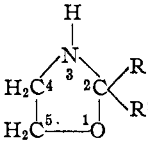
TABLE I

2-OXAZOLIDINES 

Aldehyde or ketone reacted	2-Oxazolidine	Yield, %	Boiling point °C.	Boiling point Mm.	Nitrogen, % Found	Nitrogen, % Calcd.	$n^{25}D$	d^{25}_4	Mol. ref. Found	Mol. ref. Calcd.
Isobutyraldehyde	Isopropyl	55	37–39	40	11.9	12.3	1.4531	0.9356	33.30	33.11
Acetaldehyde	Methyl	56	85–85.5	740	15.7	16.1	1.4313	.9872	22.85	23.87
Benzaldehyde	Phenyl	10	156–157	24	9.4	9.5	....	....	...	...
Butyraldehyde	Propyl	57	45–45.5	40	11.8	12.3	1.4497	.9307	33.20	33.11
Propionaldehyde	Ethyl	28	87.5–88	740	13.8	13.9	1.4481	.9415	28.80	28.49
Heptaldehyde	Hexyl	95	M. p. 38–39°		8.8	8.9	....	....	...	...
Acetone	Dimethyl	6	53–53.5	45	13.6	13.9	1.4491	.9556	28.68	28.49
Methyl *n*-amyl ketone	Methyl, *n*-amyl	5	88–89	7	9.2	8.9	1.4492	.9053	46.60	46.77

TABLE II

HYDROLYSIS PRODUCTS OF OXAZOLIDINES

2-Oxazolidine	Cubic milliliters of aldehyde or ketone Found	Cubic milliliters of aldehyde or ketone Theo.	Grams of amine hydrochloride Found	Grams of amine hydrochloride Theo.
Isopropyl	6.0	7.8	7.0	8.4
Methyl	...	...	8.4	11.2
Phenyl	6.0	6.7	5.5	6.5
Dimethyl	...	...	9.0	9.6
Propyl	6.2	7.6	7.6	8.4
Ethyl	...	...	7.0	9.6
Hexyl	8.0	8.6	5.7	6.2

recovered in sufficient amounts to indicate that these compounds are readily hydrolyzed, a characteristic property of the oxazolidines.

Attempts to prepare an oxazolidine by treating ethyleneimine with crotonaldehyde were not successful. When using the general procedure of reaction in ether solution the mixture became cherry-red after refluxing for only a few minutes and upon removal of the ether became very viscous and dark red in color. The addition of only 0.5 ml. of the imine to 10 ml. of crotonaldehyde gave a hard plastic mass of deep red color within a day.

Although oxazolidines have been reported[7] as being prepared from *p*-hydroxybenzaldehyde, *m*-hydroxybenzaldehyde and *m*-nitrobenzaldehyde by the reaction of monoethanolamine these aldehydes did not react with ethyleneimine to give the heterocyclic compound under the conditions studied. *p*-Hydroxy- and *m*-hydroxybenzaldehydes reacted with ethyleneimine to give yellowish red plastic materials which softened under 100° without a sharp melting point and were insoluble in hot butyl alcohol. Nitrogen analyses indicated one mole of ethyleneimine had reacted for each mole of aldehyde. In attempts with *m*-nitrobenzaldehyde by the general procedure there appeared to be no reaction and all the imine was recovered unchanged.

Summary

1. A new synthesis for oxazolidines has been suggested.

2. Four new oxazolidines: 2-ethyl, 2-propyl, 2-hexyl and 2,2-dimethyl have been prepared and some of their properties determined.

3. Ethyleneimine reacts with crotonaldehyde, *p*-hydroxybenzaldehyde and *m*-hydroxybenzaldehyde to give plastic products of unknown structure.

MORGANTOWN, WEST VIRGINIA

RECEIVED OCTOBER 19, 1949

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF THE JOHNS HOPKINS UNIVERSITY]

Synthetic Chlorins and Dihydrochlorins[1,2]

BY WALTER SCHLESINGER,[3] ALSOPH H. CORWIN AND LEWIS J. SARGENT

In their examination of synthetic chlorins, Fischer and Helberger[4] noted one sharp contrast in behavior between these substances and the natural chlorins derived from chlorophyll. This was the fact that the natural chlorins all gave active hydrogen determinations corresponding with the presence of two NH bonds in the nucleus while the synthetic chlorins gave zero values in the Zerewitinoff determination. These findings were confirmed by the work of Fischer and Rothemund.[5] While a formulation of a ring with no hydrogens on nitrogen and extra hydrogens on carbons in the beta positions of the porphyrin nucleus is possible, other substances suggesting such a formulation have not been discovered. It is of interest, therefore, to reëxamine the synthetic chlorins with a view to a more precise determination of their structure.

Fischer and his collaborators[6] prepared etiochlorin I by the reduction of etiohemin chloride I with sodium in absolute alcohol and in isoamyl alcohol.[5] Because of the greater availability of etioporphyrin II, our studies have been con-

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[1] Porphyrin Studies. IX. Paper VIII, Andrews, Corwin and Sharp, THIS JOURNAL, **72**, 491 (1950).

[2] A portion of this paper is from the doctoral dissertation of Walter Schlesinger, The Johns Hopkins University, 1940.

[3] William Wrigley, Jr., Co., Chicago, Ill.

[4] Fischer and Helberger, *Ann.*, **471**, 285 (1929).

[5] Fischer and Rothemund, *Ber.*, **64**, 208 (1931).

[6] Fischer, Platz, Helberger and Niemer, *Ann.*, **479**, 40 (1930).

ducted on this substance. We have followed essentially the method used by Fischer's laboratory in our preparation of etiochlorin II and have studied the effect of a number of variables on the yield of chlorin obtained.

Quantitative determinations of active hydrogen were made both with our chlorin and with etioporphyrin II. Using the Zerewitinoff method we found two active hydrogens for etioporphyrin and also *two active hydrogens for etiochlorin II.*

Because of the fact that our method of purification differed from that used by Fischer's laboratory in our use of a chromatographic separation, we examined the possibility that the process of purification might have been responsible for the difference in active hydrogen values observed. Repetition of the active hydrogen determination with a sample of crude chlorin also gave an active hydrogen value of approximately two. We conclude that this determination is not seriously affected by the manner of purification of the chlorin.

From our analyses for carbon, hydrogen and active hydrogen, we feel justified in assuming the etiochlorin II to contain two secondary and two tertiary nitrogen atoms in the ring and that it contains two hydrogen atoms more than the corresponding porphyrin from which it was obtained.

In our study of the preparation of etiochlorin II, we have confirmed the observation of Fischer and Helberger[6] that the manganese complex of etioporphyrin reduces to the chlorin and the copper complex does not. In addition, we have tried the cobalt, nickel, zinc and magnesium complexes with negative results. We conclude that the iron complex is the best for the purpose.

The rate of oxidation of ethiochlorin II by molybdicyanide was compared with that reported by Conant and his collaborators[7] for methyl pheophorbide. After twenty hours, approximately 13% oxidation had occurred in the case of the etiochlorin as compared with 93% for methyl pheophorbide in the same time. This shows that the synthetic chlorin is more resistant to oxidation than the natural one. It also demonstrates that molybdicyanide may be used for the rapid oxidation of dihydrochlorin to chlorin.

Fischer and Helberger[6] mention the appearance of a by-product "perhydrochlorin," an unstable red, oily material. It seemed probable that this nomenclature is faulty, since a completely hydrogenated chlorin of the type suggested by the term "perhydro" should be a colorless compound. We have confirmed the observation that this by-product occurs and have succeeded in separating some of the material by chromatographic means. We confirm the instability of the compound but were able to obtain enough in relatively pure form for a quantitative dehydrogenation with potassium molydicyanide.[7] Two equivalents of molydicyanide converted the "red oil" quantitatively to etiochlorin II, demonstrating that Fischer and Helberger's "perhydro" chlorin is in reality a dihydrochlorin. Attempts to prepare complexes led to oxidation with the formation of chlorin complexes.

The one diagnostic tool in the study of chlorins which permits structural determinations to be made with precision is the oxidation with chromic anhydride.[8] In most cases recorded in the literature, the total yield of recognizable fragments from the oxidation of porphyrins with this reagent has been less than 50%. It was thought of value, therefore, to carry out exploratory experiments on etioporphyrin II with a view toward isolating and characterizing other oxidation products which would account for some of the remainder of the starting material employed.

Oxidation experiments with etioporphyrin II have thus far yielded, in addition to methylethylmaleic imide, at least three low molecular weight acids as well as carbon dioxide and carbon monoxide. The latter two products together account for approximately four out of 32 carbon atoms in the molecule and might conceivably arise from the four bridge carbon atoms. The acidic products have been separated into steam volatile and non-volatile fractions.

In attempting to characterize pyruvic and homopyruvic acids, it was learned the *p*-phenylphenacyl bromide does not esterify their sodium salts in the usual manner. Thus these substances are best characterized through their ketonic derivatives.

It was found that two equivalents of chromic anhydride does not convert etiochlorin II to etioporphyrin II. When more chromic anhydride is used on the chlorin, the yields of methylethylmaleic imide as well as those of carbon dioxide and carbon monoxide were comparable with the yields of the corresponding substances obtained from etioporphyrin. The acid fraction, however, appeared to contain at least one substance which differed from those derived from etioporphyrin. This additional substance has not yet been identified.

In attempts to improve the synthesis of the etioporphyrins, we have prepared a number of dipyrrylmethanes containing the acetyl group in the beta position. Attempts to hydrogenate the acetyl groups to ethyl groups by the method used for the preparation of 2,4-dimethyl-3-ethyl-5-carbethoxypyrrole led to the recovery of the unchanged starting material. We have no explanation to offer for the refractory behavior of the acetyldipyrrylmethanes toward reduction as contrasted with the reactivity of the simple pyrrole derivative.

To extend the literature on dipyrrylmethanes the preparation and characterization of several new substances of this class is included.

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(7) Conant, Dietz, Bailey and Kamerling, THIS JOURNAL, **53**, 2387 (1931).

(8) Fischer and Wenderoth, *Ann.*, **637**, 179 (1939).

The authors wish to acknowledge a grant-in-aid from the Rockefeller Foundation which permitted this investigation to be carried out. One of us (W.S.) wishes also to acknowledge a grant from the Hynson, Westcott and Dunning Research Fund.

Experimental

Reduction of Etiohemin II.—Three grams of pure etiohemin chloride II and 20 g. of sodium were refluxed under hydrogen in 300 cc. of dry isoamyl alcohol. In six to ten minutes the reaction mixture turned green. After twenty minutes 200 cc. of ethanol was added very cautiously, still keeping the reaction mixture under hydrogen. When all of the excess sodium had reacted, 150 cc. of concentrated hydrochloric acid was added carefully to the hot mixture, still under hydrogen. Once all the acid has been added, the reaction mixture is no longer sensitive to air and the atmosphere of hydrogen can be dispensed with. The acid solution was poured into two liters of water and extracted several times with ether. Practically all of the color went into the ether solution. This was washed with water five or six times and then extracted with 4% hydrochloric acid until no more porphyrin was removed. The ether solution was then extracted with 20% hydrochloric acid saturated with ether until no more chlorin went into the aqueous layer. The combined water extracts were then diluted with an equal volume of water and extracted with chloroform. All of the chlorin went into the chloroform layer. The chloroform was evaporated at room temperature, leaving a mixture of chlorin and isoamyl alcohol. This was poured into enough water to dissolve all the alcohol (about 20 l.). The aqueous solution was made slightly alkaline and the chlorin, which was oily at first, gradually solidified. It was filtered and dried in a vacuum desiccator in a darkened place. The yield of crude chlorin–dihydrochlorin mixture was 2.0 g. or 79%.

Separation of Etiochlorin II and Dihydroetiochlorin II.—The crude chlorin obtained by the above procedure was dissolved in hexane, filtered and chromatographed over a column of magnesium oxide. The chlorin was all adsorbed from the hexane. The column was then developed with a mixture of 70% benzene and 30% hexane. The first colored product that came through was rich in dihydrochlorin. The later fractions were relatively richer in the green component. The yield from 6.0 g. of the mixture was 2.6 g. of enriched chlorin and 2.4 g. of enriched dihydrochlorin. By repeated fractional chromatographing in this manner it was possible to isolate the green material free from the red and the red free from the green. The yield of purified chlorin was 3.4 g. from 4.3 g. of the enriched fraction.

Chromatographing and other operations with chlorin mixtures containing the red material are best carried out under nitrogen and in subdued light, since under alkaline conditions light destroys the red pigment. In the presence of chlorin this reaction appears to be quite rapid. In the absence of chlorin it appears to take place much more slowly.

Etiochlorin II.—The chlorin is a very intensely colored substance which crystallizes in dark blue-black crystal clusters from hexane–alcohol. The crystals are so intensely colored that they do not transmit light when examined under the microscope and consequently must be illuminated from above for microscopic investigation.

Etiochlorin is very soluble in chloroform, hexane, pyridine and benzene. It is only slightly soluble in alcohol. Dilute solutions of the chlorin are green with a very faint red fluorescence. More concentrated solutions appear to be deep crimson due to dichroism.

Crystals of etiochlorin hydrochloride may be obtained by passing dry gaseous hydrogen chloride into a hot solution of 50 mg. of the chlorin in 50 cc. of pure, dry benzene. The hot solution is immediately placed in a quiet, dust-free place to cool. After twenty-four hours the crystals are filtered and examined microscopically. Beautiful, deep violet-blue octahedra are obtained in this way. These crystals also do not transmit light.

The hydrochloride is soluble in ethanol, methanol, chloroform and acetone. It is insoluble in benzene and hexane. The color of the hydrochloride in solution varies from deep violet-blue to reddish violet, depending on the solvent.

For purification, the best method of crystallizing the chlorin after chromatographing is to dissolve it in a small amount of hexane, filter hot, then add boiling ethanol to the filtrate and allow the chlorin to crystallize. The first few crystallizations showed the presence of dark tarry materials in the chlorin but these were removed by subsequent crystallizations.

For analysis, the etiochlorin II was chromatographed over activated alumina, then magnesia. It was then recrystallized from hexane or hexane–alcohol, as indicated.

Anal. Calcd. for $C_{32}H_{38}N_4$ (etioporphyrin): C, 80.29; H, 8.00. For $C_{32}H_{40}N_4$ (dihydroporphyrin): C, 79.95; H, 8.39. For $C_{32}H_{42}N_4$ (tetrahydroporphyrin): C, 79.62; H, 8.77. Found: C, 79.61,[a] 79.53,[b] 79.72,[c] 79.66[d]; H, 8.37,[a] 8.43,[b] 8.29,[c] 8.33.[d]

[a] Recrystallized twice from hexane. [b] Recrystallized once from hexane, once from hexane–ethanol. [c] Recrystallized from hexane, then twice from hexane–ethanol. [d] Recrystallized from hexane three times, then twice from hexane–ethanol.

Absorption spectrum of etiochlorin II in hexane: I, 640–658 mμ; II, 635–637; III, 615–620; IV, 586–600; V, 544–546; VI, 517–521; VII, 494–499; VIII, 480–490. End absorption, 422 mμ. Order of intensity: I, VII, VIII, IV, III, II, VI, V.

Absorption spectrum of etiochlorin II Mg complex, obtained from succeeding experiment: I, 605–633 mμ; II, 595; III, 564–578; IV, 552; V, 506–517. End absorption, 425 mμ.

Active Hydrogen Determinations.—The active hydrogens in etioporphyrin II were determined by treating a weighed sample of the porphyrin with an excess of methylmagnesium iodide in dibutyl ether and measuring the volume of methane evolved over dibutyl phthalate. Sample, 0.1065 g.: CH_4, 11.7 cc. at 302 °K. and 760.4 mm. Active H, 2.1. Etiochlorin II. Sample, 0.1080 g. (analytically pure): CH_4, 11.6 cc. at 760.8 mm. and 303 ° K. Active H, 2.08. Etiochlorin II (crude). Sample, 0.086 g.: CH_4, 10.0 cc. at 761.5 mm. and 304 °K. Active H, 2.2.

Attempted Quantitative Dehydrogenation.—An attempt was made to determine the oxidation equivalent of etiochlorin II using the technique of Conant, Dietz, Bailey and Kamerling.[7] After exposure to the molybdicyanide reagent for 1200 minutes, only 13% oxidation had taken place. This resistance to oxidation makes it possible to oxidize dihydroetiochlorin to etiochlorin without appreciable overshooting.

Another oxidation was performed with ceric sulfate. Twenty-five milligrams of etiochlorin was placed in each of three 50-ml. Erlenmeyer flasks and dissolved in 15 cc. of a solution made up to equimolar quantities of purified pyridine and glacial acetic acid. The first sample was treated with 2.4 cc. (2 equiv.) of 0.043 *N* ceric sulfate, the second with 4.8 cc. (4 equiv.), and the third with 7.2 cc. (6 equiv.). After eighteen hours the spectrum of etioporphyrin had begun to appear in all of these solutions; after ninety hours the solutions all began to deposit small amounts of etioporphyrin. This experiment shows that ceric sulfate in pyridineacetic acid will oxidize the chlorin slowly.

Variations in the Etiochlorin Preparation.—The effect of water was assayed by treating 50 mg. of etiohemin with 25 cc. of isoamyl alcohol, 1 cc. of water and 5 g. of sodium. Unreacted porphyrin was recovered and no chlorin was formed.

Absolute ethanol at the boil was substituted for boiling isoamyl alcohol. Assay showed that the conversion was incomplete. Absolute *n*-propanol was tried with the same results. Absolute *n*-butanol gave yields comparable with those obtained with isoamyl alcohol.

The technique used in the reduction of etiohemin II was repeated on the cobalt, copper, manganese, nickel, zinc and magnesium complexes of etioporphyrin II. The copper and magnesium complexes gave no chlorin. The cobalt complex gave a trace of chlorin. The nickel and zinc complexes gave a trace of dihydrochlorin. The manganese complex gave a crude chlorin yield of 53%.

Dihydroetiochlorin.—After chromatographic separation of the dark, blue-green chlorin from the adhering red oil, a hexane solution of the latter was repeatedly chromatographed over a column of magnesium oxide until freed from any blue-green color. The hexane solution of the purified red oil was filtered and concentrated on the steam-bath under reduced pressure in an atmosphere of hydrogen. The product consisted of a dark-red sirup which solidified to a waxy cake after about one week; yield 1.6 g. from 2.4 g. of enriched dihydrochlorin fraction.

Quantitative Dehydrogenation of Dihydroetiochlorin.—In view of the stability of etiochlorin to molybdicyanide reagent, the state of oxidation of the red oil can be determined by treatment with this reagent, first with an excess and then with a deficiency. The reagent consisted of 0.003 *M* potassium molybdicyanide[9] in equimolar pyridine–acetic acid. Twenty-five milligrams of the dried red solid from the preparation above was placed in each of four glass-stoppered Erlenmeyer flasks and covered with different amounts of the molybdicyanide reagent. Aliquots of 0.7 cc. were removed from each sample after varying intervals of time and back-titrated with 0.001 *M* potassium ferrocyanide. It was learned in this manner that the reaction is about 90% complete in twenty-five minutes and is essentially complete in 6–6.5 hours. In this time the maximum amount of chlorin produced which could be oxidized would vary from 0 to 3% in the four experiments. The amounts of molybdicyanide reagent used in four experiments were: (a) 37.6 cc. (2.17 equiv.); (b) 75.2 cc. (4.3 equiv.); (c) 112.8 cc. (6.5 equiv.); (d) 18.8 cc. (1.09 equiv.). Molecular weight, calcd. for $C_{32}H_{42}N_4$, 483. Equivalent weight, 241.4. Found, from back titration with ferrocyanide: (a) 231; (b) 233; (c) 239. In experiment (d) all the molybdicyanide was consumed and the spectroscope showed a mixture of chlorin and dihydrochlorin spectrum. This establishes the fact that oxidation of the dihydrochlorin does not take place in the absence of the reagent. Chlorin was isolated from the first three solutions. The yields were (a) 82.5%; (b) 86%; (c) 83%. Since the isolation procedure is not quantitative, this establishes the fact that essentially the same amount of chlorin is formed by 2, 4 and 6 equivalents of molybdicyanide. Experiment (d) establishes that one equivalent is insufficient for complete conversion to chlorin. From these facts it follows that the red material is a dihydrochlorin.

Complex Formation.—Attempts to prepare iron, copper, zinc and magnesium complexes of the dihydrochlorin under hydrogen by treatment with ferrous chloride, cupric acetate, zinc acetate and methylmagnesium iodide, respectively, all resulted in the formation of the corresponding metallo-complexes of the green chlorin, as determined by absorption spectra.

Oxidation of Etioporphyrin II with Chromic Anhydride.—The reaction was conducted in a three-necked flask equipped with funnel, an inlet for carbon dioxide-free oxygen, and a gas outlet which bubbled through a barium hydroxide absorption tube for the determination of carbon dioxide, a potassium hydroxide tube for drying and removal of acidic impurities, a hopcalite tube maintained at 150° for the oxidation of carbon monoxide and finally through a second barium hydroxide tube for the determination of carbon dioxide. Five hundred milligrams of etioporphyrin II was dissolved in 20 cc. of concentrated sulfuric acid and cooled with an ice-bath. Twenty-five grams of crushed ice and a trace of ferrous sulfate as a catalyst[10] were added. A solution of 1.7 g. of chromic anhydride in 8 cc. of water and 5 cc. of concentrated sulfuric acid was then added dropwise over a period of forty-five minutes. During all this time, the reaction was swept with oxygen to remove carbon monoxide and carbon dioxide. In two experiments, carbon dioxide equivalent to 3.54 and 3.24 carbon atoms was recovered and carbon monoxide equivalent to 0.19 and 0.13 carbon atoms, making a total of 3.73 and 3.37 carbon atoms accounted for by these materials. In four experiments, methylethylmaleic imide was isolated[10] in yields corresponding to 1.16, 1.66, 1.60 and 1.80 pyrrole rings out of the four present in the porphyrin. This indicates that other fragments corresponding approximately to two pyrrole rings should be found. The acid residue was treated quantitatively for the isolation of ammonia in three experiments and amounts corresponding to 1.76 and 1.92 and 2.04 atoms of nitrogen were found indicating rupture of the two rings with the production of ammonia and other products, probably acidic.

The acid oxidation mixture from 0.61 millimole (300 mg.) of etioporphyrin was steam distilled. The alkali neutralized by the steam distillate was 2.54 millimoles. Attempts to prepare the *p*-phenylphenacyl ester of the sodium salt of this acid mixture led only to the production of *p*-phenylphenacyl alcohol, m. p. 126–129°.[11] Attempts to prepare *p*-phenylphenacyl esters of pyruvic, homopyruvic and methylethylmaleic acids all led to the formation of the same alcohol and no ester.

The residue from the steam distillation was neutralized and then acidified and extracted with ether. The yield was 1.88 millimoles. The sodium salts, when dried, weighed 0.21 g. The correspondence between weights and equivalence would be correct for a mixture of acetic and propionic acids. The *p*-phenylphenacyl ester of this salt was prepared and melted in the range of 85–100° in different preparations. The m. p. of the acetate is 109.5–111° and of the propionate 101–102°. A mixed m. p. between acetate and propionate was 90–93°.

To obtain larger quantities of these acids, several oxidation runs for the preparation of methylethylmaleic imide were combined; m. p. of *p*-phenylphenacyl ester, 84.5–87.5°. After four recrystallizations, a sample melting at 100–104° was obtained; mixed m. p. with the propionate, 87–89°. A sample melting at 88.5–89° was mixed with an equal amount of the mixture of acetate and propionate esters melting at 90–93°, mixed m. p. 88–91°; remelt, 87.5–90.5°. This gives an inconclusive indication that the substance is a mixture of *p*-phenylphenacyl acetate and propionate.

Oxidation of Etiochlorin II.—A sample of etiochlorin II was treated with just enough chromic anhydride in sulfuric acid to convert it to etioporphyrin. On examination of the product, no etioporphyrin was found. This shows that the reagent has been consumed in the destruction of the molecule and not in its conversion to porphyrin.

A quantitative oxidation was performed in the manner described for the porphyrin, except that the carbon monoxide was not determined. Carbon dioxide accounted for 3.5 carbon atoms. Methylethylmaleic imide accounted for 1.16 pyrrole rings. The acid fraction was isolated as described immediately above, with the omission of the steam distillation. The mixed sodium salts were treated with *p*-phenylphenacyl bromide and an ester was obtained melting with decomposition at 160–165° after crystallization from hot benzene. This was not identified.

3,5,3′,5′-Tetramethyl-4,4′-diacetyl-*meso*-dimethyldipyrrylmethane.—One gram of 2,4-dimethyl-3-acetylpyrrole was dissolved in 20 cc. of ethanol. Five cubic centimeters of acetone and two drops of concentrated hydrochloric acid were added and the mixture refluxed for fifteen minutes. Thirty cubic centimeters of water was added and the mixture allowed to stand overnight. The precipitate was recrystallized from acetone, then twice from alcohol; m. p. 233–235°.

Anal. Calcd. for $C_{19}H_{26}O_2N_2$: C, 72.58; H, 8.34. Found: C, 72.53; H, 8.40.

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[9] Fieser, THIS JOURNAL, **52**, 5226 (1930).

[10] Ellingson and Corwin, *ibid.*, **68**, 1114 (1946).

[11] Drake and Bronitsky, *ibid.*, **52**, 3715 (1930); Allen and Ball, *Can. J. Research*, **7**, 643 (1932).

Attempts to reduce the acetyl group to ethyl, using palladium chloride on Norite catalyst under hydrogen,[12] were unsuccessful.

3-Ethyl-4,3′,5′-trimethyl-5-carbethoxy-4′-acetyldipyrrylmethane.—Six grams of 2-bromomethyl-3-ethyl-4-methyl-5-carbethoxypyrrole was added slowly to a boiling solution of 3.2 g. of 2,4-dimethyl-3-acetylpyrrole in 40 cc. of boiling methanol. The mixture was refluxed for five minutes. Water was added to incipient turbidity and the solution allowed to cool. The methane which separated was recrystallized from alcohol–water; m. p. 174–175°; yield after one recrystallization, 6.3 g. or 87%.

Anal. Calcd. for $C_{19}H_{26}O_3N_2$: C, 69.06; H, 7.93. Found: C, 69.05; H, 7.99.

Attempts to reduce the acetyl group in this methane to ethyl by the catalytic method were unsuccessful.

3,4′-Diacetyl-4,3′,5′-trimethyl-5-carbethoxydipyrrylmethane.—One gram of 2-chloromethyl-3-acetyl-4-methyl-5-carbethoxypyrrole was added to a boiling solution of 560 mg. of 2,4-dimethyl-3-acetylpyrrole in 10 cc. of boiling methanol. The mixture was refluxed for fifteen minutes, then allowed to cool overnight in the icebox. The methane was recrystallized from alcohol–water; m. p. 210°.

Anal. Calcd. for $C_{19}H_{24}O_4N_2$: C, 66.26; H, 7.03. Found: C, 66.00; H, 7.03.

Attempts to hydrogenate the acetyl groups to ethyl groups by the usual method were unsuccessful.

3,4,3′,5′-Tetramethyl-4,4′-diethyl-*meso*-dimethyldipyrrylmethane.—Three-tenths of a cubic centimeter of freshly distilled 2,4-dimethyl-3-ethylpyrrole was dissolved in 10 cc. of ethanol. Two cubic centimeters of acetone and one drop of 48% hydrobromic acid were added. The mixture was refluxed under nitrogen for fifteen minutes, poured into water and allowed to stand overnight. The precipitate, which was oily at first, solidified. It was filtered and recrystallized from ethanol, then from methanol; yield, 120 mg.; m. p. 156°.

Anal. Calcd. for $C_{19}H_{30}N_2$: C, 79.66; H, 10.56. Found: C, 79.50; H, 10.50.

Attempts to prepare dicryptopyrrylmethane from cryptopyrrole and formaldehyde by the method above gave only tarry products.

3,5,4′-Trimethyl-4-acetyl-3′,5′-dicarbethoxydipyrrylmethane.—Five hundred milligrams of 2,4-dimethyl-3-acetylpyrrole was dissolved in 25 cc. of hot ethanol and to the boiling solution 200 mg. of 2-chloromethyl-3,5-dicarbethoxy-4-methylpyrrole was added. The mixture was refluxed for thirty minutes, water added and the precipitate allowed to stand for twenty-four hours. Two recrystallizations from ethanol gave a product melting at 274°.

Anal. Calcd. for $C_{20}H_{26}O_5N_2$: C, 64.15; H, 7.00. Found: C, 64.20; H, 7.04.

Attempts to hydrogenate the acetyl group were unsuccessful.

Summary

1. Our preparations of etiochlorin II assay for two active hydrogen atoms, paralleling in this the behavior of the natural chlorins.

2. The rate of oxidation of etiochlorin II is much slower than that of methyl pheophorbide when treated with potassium molybdicyanide.

3. The "red oil" formed as a by-product in the preparation of ethiochlorin has been shown to be a dihydrochlorin by quantitative oxidation with potassium molybdicyanide.

4. Certain new fragments have been separated in the oxidation of etioporphyrin with chromic anhydride but identification is not complete.

5. Chromic anhydride does not convert etiochlorin II to etioporphyrin II.

6. Attempts to prepare *p*-bromophenacyl esters of pyruvic and homopyruvic acids by the usual method were unsuccessful leading to the conclusion that these substances should be identified through their ketonic derivatives.

7. In contrast to 2,4-dimethyl-3-acetyl-5-carbethoxypyrrole, four different dipyrrylmethanes with acetyl groups in beta positions failed to reduce when treated with hydrogen and palladium.

8. Several new dipyrrylmethanes, prepared in the course of this work, have been described.

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[12] Compare Corwin and Quattlebaum, THIS JOURNAL, **58**, 1084 (1936).

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

Preparation and Reactions of Methylenecyclopentane

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In an earlier paper from this Laboratory[2] it was shown that methylenecyclohexane reacts with formaldehyde, maleic anhydride and sulfur trioxide (as its dioxane complex) to form 1–1 adducts. Only in the case of the product resulting from the formaldehyde–olefin reaction was an independent synthesis accomplished.

By modification of several earlier procedures, a convenient synthesis for methylenecyclopentane (I) has now been effected. This "isobutylene type" olefin has been treated with formaldehyde, maleic anhydride and sulfur trioxide (as its dioxane complex). In each case 1–1 adducts were isolated and assigned structures III, IV and II, respectively.

Compound II when treated with bromine water does not liberate sulfate ion and therefore cannot have α,β-unsaturation.[3,4,5]

Alcohol (III) was prepared independently by reducing 1-cyclopentenylacetic acid with lithium aluminum hydride.[6]

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[1] This material is taken from a Ph.D. thesis submitted to the Graduate Faculty of the University of Minnesota by Roger W. Amidon, June, 1949.

[2] Arnold and Dowdall, THIS JOURNAL, **70**, 2590 (1948).

[3] Suter and Malkemus, *ibid.*, **63**, 978 (1941).

[4] Suter and Bordwell, *ibid.*, **65**, 507 (1943).

[5] Kohler, *ibid.*, **20**, 680 (1898).

[6] Nystrom and Brown, *ibid.*, **69**, 2548 (1947).