidine) rapidly became discolored on standing in the presence of air, this fraction was again subjected to hydrogenation using platinum oxide in a neutral alcoholic solution. Only a very small amount of hydrogen was absorbed but after this second reduction the product was obtained as a stable, light yellow oil; b. p. 87–89° at 0.5 mm.; $n^{20}D$ 1.5392.

Anal. Calcd. for $C_{15}H_{21}N$: C, 83.66; H, 9.83. Found: C, 83.55; H, 9.87.

The **picrate** of **4-phenylquinolizidine** formed readily in alcohol and was obtained as yellow crystals, m. p. 195–215°. The wide melting point range is evidently due to the presence of diastereoisomers since the crude sample gave the expected composition on analysis. After four recrystallizations from ethanol a pure sample of one of the racemates, m. p. 213–214°, was obtained.

Anal. Calcd. for $C_{21}H_{24}N_4O_7$: C, 56.75; H, 5.44. Found (sample, m. p. 213–214°): C, 56.57; H, 5.33. Found (crude sample, m. p. 200–215°); C, 56.57; H, 5.23.

The **methiodide of 4-phenylquinolizidine** was prepared by heating 1.0 g. of 4-phenylquinolizidine with 2.0 ml. of methyl iodide in 2 ml. of methanol for one and one-half hours. The methanol was then removed and the residue was washed with ether. After recrystallization from an alcohol–ethyl acetate mixture, the methiodide was obtained as light tan crystals, m. p. 175–225°. Several more recrystallizations from the same solvent mixture gave one of the racemates in slightly impure form as white crystals, m. p. 152–159°.

Anal. Calcd. for $C_{16}H_{24}NI$: C, 53.78; H, 6.77. Found: C, 53.78; H, 6.71.

Phenyl-γ-(2-pyridyl)-propylcarbinol.—Into a 3-necked flask, equipped with stirrer, dropping funnel, reflux condenser and calcium chloride tubes protecting each opening, and containing 0.015 mole of lithium aluminum hydride (in dry ether), was added 7 g. (0.03 mole) of phenyl γ-(2-pyridyl)-propyl ketone in 20 ml. of ether at a rate just fast enough to produce gentle boiling. The excess lithium aluminum hydride and the organo-metallic complex were decomposed by the addition of moist ether. After the precipitate of aluminum hydroxide and lithium hydroxide had been filtered off and the ether solution had been dried over Drierite, the ether was evaporated under reduced pressure, leaving 6 g. of a pale yellow solid, m. p. 65–67°. After four recrystallizations from hexane there was obtained 3.8 g. (54%) of beautiful clusters of white needles, m. p. 66.5–67°.

Anal. Calcd. for $C_{15}H_{17}NO$: C, 79.26; H, 7.54. Found: C, 78.93; H, 7.37.

The **picrate** of **phenyl-γ-(2-pyridyl)-propylcarbinol** was obtained from alcohol as clusters of yellow needles, m. p. 112.5–114°.

Anal. Calcd. for $C_{21}H_{20}N_4O_7$: C, 55.26; H, 4.42. Found: C, 55.49; H, 4.43.

Summary

In an effort to obtain model compounds of possible relationship to β-erythroidine the synthesis of certain lactones derived from quinolizidine has been investigated. In the course of this work a new compound, phenyl-γ-(2-pyridyl)-propylcarbinol, having a central action in effecting muscular paralysis was discovered.

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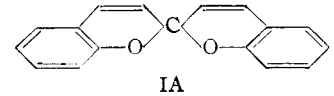
[CONTRIBUTION FROM THE WEIZMANN INSTITUTE OF SCIENCE, REHOVOTH, ISRAEL]

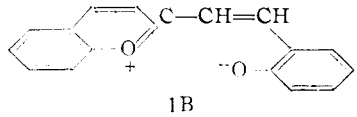
Structure and Polarity of Some Polycyclic Spirans

BY ERNST D. BERGMANN, ANNA WEIZMANN AND ERNST FISCHER

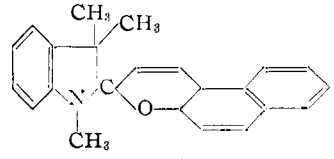
Certain polycyclic spirans show the effect of thermochromy. Thus 1,3,3-trimethylindolino-β-naphthopyrylospiran (II) is a colorless substance, but its melt is blue, and its solutions in non-polar solvents, which are pink at room temperature, turn intensely red upon heating. The phenomenon is reversible and has been interpreted as being due to variation in the contribution of the polar (colored) mesomeric structure (IIB).[1,2] The colorless dibenzospiropyran (I) does not show the above phenomenon. It is, therefore, assumed



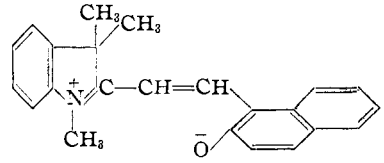
IA



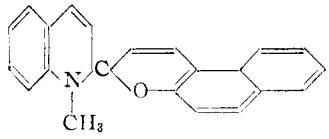
IB



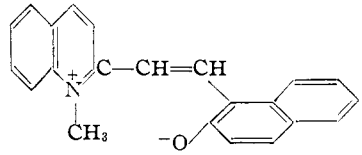
IIA



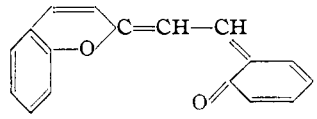
IIB



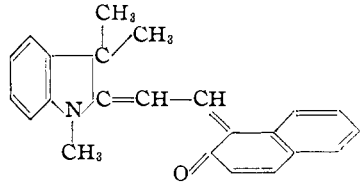
IIIA



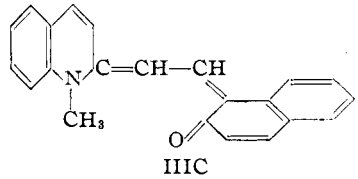
IIIB



IC



IIC



IIIC

that a possible polar form (IB) does not contribute to the structure of this molecule under the experimental conditions employed.

On the other hand, N-methylquinolino-β-naphthopyrylospiran (III) is blue-green even in

(1) Loewenbein and Katz, *Ber.*, **59**, 1377 (1926); Dilthey and co-workers, *Ber.*, **59**, 1856 (1926); **61**, 963 (1928); *J. prakt. Chem.*, [2] **114**, 179 (1926); Heilbron and co-workers, *J. Chem. Soc.*, 1699 (1927); 2077 (1928); 936 (1929); 1336 (1931); 430, 1263 (1933); 1571 (1934); 1380 (1936).

(2) Wizinger and Wenning, *Helv. Chim. Acta*, **23**, 247 (1940).