

carried out over a 4-hour period, the time required for the complete reaction and dissolution of VI. The solvent was removed in a current of dry air and finally *in vacuo* to give

a colorless sirup, whose infrared spectrum was *identical* to that of the product obtained from V. NEW YORK 27, N. Y.

[CONTRIBUTION FROM THE CHARLES F. KETTERING FOUNDATION FOR THE STUDY OF CHLOROPHYLL AND PHOTOSYNTHESIS AND THE DEPARTMENT OF CHEMISTRY, THE OHIO STATE UNIVERSITY]

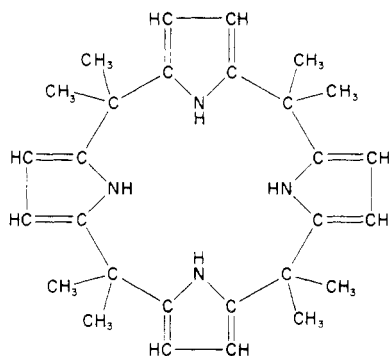
Concerning the Structure of "Acetonepyrrole"

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RECEIVED NOVEMBER 26, 1954

The structure of "acetonepyrrole" proposed by Chelintzev and Tronov has been partially confirmed. It is shown that at least three of the four bridge carbons are linked to the pyrrole nuclei in the α -positions.

The acid-catalyzed reaction of pyrrole and acetone yields "acetonepyrrole," $C_{28}H_{36}N_4$.² A structure has been proposed by Chelintzev and Tronov (I)^{2d} and given the name $\alpha,\beta,\gamma,\delta$ -octamethylporphyrinogen by Fischer.³ This configuration is based on the isolation of maleimide by oxidation with chromic acid^{3d} and pyrrole and 2-isopropylpyrrole by a pyrolytic reaction.^{2b} The uncertainty of the linkage of the bridge carbons to the pyrrole nuclei, whether to the α - or β -positions, warranted further investigation because of the close similarity of the proposed structure of "acetonepyrrole" to the porphyrins and on account of the failure, thus far, to convert "acetonepyrrole" to a porphyrin.



High-pressure hydrogenation of "acetonepyrrole" with Nickel Pellet Catalyst (UOP)⁴ at 265–270° and 204 atm. of hydrogen and copper chromite catalyst⁵ at 215° and 204 atm. yielded pyrrole, 2-isopropylpyrrolidine, 2-isopropylpyrrole, 2,5-diisopropylpyrrolidine and 2,5-diisopropylpyrrole. Also, with the latter catalyst, a small amount of a crystalline product, $C_{14}H_{24}N_2$, was obtained. The nature and quantity of the products isolated from the above hydrogenolyses definitely establish that at least three of the four bridge carbons are bonded

to the α -positions of the pyrrole nuclei. The remaining bridge carbon is probably bonded in a like manner since at no time in this investigation has a β -substituted pyrrole been isolated.

Of these reaction products only pyrrole and 2-isopropylpyrrole have been reported; therefore, the other reaction products were synthesized and compared with the product derived from the hydrogenolysis of "acetonepyrrole," and also with the products obtained from the zinc dust pyrolytic degradation of "acetonepyrrole." The latter yielded pyrrole, 2-isopropylpyrrole, 2-ethyl-5-isopropylpyrrole and two crystalline solids of unknown structure, $C_9H_{11}N$ and $C_{13}H_{17}N$. The latter two compounds appear to be pyrroles with unsaturated side-chains, and their structure will be further investigated.

The isolation of 2-ethyl-5-isopropylpyrrole was unexpected but not improbable considering the drastic pyrolytic conditions of the experiment. It is significant that the hydrogenolysis conducted at a temperature at least 100° below the pyrolytic degradation gave no 2-ethyl-5-isopropylpyrrole or corresponding pyrrolidine.

The synthetic pyrroles were prepared by the reaction of the appropriate pyrrole Grignard reagent with isopropyl bromide which yielded a mixture of mono- and poly-substituted pyrroles. Hydrogenation in dioxane with Raney Nickel W-4 catalyst⁶ gave the corresponding pyrrolidines in 45–55% yield.

Experimental⁷

Pyrrole obtained from Eastman Kodak Company, white label, was distilled over sodium⁸ from a Claisen flask just prior to use; boiling range 128–130°.

"Acetonepyrrole."—The procedure of Dennstedt^{2b} was followed except that methanesulfonic acid⁹ was used as the catalyst; yield 94 g., 88% of theory. Immediate extraction and recrystallization from acetone gave a white crystalline product, m.p.K. 296°, which kept for several months without discoloration.

Hydrogenolysis of "Acetonepyrrole."—A 500-ml. rocker-type autoclave¹⁰ was charged with 55 g. of recrystallized "acetonepyrrole," 10 g. of pulverized Nickel Pellet Catalyst (UOP)⁶ and 200 ml. of dry, peroxide-free dioxane. The contents of the bomb were brought to 157 atm. of hydrogen

(1) Taken in part from a dissertation presented by Clarke L. Gage, to the Faculty of the Department of Chemistry, The Ohio State University, in partial fulfillment of the requirements for the degree of Doctor of Philosophy, December, 1951.

(2) (a) A. Baeyer, *Ber.*, **19**, 2184 (1886); (b) M. Dennstedt and J. Zimmermann, *ibid.*, **20**, 850, 2449 (1887); *ibid.*, **21**, 1478 (1888); (c) M. Dennstedt, *ibid.*, **23**, 1370 (1890); (d) V. V. Chelintzev and B. V. Tronov, *J. Russ. Phys. Chem. Soc.*, **48**, 105, 127 (1916); (e) Th. Sabalitschka and H. Haase, *Arch. Pharm.*, **226**, 484 (1928).

(3) H. Fischer and H. Orth, "Die Chemie des Pyrrols," Akademische Verlagsgesellschaft m.b.H., Leipzig, 1934, p. 20.

(4) Wilkens-Anderson Company, Chicago, Illinois.

(5) T. W. Riener, *This Journal*, **71**, 1130 (1949).

(6) A. A. Pavlic and H. Adkins, *ibid.*, **68**, 1471 (1946).

(7) Boiling points are uncorrected. Melting points were taken either on a Fisher-Johns melting point block or on a Kofler hot stage mounted on a "Federal" microscope stand. The latter are designated m.p.K.

(8) R. Willstätter and D. Hatt, *Ber.*, **45**, 1477 (1912).

(9) Supplied by Indoil Chemical Company, Chicago, Illinois.

(10) American Instrument Company, Silver Springs, Maryland, Double Pedestal Rocking Type Autoclave.

and 240° and held at this temperature for 22.5 hours. A pressure drop of 82 atm. was observed. The catalyst was removed by filtration and the dioxane stripped off at atmospheric pressure. No evidence of pyrrolidine, b.p. 89°, was found. A preliminary distillation, at 10 mm. pressure, gave indications of decomposition during the latter part of the distillation, leaving a charred residue of 12–13 g.

Refractionation, at 10 mm. pressure, through a Todd column¹¹ gave: fraction 1, 6.0 g. of a colorless liquid, b.p. 27–40°. This was further separated by distillation through the same column at 740 mm. to yield 2 g. of pyrrole, b.p. 130–132°, n_D^{25} 1.502, and 1.5 g. of 2-isopropylpyrrolidine, b.p. 141–142°, n_D^{25} 1.450, d_4^{25} 0.898. Fraction 2, 20.5 g. of a colorless oil, b.p. 63–65°, n_D^{25} 1.487, d_4^{25} 0.898. After three extractions with 25-ml. portions of *N* HCl the residual liquid was taken up in ether, dried and distilled to yield: 10.5 g. of 2-isopropylpyrrole, b.p. 171–172° (741 mm.), n_D^{25} 1.491, d_4^{25} 0.908 (18.8%).¹² Neutralization and extraction with ether of the hydrochloric acid fraction gave upon distillation (a) 1.5 g. of 2,5-diisopropylpyrrolidine, b.p. 171–173° (741 mm.), n_D^{25} 1.451, d_4^{25} 0.832 (3.8%).¹² Chloroplatinate, yellow-orange crystals, m.p.K. 199–201°; and (b) 4.5 g. of a pale-yellow oil, diisopropylpyrrole,¹³ b.p. 167–171° (22 mm.), n_D^{25} 1.505, d_4^{25} 0.956 (8.1%).¹² Hydrochloride, m.p. 184–186°. Fraction 3, 14.0 g. of 2,5-diisopropylpyrrole, b.p. 83–86°, n_D^{25} 1.484, d_4^{25} 0.887, (36.2%).¹² This represents a total of 69.4% of the number of bridge carbon atoms from purified material, not counting losses due to distillation.

A second hydrogenolysis of 26.8 g. of "acetonepyrrole," 10 g. of copper chromite catalyst⁸ and 175 ml. of dry, peroxide-free dioxane at 215° and 204 atm. gave a pressure drop of 37.4 atm. in 6.5 hours. After removal of spent catalyst, and of the dioxane, a crystalline material precipitated from the residual liquid on standing. Precipitation could be promoted by the addition of methanol. Shaking the solid with cold acetone and concentration of the filtrate gave white needles of unchanged "acetonepyrrole," m.p. 296° (darkening). The residual solid was recrystallized from ethyl acetate, decolorizing with Darco charcoal G-60. A second recrystallization from boiling acetone gave white needles, m.p.K. 197.5–198.0°, after drying under vacuum at 100° over phosphorus pentoxide.

Anal. Calcd. for $C_{14}H_{24}N_2$: C, 76.30; H, 10.98; N, 12.72; mol. wt., 220.35. Found: C, 76.4, 76.9, 76.7; H, 11.2, 11.3, 10.7; N, 12.4, 12.7; mol. wt. (Rast), 229.

It readily gave a hydrochloride which gradually darkened on heating and did not melt below 350°.

Anal. Calcd. for $C_{14}H_{24}N_2 \cdot HCl$: C, 65.47; H, 9.81; N, 10.91; Cl, 13.81; mol. wt., 256.82. Found: C, 65.2, 65.3; H, 10.0, 10.0; N, 10.8, 10.7; Cl (Carius), 13.6, 13.5.

A picrate was also formed (by addition of alcoholic picric acid to an acetone solution of the $C_{14}H_{24}N_2$ compound). Recrystallization from methanol gave yellow needles which sublimed at 235°, decomposed at 285°. Cleavage of the picrate on alumina indicated a 1:1 ratio of $C_{14}H_{24}N_2$ to picric acid.

Anal. Calcd. for $C_{14}H_{24}N_2 \cdot C_6H_3N_3O_7$: C, 53.44; H, 6.06; N, 15.58; O, 24.92; mol. wt., 449.46. Found: C, 53.3, 53.5; H, 6.3, 6.3; N, 15.5, 15.4.

Pyrolytic Degradation of "Acetonepyrrole."^{2b,c}—In a 500-ml. r.b. flask, half embedded in a sand-bath and bearing a 12 mm. bore side arm sealed 3 cm. above the bulb which led to a water-cooled receiver, was placed an intimate mixture of 200 g. of "acetonepyrrole" and 50 g. of zinc dust. By heating with an open flame, 131 g. of yellow oil was distilled over. A preliminary distillation from a 125-ml. pear-shaped Claisen-type flask, with a 5 inch vacuum-jacketed Vigreux column, gave three main fractions: fraction 1, up to 65° at 10 mm.; fraction 2, 65–110° at 10 mm.; fraction 3, 95–138° at 2 mm.; residue, 30 g.

Redistillation of fraction 1 through a Todd column gave 42.0 g. of pyrrole, b.p. 27–35° (10 mm.), n_D^{25} 1.508. Fraction 2 gave (a) 13.0 g. of 2-isopropylpyrrole, b.p. 67–70° (11 mm.), n_D^{25} 1.492, d_4^{25} 0.910, and (b) 4.5 g. of 2-ethyl-5-

isopropylpyrrole, b.p. 85–88° (11 mm.), n_D^{25} 1.488, d_4^{25} 0.889. Fraction 3 gave (a) 3 g. of a light yellow oil, b.p. 142–145° (10 mm.), n_D^{25} 1.568, d_4^{25} 1.011. Partial crystallization was induced by cooling with Dry Ice to yield pale yellow needles. After drying on a porous plate, two recrystallizations from ethanol gave white needles, m.p.K. 101–101.5°.

Anal. Calcd. for $C_9H_{11}N$: C, 81.16; H, 8.33; N, 10.51; mol. wt., 133.19. Found: C, 81.2, 80.9; H, 8.3, 8.1; N, 10.2, 10.2; mol. wt. (Rast), 136, and (b) 6 g. of a bright yellow oil, b.p. 148–150° (6 mm.), n_D^{25} 1.558, d_4^{25} 0.986. Partial crystallization occurred after cooling with Dry Ice to yield long needles in a viscous oil. Drying on a porous plate and recrystallization from the melt gave white needles, m.p.K. 58–60°.

Anal. Calcd. for $C_{13}H_{17}N$: C, 83.37; H, 9.15; N, 7.48; mol. wt., 187.28. Found: C, 83.2, 83.7; H, 9.2, 9.0; N, 7.4, 7.4; mol. wt. (Rast), 182.

Synthesis of Isopropyl Substituted Pyrroles.—The pyrrole Grignard reagent was first prepared by the combination of pyrrole and methylmagnesium iodide in ether solution. Its subsequent reaction with isopropyl bromide led to the formation of a mixture of isopropylpyrroles. After hydrolysis with aqueous ammonium chloride the mixture was steam distilled to remove tars and resins and then fractionally distilled through a Todd column. The products depended upon the ratio of methylmagnesium iodide to pyrrole, and on the manner of their combination.

Method 1.—Dropwise addition of one mole of pyrrole in 150 ml. of dry ether to one mole of methylmagnesium iodide in 500 ml. of ether, was followed by the addition of one mole of isopropyl bromide and refluxing for 2.5 hours. Fractionation gave (a) 18 g. of pyrrole, b.p. 27–32° (10 mm.), n_D^{25} 1.508; (b) 30 g. of 2-isopropylpyrrole, b.p. 67.5–70.5° (10 mm.), n_D^{25} 1.492, d_4^{25} 0.906, yield 15.9%¹⁴ and (c) 16 g. of 2,5-diisopropylpyrrole, b.p. 87–90° (11 mm.), n_D^{25} 1.484, d_4^{25} 0.886, yield 6.5%¹⁴.

Anal. Calcd. for $C_{10}H_{17}N$: C, 79.40; H, 11.30; N, 9.26. Found: C, 79.6, 79.1; H, 11.4, 11.6; N, 9.3, 9.4.

Method 2.—As method 1, but two moles of methylmagnesium iodide in 1 liter of dry ether. A reflux time of 2 hours gave (a) 8.5 g. of 2-isopropylpyrrole, b.p. 67–70° (11 mm.), n_D^{25} 1.490, d_4^{25} 0.906, yield 7.8%¹⁴; (b) 17.0 g. of 2,5-diisopropylpyrrole, b.p. 87–90° (11 mm.), n_D^{25} 1.486, d_4^{25} 0.886, yield 11.2%¹⁴ and (c) 23 g. of 2,3,5-triisopropylpyrrole, b.p. 99–102° (10 mm.), n_D^{25} 1.481, d_4^{25} 0.871, yield 11.9%¹⁴.

Anal. Calcd. for $C_{13}H_{23}N$: C, 80.77; H, 11.99; N, 7.24. Found: C, 81.1, 81.6; H, 12.2, 12.2; N, 7.3, 7.1.

Method 3.—Dropwise addition of one mole of methylmagnesium iodide in 500 ml. of dry ether to one mole of pyrrole in 500 ml. of dry ether and subsequent reaction with one mole of isopropyl bromide for 2 hours gave: (a) 32.0 g. of unreacted pyrrole, b.p. 28–33° (10 mm.), n_D^{25} 1.506; (b) 17.5 g. of 2-isopropylpyrrole, b.p. 65–70° (10 mm.), n_D^{25} 1.491, d_4^{25} 0.908; yield 10.5%¹⁴ and (c) 2.0 g. of 2,5-diisopropylpyrrole, b.p. 85–90° (10 mm.), n_D^{25} 1.484, d_4^{25} 0.886; yield 0.9%¹⁴.

2-Ethyl-5-isopropylpyrrole.—2-Isopropylpyrrole and magnesium bromide was prepared as in method 1 from 27.3 g. (0.25 mole) of 2-isopropylpyrrole and 0.30 mole of ethylmagnesium bromide in 200 ml. of dry ether, followed by the addition of 27.2 g. (0.25 mole) of ethyl bromide and refluxing for 1 hour. Fractionation gave: (a) 9.5 g. of unreacted 2-isopropylpyrrole, b.p. 66–70° (10 mm.), n_D^{25} 1.491; and (b) 9.5 g. of 2-ethyl-5-isopropylpyrrole, b.p. 81–84° (10 mm.), n_D^{25} 1.489, d_4^{25} 0.898; yield 42.5% (based on the amount of 2-isopropylpyrrole consumed).

Anal. Calcd. for $C_9H_{13}N$: C, 78.77; H, 11.02; N, 10.21. Found: C, 78.9, 78.6; H, 11.1, 11.5; N, 10.3, 10.4.

Synthesis of Isopropyl Substituted Pyrrolidines.—The appropriate pyrrole with Raney Nickel W-4 catalyst⁶ and dry, peroxide-free dioxane was charged to a Pyrex glass liner of the hydrogenation apparatus and hydrogen admitted under pressure. After continuous rocking at elevated temperatures, the bomb was cooled, spent catalyst removed by filtration, and the filtrate fractionated in the Todd column.

2-Isopropylpyrrolidine.—Twenty grams of 2-isopropylpyrrole, 3 g. of catalyst⁶ and 25 ml. of dioxane, at 204 atm.

(11) Todd Precise Fractionation Assembly (50-plate column); F. Todd, *Ind. Eng. Chem., Anal. Ed.*, **17**, 175 (1945).

(12) Percentage of total number of bridge carbon atoms.

(13) C. F. H. Allen, M. R. Gilbert and D. M. Young, *J. Org. Chem.*, **2**, 227, 235 (1937).

(14) Based on amount of pyrrole consumed.

of hydrogen and 190° for 8 hours gave 9.5 g. of 2-isopropylpyrrolidine, b.p. 48–51° (20 mm.), n_D^{25} 1.442, d_4^{25} 0.835, conversion 45.8%.

Anal. Calcd. for $C_7H_{15}N$: C, 74.27; H, 13.36; N, 12.37. Found: C, 73.9, 74.1; H, 13.8, 13.5; N, 12.6, 12.1; chloroplatinate, m.p. 138–140°.

Anal. Calcd. for $C_7H_{15}N \cdot H_2PtCl_6$: C, 26.42; H, 5.07, Pt, 30.68. Found: C, 26.0, 26.7; H, 5.5, 5.3; Pt, 30.8, 31.2.

2,5-Diisopropylpyrrolidine.—Fifteen grams of 2,5-diisopropylpyrrole, 3 g. of catalyst in 25 ml. of dioxane, were hydrogenated at 192 atm. and 185° for 5 hours. Fractional distillation gave 8.5 g. of 2,5-diisopropylpyrrolidine, b.p. 63–67° (10 mm.), n_D^{25} 1.442, d_4^{25} 0.826, conversion 55.2%.

Anal. Calcd. for $C_{10}H_{21}N$: C, 77.34; H, 13.63; N, 9.03. Found: C, 77.1, 77.0; H, 13.9, 13.5; N, 9.1; chloroplatinate, m.p. 198–200°.

Anal. Calcd. for $2 C_{10}H_{21}N \cdot H_2PtCl_6$: C, 33.34; H, 6.16; Pt, 27.09. Found: C, 33.4; H, 5.8; Pt, 27.2.

2-Ethyl-5-isopropylpyrrolidine.—Eight and one-half grams of 2-ethyl-5-isopropylpyrrole, 3 g. of catalyst in 25

ml. of dioxane, were hydrogenated at 190° and 153 atm. for 4 hours; yield 4.5 g. of 2-ethyl-5-isopropylpyrrolidine, b.p. 171–172° (743 mm.), n_D^{25} 1.442, d_4^{25} 0.832, conversion 53.0%.

Anal. Calcd. for $C_9H_{19}N$: C, 76.52; H, 13.56; N, 9.92. Found: C, 76.3, 76.2; H, 13.6, 13.5; N, 9.8, 9.8. Hydrochloride, m.p. 195–200°.

Anal. Calcd. for $C_9H_{19}N \cdot HCl$: C, 60.82; H, 11.35; N, 7.88; Cl, 19.95. Found: C, 60.7, 60.7; H, 11.5, 11.6; N, 7.7, 7.8; Cl, 19.6, 19.8.

Acknowledgment.—One of us (CLG) is indebted to the Kettering Foundation for the Fellowship which made this study possible. The generous loan of hydrogenation and fractionation equipment, by the Chemistry Department of Antioch College, is gratefully acknowledged.

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

The Structure of α -Erythroidine¹

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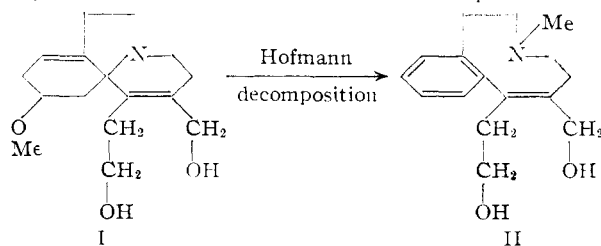
RECEIVED JANUARY 5, 1955

α -Erythroidine has been carried through a sequence of degradations which provides convincing evidence that the original molecule contains the partial structure shown by formula III. The key reaction in this sequence was the rearrangement and aromatization that occurred when dihydro- α -erythroidinol (V) was subjected to the conditions of the Hofmann exhaustive methylation procedure. From III, it can be seen that α -erythroidine possesses the same carbon skeleton as β -erythroidine but differs from it in the arrangement of the lactone ring. Although the positions of the methoxyl group and the two aliphatic double bonds in rings A and B remain uncertain, formula XV is tentatively proposed for the over-all structure of α -erythroidine.

In a previous publication,³ the characterization of α -erythroidine was described and evidence was presented emphasizing the differences between α - and β -erythroidine in their behavior and properties. Although these two alkaloids had been named on the supposition that they were diastereoisomers,⁴ the conclusion drawn in our previous study was that this was unlikely. In order to investigate this point further, we have now made a study of the Hofmann degradation of dihydro- α -erythroidinol following the same general approach which had been used successfully in the case of β -erythroidine.⁵

In the previous studies on β -erythroidine it was found that when dihydro- β -erythroidinol (I) was subjected to the conditions of the Hofmann exhaustive methylation procedure, rupture of the carbon-nitrogen bond was accompanied by aromatization with loss of the elements of methanol to give compound II.^{5,6} Since this transformation removes the features responsible for optical activity, it would be

expected that, if α -erythroidine were a diastereoisomer of β -erythroidine, a similar degradation of α -erythroidine would lead to the identical product II.



To test this hypothesis it was necessary to prepare dihydro- α -erythroidinol and this was accomplished as follows. α -Erythroidine was treated with lithium aluminum hydride to effect reduction of the lactone ring and give the corresponding diol, α -erythroidinol. This, on hydrogenation using Raney nickel as catalyst, gave the desired dihydro- α -erythroidinol in good yield. Although it was also shown that α -erythroidine could be catalytically reduced to dihydro- α -erythroidine following the same procedure, the further reduction of dihydro- α -erythroidine with lithium aluminum hydride as an alternate route to dihydro- α -erythroidinol was not investigated.

When dihydro- α -erythroidinol was subjected to the conditions of the Hofmann exhaustive methylation procedure, a smooth reaction occurred to give the corresponding des-base as a light yellow gum in 89% yield. From the analytical data, it was appar-

(1) Aided by a grant from the United Cerebral Palsy Association.

(2) Du Pont Postgraduate Fellow, 1953–1954.

(3) V. Boekelheide and M. F. Grundon, *THIS JOURNAL*, **75**, 2563 (1953).

(4) K. Folkers and R. T. Major, British Patent 543,187; K. Folkers and R. T. Major, U. S. Patent 2,373,952.

(5) J. Weinstock and V. Boekelheide, *THIS JOURNAL*, **75**, 2546 (1953).

(6) The style of representing the formulas of these alkaloids has been changed from that used in our previous publications in order to obtain a uniform presentation for all of the erythrina alkaloids (see Boekelheide and Prelog, "Progress in Organic Chemistry," Vol. III, Academic Press, Inc., New York, N. Y., 1955).