Cox and Wolfenden's suggestion that this effect is approximately an additive property of the ions has been confirmed.

4. It is shown for the first time that permanganates have the property of diminishing the viscosity of water.

5. The extended Jones and Dole equation is found to fit our data better and over a greater range of concentration than any other known equation.

6. The results confirm the equation of Falkenhagen and Vernon for the computation of the influence of interionic attraction on the viscosity.

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[CONTRIBUTION FROM THE C. F. KETTERING FOUNDATION FOR THE STUDY OF CHLOROPHYLL AND PHOTOSYNTHESIS]

A New Porphyrin Synthesis. The Synthesis of Porphin[1]

BY PAUL ROTHEMUND

Recently we reported on the formation of porphyrins from pyrrole and aldehydes (formaldehyde, acetaldehyde and furaldehyde),[2] and we announced further studies to ascertain the applicability of the reaction to other aldehydes. It was found that the reaction can be used for the synthesis of a large number of porphyrins, when pyrrole is used as one component and a substance with aldehydic function as the other component. In this paper the reaction between pyrrole and formaldehyde will be described, as the reaction product, porphin[3] (Fig. 1), is of interest as the fundamental ring system in all the porphyrins, and hence also in the important pigments hemin and chlorophyll.

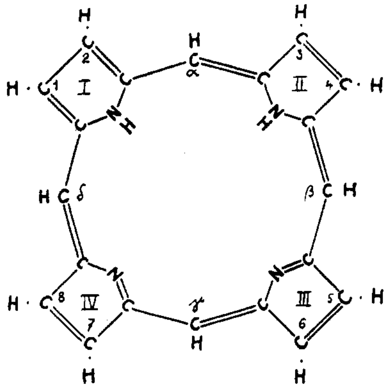

Fig. 1.—Porphin.

Attempts to prepare this ring system had been made by different investigators in the field,[4,5] but the reaction products obtained did not exhibit the characteristic properties of porphyrins. Very recently Fischer[6] reported a synthesis of porphin, brought about by adding pyrrole-α-aldehyde to boiling formic acid; his spectroscopic data for porphin checked with those published from this Laboratory.[2]

Our porphin synthesis may be represented by the scheme shown in Fig. 2. When formaldehyde and pyrrole were used, porphin (Fig. 1) was obtained; with pyrrole and another aldehyde a porphin with substitution in the positions α, β, γ and δ resulted.

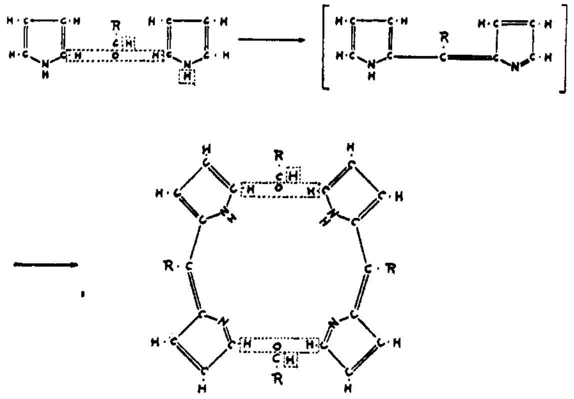

Fig. 2.

If the synthesis with formaldehyde and pyrrole was performed at a temperature of 145–155° instead of 90–95° as described for porphin in the experimental part, a porphyrin resulted which differed from porphin spectroscopically in the positions of the two main absorption bands: these bands were shifted approximately 100 Å. toward the red region of the spectrum. The hydrochloric acid number was much lower than that of porphin. Studies are now in progress to deter-

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[1] This investigation was carried out with the experimental cooperation of T. Londergan in partial fulfilment of the requirements for his Bachelor's degree under the Antioch Coöperative Plan.

(2) Rothemund, THIS JOURNAL, **57**, 2010 (1935).

(3) Fischer and Halbig, *Ann.*, **448**, 193 (1926); Fischer, Halbig, and Walach, *ibid.*, **452**, 268 (1927).

(4) Chelintzev and Maksorov, *J. Russ. Phys.-Chem. Soc.*, **48**, 748 (1916); quoted from *C. A.*, **11**, 782 (1917).

(5) Godnew and Naryschkin, *Ber.*, **58**, 2703 (1925); *ibid.*, **59**, 2897 (1926).

(6) Fischer and Gleim, *Ann.*, **521**, 157 (1935).

mine whether or not this porphyrin is an isomer of porphin.

The reaction has been tested with a number of other aldehydes (acetaldehyde, propionaldehyde, *n*-butyraldehyde, benzaldehyde and α-furaldehyde), and has led to crystallized porphyrins; with chloral hydrate, glyoxylic acid, *o*-nitrobenzaldehyde, vanillin, *p*-dimethylaminobenzaldehyde, and pyrrole-α-aldehyde, porphyrin formation was observed spectroscopically.

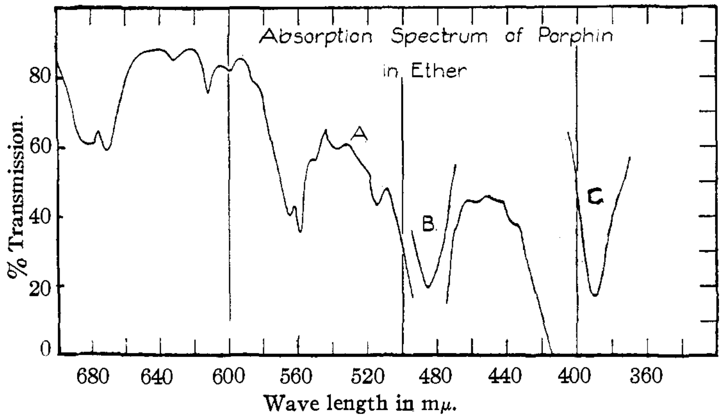

Fig. 3.—Absorption spectrum of porphin in ether.—The letters B and C refer to determinations with the concentrations 50 and 25%, respectively, of the initial concentration A.

The description of the *ms*-substituted porphins prepared will be reported subsequently. An investigation of the absorption spectra and of the fluorescence spectra of the new porphyrins and their metal complex salts is now being carried out at Antioch College by Dr. Albers and Dr. Knorr, to whom I am indebted for the absorption spectrum curve of porphin in pyridine–ether,[7] reproduced in Fig. 3.

Experimental

Solution of Formaldehyde in Methanol.—Gaseous formaldehyde was generated by heating 50 g. of paraformaldehyde and 50 cc. of 10% sulfuric acid in a round-bottom flask. The gas passed a reflux condenser and was then absorbed in 250 cc. of methanol under cooling with ice water. The highest concentration obtained by this method was 2% formaldehyde in methanol. The determination was performed according to Romijn.[8]

Synthesis of Porphin.—The reaction vessels were made from Pyrex glass. Tubes of 250 mm. length and 38 mm. inside diameter were closed at one end; to the other end a piece of Pyrex tubing of 200 mm. length and 8 mm. inside diameter was fused. The containers had a capacity of about 200 cc. They were filled with 10 cc. of a 5 molar solution of pyrrole in methanol (corresponding to 3.35 g. of pyrrole), 100 cc. of 2% formaldehyde solution in methanol, and 10 cc. of pyridine. The air above the reaction mixture was replaced by nitrogen in order to render the sealing of the tubes less dangerous. The sealed tubes were heated in a water-bath to 90–95° for thirty hours and opened after cooling by breaking off the seal at the end of the narrow tube.

The contents of five tubes was filtered into a standard taper round-bottomed flask, the residue in the tubes and on the filter was extracted with pyridine and the filtered pyridine extract was added to the original filtrate. The solution was heated on a steam-bath to distil the methanol off, and then concentrated *in vacuo* to a volume of approximately 30 cc. The contents of the flask was taken up into 2 liters of ether and filtered. (The remaining flakes were tested for porphin by extraction with hot pyridine, addition of ether and water, and spectroscopic examination of the ether layer. Usually the flakes were porphin-free; in the case of a positive porphin test the ether was filtered and combined with the main ether solution.) The ether solution of porphin was washed with two 200-cc. portions of water, followed by two extractions with 20 cc. of 50% acetic acid; finally, the ether solution was extracted with three 20-cc. portions of a saturated solution of acid sodium sulfite in water, and washed with water until neutral. The dark red-brown ether solution was then subjected to fractionation with hydrochloric acid by Willstätter's method.[9] The hydrochloric acid concentrations used for the first fractionation were: 5, 10, 15 and 25%. Each fraction was transferred into fresh ether by means of sodium acetate in the case of the lower concentrations, and by partial neutralization with 10% sodium hydroxide and addition of sodium acetate for the higher concentrations. Porphin entered the 5 and 10% fractions. These two fractions were combined and the porphin transferred into 1.5 liters of ether by means of sodium acetate. After washing with water, the red ether solution was fractionated with 1, 3 and 10% hydrochloric acid. The 3% fraction was the main fraction and contained porphin in very pure form. The porphin was transferred back into 1.5 liters of ether, the ether was washed and then dried with sodium sulfate, filtered and concentrated to a volume of 10 cc. Porphin crystallized from this ether in dark auburn platelets with a violet metallic surface luster. The yield was approximately 1 mg. of pure porphin for every gram of pyrrole used. The hydrochloric acid number was 3.3. The substance was soluble in pyridine, chloroform, or acetic acid; it was only slightly soluble in ether or methanol.

Anal. Material crystallized from ether and recrystallized twice from pyridine–ether; dried at 120° *in vacuo* over phosphorus pentoxide. Calcd. for $C_{20}H_{14}N_4$: C, 77.38; H, 4.55; N, 18.07. Found: C, 77.2; H, 4.8; N, 17.9.—Determination of the "active" hydrogen (Roth's[10] modification of the method of Tschugaeff–

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[7] Kirstahler, *Tabulae Biologicae Periodicae*, **1**, 258 (1931).

[8] Meyer, "Lehrbuch der organisch-chemischen Methodik," Julius Springer, Berlin, 1933, Vol. 2, p. 50.

[9] Willstätter and Mieg, *Ann.*, **350**, 1 (1906).

[10] Roth, *Mikrochemie*, **11**, 140 (1932); *cf.* Flaschenträger, *Z. physiol. Chem.*, **146**, 219 (1925).

Zerewitinoff): Calcd. two active hydrogen atoms in the molecule. Found: CH_4 corresponding to 1.8 active hydrogen atoms.

Magnesium Complex Salt of Porphin (Porphin Phyllin).—Five milligrams of porphin, 15 mg. of magnesium oxide, 0.5 cc. of pyridine, and 7.5 cc. of 40% methanolic potassium hydroxide were heated in a sealed tube for three hours to 140-150°. After cooling, the alkaline solution exhibited the typical phyllin spectrum. The phyllin was transferred to 500 cc. of ether by addition of 80 cc. of water, and the ether was washed alkali-free. Drying with sodium sulfate, filtration and evaporation to a volume of approximately 20 cc. yielded the phyllin in red needle-shaped crystals.

Anal. Calcd. for $C_{20}H_{12}N_4Mg$: C, 72.19; H, 3.64; N, 16.85; Mg, 7.32. Found: N, 16.6; Mg, 7.0.

Heating of the phyllin with 10% hydrochloric acid on a steam-bath eliminated the complexly linked magnesium atom; the thus regenerated porphin was transferred into ether by means of sodium acetate and identified spectroscopically and by crystallization.

Hemin of Porphin.—Five milligrams of porphin was dissolved in 1.5 cc. of glacial acetic acid, heated to boiling. 50 mg. of ferric chloride and 150 mg. of sodium acetate were added, and the boiling continued for two minutes. The resulting hemin was transferred into 50 cc. of ether by addition of 25 cc. of water. The hemin, isolated from the ether in the usual manner, crystallized in form of brown cubes.

Anal. Calcd. for $C_{20}H_{12}N_4FeCl$: C, 60.09; H, 3.03; N, 14.03; Fe, 13.98; Cl, 8.87. Found: N, 13.6; Cl (Carius), 8.4.

Copper Complex Salt of Porphin.—Preparation analogous to the preparation of the hemin, except that ferric chloride was replaced by copper acetate; brick-red needles from ether.

Anal. Calcd. for $C_{20}H_{12}N_4Cu$: C, 64.57; H, 3.25; N, 15.08; Cu, 17.10. Found: N, 15.3.

Absorption Spectra

Porphin.—(a) in pyridine-ether:[7] I, 637.0-(632.3)-627.5; II, 620.5-(617.8)-615.0; III, 608.6-(605.4)-602.2; IV, 593.0-(590.6)-588.1; V, 583.3---575.0-(571.6)-568.1; VI, 564.7-(561.9)-559.1; VII, 554.6-(552.7)-550.7; VIII, 529.3-(522.4)-515.4; IX, 506.7-(489.9)-473.2; shadow 460.0; E. A. 433.0. Intensity: IX, VI, V, II, VIII, VII, IV, I = III.

(b) In 3% hydrochloric acid: I, 578.5-(572.3)-566.0; II, 548.7-(543.0)-534.2; III, 514.3-(505.4)-496.4; E. A. 414.0. Intensity: II, III, I.

Porphin Phyllin.—(a) in pyridine-ether:[7] I, 609.6-(605.2)-600.8; II, 574.9-(569.6)-564.3 (double band with maxima measured at 572.2 and 566.0); III, 551.5-(535.3)-519.0; IV, 501.0-(491.0)-481.0; E. A. 427.0. Intensity: III, I = II, IV.

(b) In the alkaline reaction mixture: I, 577.8-(572.2)-566.6; II, 551.7---540.9-(535.9)-530.9---522.8; III, 510.1-(498.6)-487.1; E. A. 420.0. Intensity: II, I, III.

Porphin Hemin.—(a) in pyridine-ether:[7] I, maximum 579.5; II, 555.5-(549.9)-544.3; III, 528.0-(520.0)-512.0; E. A. 422.0. Intensity: III, II, (I).

(b) In chloroform: I, 646.2-(638.1)-630.0; II, 601.0---585.0-(575.8)-566.7; III, 544.9-(517.9)-491.0; shadow 610.0; E. A. 420.0. Intensity: III, II, I.

(c) In chloroform + hydrazine hydrate: I, 648.0-(641.8)-635.5---630.5; II, 605.0---583.5-(571.8)-560.0; III, 543.0-(536.6)-530.1; IV, 516.0-(502.0)-488.0; E. A. 451.0. Intensity: IV, III, II, I.

Porphin Copper Complex Salt (in pyridine-ether[7]).—I, 552.6-(548.7)-544.8; II, 529.1---520.3-(515.0)-509.7---502.8; III, 489.6-(485.2)-480.8; E. A. 423.5. Intensity: II, I, (III).

Summary

1. A porphyrin synthesis is described, in which pyrrole is used as one component and a substance with aldehydic function as the other component for the condensation.

2. Porphin and five *ms*-substituted porphins have been synthesized by the method so far, using pyrrole and one of the following aldehydes: formaldehyde, acetaldehyde, propionaldehyde, *n*-butyraldehyde, benzaldehyde and α-furaldehyde; for six more aldehydes porphyrin formation with pyrrole has been demonstrated spectroscopically.

3. The synthesis of porphin, the fundamental structure of the physiologically important pigments hemin and chlorophyll, from pyrrole and formaldehyde is described in detail as an example of the reaction.

4. The hemin, phyllin and copper complex salts of porphin have been prepared.

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