The Synthesis of Four Isomeric Tetramethyltetracarbethoxyporphyrins[1]

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The synthesis of each of the four isomeric tetramethyltetracarbethoxyporphyrins analogous to the etio-, copro-, and uroporphyrins of isomer types I–IV is described. These syntheses have been achieved using dipyrrylmethenes bearing α-chloro- and α-methyl-substituent groups. In each case the methenes underwent condensation in naphthalene solution in the presence of cupric acetate to give the porphyrin copper complex, from which the corresponding porphyrin free base was obtained upon subsequent treatment with concentrated sulfuric acid. The present work represents the first reported synthesis of the type III and IV isomers and provides an alternative synthetic route to types I and II. The four isomeric tetramethyltetracarbethoxyporphyrins exhibit significant differences in their ultraviolet and visible absorption spectra and in their solubilities in organic solvents. The four isomers also afford distinctly different X-ray powder patterns.

The initial objective of a research program begun sometime ago was to synthesize the four isomeric tetramethyltetracarbethoxyporphyrins analogous to the etio-, copro-, and uroporphyrins of types I–IV. It was proposed to synthesize these four tetramethyltetracarbethoxyporphyrins, then to undertake a comparative study of their physical and chemical properties. It was anticipated that the results of such a study would serve to illuminate the effects of molecular symmetry in the porphyrin system upon these properties. The present article describes the synthesis of these four isomeric porphyrins and reports some results of a preliminary study of certain of their physical properties.

The problem of distinguishing between isomeric porphyrins by means of their physical or chemical properties frequently proves a difficult one. Such widely used criteria of identity as melting point or mixture melting point are often of little utility.[3] The visible absorption spectra of coproporphyrins I–IV are essentially identical.[4] The same holds true for the fluorescence spectra of certain isomeric porphyrins,[5] although the fluorescence spectra of isomers have been found to exhibit different pH dependencies.[6] However, differences in the infrared spectra have been observed[7,8] in comparing coproporphyrins I and III as well as uroporphyrins I and III. In addition, at the time when this work was undertaken the X-ray powder pattern had been used successfully in two instances to distinguish between isomeric porphyrins.[9] More recently, Klesper, Corwin, and Iber[10] have further demonstrated the general utility of this latter method. Two groups of workers[11] have, moreover, observed significant differences in comparing the proton magnetic resonance spectra of porphyrin isomers.

Several considerations prompted the selection of the isomeric tetramethyltetracarbethoxyporphyrins for synthesis and subsequent study. Two of these in particular deserve mention. First, it was our expectation that the vastly dissimilar nature of the methyl and carbethoxy groups as substituents would give rise to pronounced symmetry effects upon the physical and chemical properties in this series of porphyrin isomers. Secondly, the synthetic versatility of the carbethoxy group permits its replacement[12] by many other substituent groups. Thus these porphyrins are of interest as intermediates for the synthesis of a wide variety of porphyrins.

When this study was initiated, synthesis of the tetramethyltetracarbethoxyporphyrins of isomer type I[13] and isomer type II[12] had been reported. More recently an additional synthesis each of type I[14] and of type II[15] has been described. The less symmetrically substituted and thus less readily accessible isomers of types III and IV, on the other hand, have not been synthesized previously.

Since it appeared that chlorinated methenes had received little previous attention[16] as intermediates of potential utility in porphyrin synthesis, we were prompted to explore the feasibility of employing dipyrrylmethenes bearing α-chloro- and/or α-methyl-substituent groups for the synthesis of each of the four tetramethyltetracarbethoxyporphyrins. The vast majority of synthetic porphyrins reported in the literature to date have been prepared from analogous brominated methenes.

The utility of metals and their compounds in promoting condensation reactions leading to the phthalocyanines has long been recognized. Similar effects have been demonstrated in the case of certain porphyrin syntheses[13,14,17–21] from monopyrryl and dipyrryl intermediates, although the precise mode of action of the metal, metallic salt, or the organometallic compound is not yet clearly understood. Several examples of the

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(3) E. M. Jope and J. R. P. O'Brien, *Biochem. J.*, **39**, 239 (1945).

(4) A. Stern and H. Wenderlein, *Z. Physik. Chem.*, **A170**, 337 (1934).

(5) A. Stern and H. Molvig, *ibid.*, **A175**, 38 (1935).

(6) H. Fink and W. Hoerburger, *Z. Physiol. Chem.*, **232**, 28 (1935).

(7) C. H. Gray, A. Neuberger, and P. H. A. Sneath, *Biochem. J.*, **47**, 87 (1950).

(8) J. E. Falk and J. B. Willis, *Australian J. Sci. Res.*, **A4**, 579 (1951).

(9) O. Kennard and C. Rimington, *Biochem. J.*, **55**, 105 (1953).

(10) E. Klesper, A. H. Corwin, and P. K. Iber, *Anal. Chem.*, **33**, 1091 (1961).

(11) (a) R. J. Abraham, A. H. Jackson, and G. W. Kenner, *J. Chem. Soc.*, 3468 (1961); (b) R. J. Abraham, P. A. Burbidge, A. H. Jackson, and G. W. Kenner, *Proc. Chem. Soc.*, 134 (1963); (c) E. D. Becker, R. B. Bradley, and C. J. Watson, *J. Am. Chem. Soc.*, **83**, 3743 (1961).

(12) J. S. Andrews, A. H. Corwin, and A. G. Sharp, *ibid.*, **72**, 491 (1950).

(13) A. H. Corwin and V. L. Sydow, *ibid.*, **75**, 4484 (1953).

(14) W. S. Caughey, A. H. Corwin, and R. Singh, *J. Org. Chem.*, **25**, 290 (1960).

(15) G. P. Arsenault, E. Bullock, and S. F. MacDonald, *J. Am. Chem. Soc.*, **82**, 4384 (1960).

(16) H. Fischer, E. Baumann, and H. J. Riedl, *Ann.*, **475**, 205 (1929).

(17) G. G. Kleinspehn and A. H. Corwin, *J. Am. Chem. Soc.*, **82**, 2750 (1960).

(18) J. H. Priesthoff and C. V. Banks, *ibid.*, **76**, 937 (1954).

(19) U. Eisner and R. P. Linstead, *J. Chem. Soc.*, 3742 (1955).

(20) U. Eisner, R. P. Linstead, E. A. Parkes, and E. Stephen, *ibid.*, 1655 (1956).

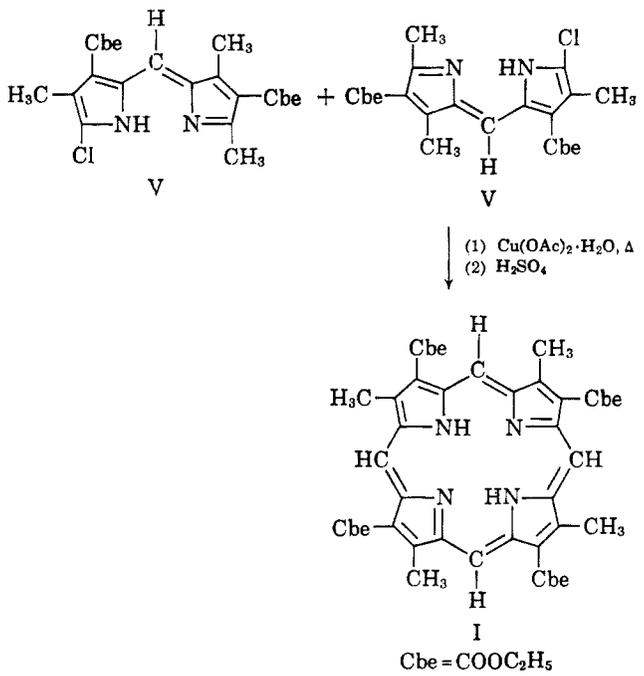
(21) U. Eisner, A. Lichtarowicz, and R. P. Linstead, *ibid.*, 733 (1957).

advantageous use of metallic derivatives appear in the literature, and in most cases the product is a porphyrin metal complex.

In the present instance cupric acetate was selected as the metallic salt of choice for promoting condensation of the chlorinated methenes to porphyrins after a number of preliminary condensation experiments indicated its suitability.

The synthesis of the type I porphyrin isomer, 1,3,5,7-tetramethyl-2,4,6,8-tetracarbethoxyporphyrin (I) (Chart I), was accomplished *via* the self-condensa-

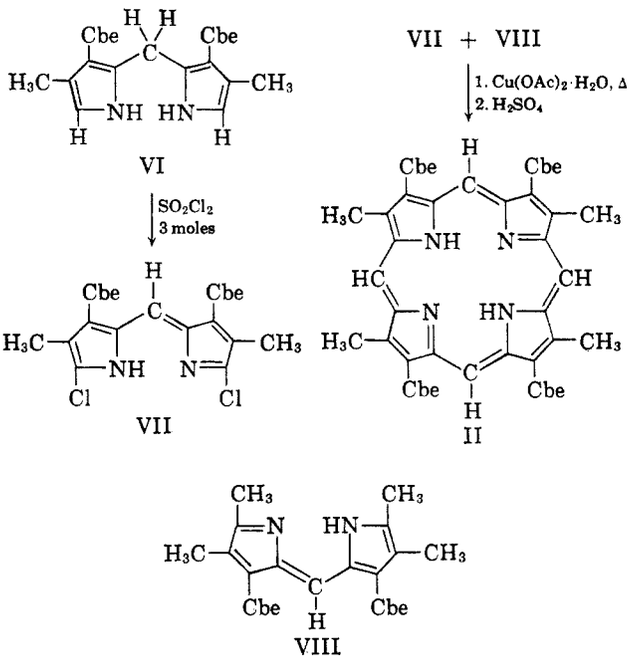
CHART I



tion of monochlorodipyrrylmethene V in the presence of cupric acetate at 180–220°. Corwin and Sydow[13] had previously synthesized I employing the analogous monobromodipyrrylmethene and cuprous chloride. In both instances the first product isolated was the cupric complex of I, which after preliminary purification was converted by concentrated sulfuric acid, without ester hydrolysis, to the metal-free porphyrin. Following further purification by chromatography and recrystallization, a 7% yield of the *analytically pure* porphyrin tetraester I was obtained based upon V. In the process of working up the present methene condensation reaction mixture it became readily apparent that substantial losses of porphyrin attend the purification sequence designed to remove nonporphyrin impurities. In fact, from weights of crude product and from spectrophotometric assay it could be estimated that the porphyrin copper complex was generally present in the crude reaction mixture in a yield approximating 20%. These same remarks apply to the analogous methene condensations leading to porphyrin isomers II–IV. Purification losses were apparently much greater in the case of isomers I and II.

The type II isomer, 1,4,5,8-tetramethyl-2,3,6,7-tetracarbethoxyporphyrin (II), has been prepared in good yield by two different methods.[12,15] We synthesized II *via* condensation of α,α'-dimethyldipyrrylmethene (VIII) with the previously unreported

CHART II



α,α'-dichlorodipyrrylmethene (VII). The dichlorinated methene was obtained by the chlorination of dipyrrylmethane VI (Chart II) using 3 moles of sulfuryl chloride; the other methene, VIII, by the method of Brunings and Corwin.[22] Condensation of methenes VII and VIII in the presence of cupric acetate afforded *via* the cupric complex of II a 5% yield of analytically pure type II metal-free porphyrin. Our product was compared with isomer II prepared by the method of Andrews, Corwin, and Sharp.[12] The two products exhibited indistinguishable ultraviolet and visible absorption spectra and very similar X-ray powder patterns and solubility characteristics.

The dichloromethene VII was also utilized for the synthesis of the type III isomer, 1,3,5,8-tetramethyl-2,4,6,7-tetracarbethoxyporphyrin (III). The second methene required for the final condensation was the unsymmetrical dipyrrylmethene IX, a previously unreported compound. Methene IX was obtained *via* two routes in order to authenticate its structure. The first route involved condensation of α-free pyrroles X and XI (Chart III) with formaldehyde to give the unsymmetrical dipyrrylmethane XII, which was subsequently oxidized to methene IX. The successful synthesis of XII was patterned after Corwin and Brunings' similar preparation of a mono-N-methyldipyrrylmethane.[23] The second route employed the condensation of pyrrolecarboxaldehyde XIII with α-free pyrrole XI. The methene products obtained *via* the first and second routes showed no depression during a mixture melting point determination. The analytically pure porphyrin isomer III was then obtained in a yield of 13% by condensing methenes VII and IX in the presence of cupric acetate.

The type IV isomer, 1,4,6,7-tetramethyl-2,3,5,8-tetracarbethoxyporphyrin (IV), was synthesized *via* condensation of dipyrrylmethenes VII and XIV (Chart IV). Here, as in the case of each of the other

(22) K. J. Brunings and A. H. Corwin, *J. Am. Chem. Soc.*, **66**, 337 (1944).
(23) A. H. Corwin and K. J. Brunings, *ibid.*, **64**, 2106 (1942).

TABLE I

ELECTRONIC SPECTRAL DATA FOR ISOMERIC PORPHYRINS IN CHLOROFORM AT 30°[a]

Isomer type	λ_{max}, mμ						
	1	2	3	4	Soret	Ultraviolet	
I	654	598	558	522	428	322	271
II	654	598	557	520	423	326	279
III	651	595	556	521	426.5	318	265
IV	648	595	556	523	427.5	317	266
	$\epsilon_{max} \times 10^{-3}$						
	1	2	3	4	Soret	Ultraviolet	
I	3.5	5.8	6.5	15.5	284	17.1	29.0
II	4.8	5.6	7.9	14.9	287	17.3	24.5
III	2.8	5.7	5.9	15.5	251	16.7	23.4
IV	1.8	5.7	5.2	15.6	247	16.2	24.6

[a] These data were obtained using a Cary Model 11 spectrophotometer. The solvent was J. T. Baker reagent chloroform (No. 9180) containing about 0.2% ethanol as preservative. The chloroform was stored over calcium oxide and was filtered just prior to use.

CHART III

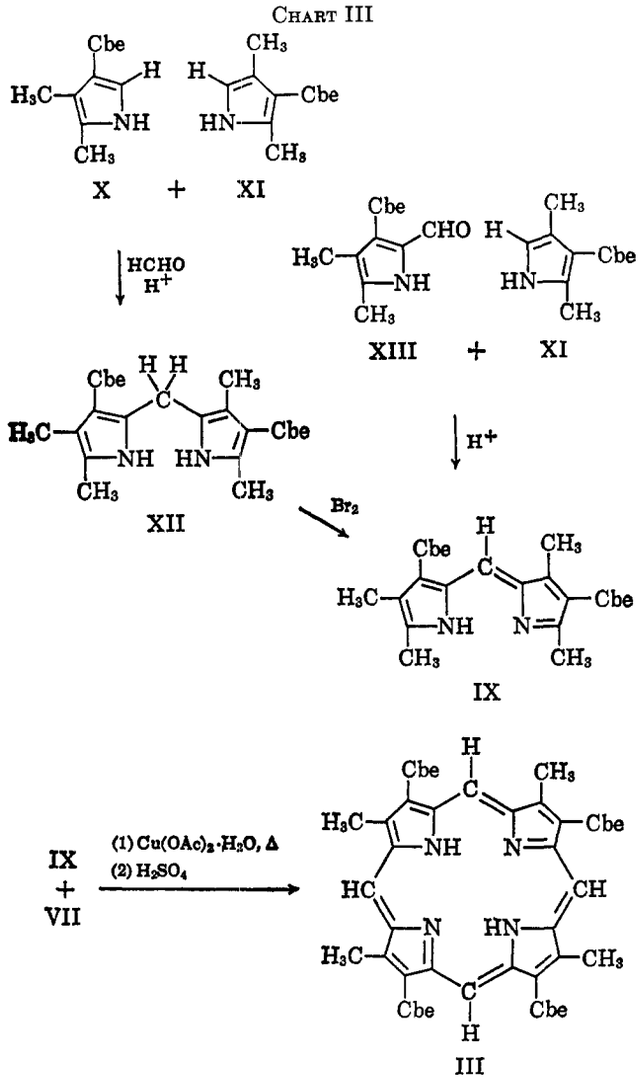
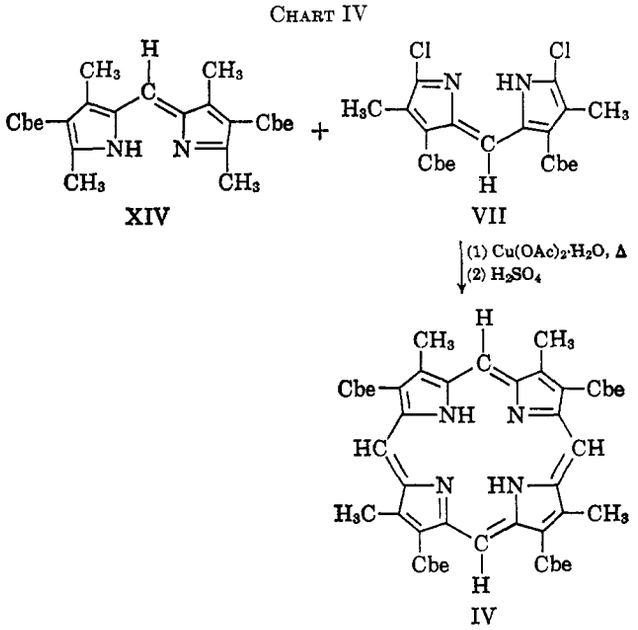


CHART IV



three isomers, copper was removed from the initially formed porphyrin–copper complex upon treatment with sulfuric acid to afford the porphyrin free base. In the present instance the analytically pure porphyrin base IV was obtained from VII and XIV in 17% yield.

Table I compares the ultraviolet and visible absorption spectra of the four isomeric tetramethyltetracarbethoxyporphyrins in chloroform solution. The spectral differences, while not great in magnitude, are nevertheless sufficient to render the four isomers distinguishable from one another. Although there are significant differences to be noted in comparing λ_{max} values (particularly in the ultraviolet), the relative ϵ_{max} values are perhaps more definitive for identification purposes. Porphyrin IV is unique among the isomers in exhibiting a porphyrin spectrum of the "phyllo type," *i.e.*, one in which the molecular extinction coefficients of its visible absorption peaks decrease in the order 4 > 2 > 3 > 1. The remaining three isomers show spectra of the "etio type" (4 > 3 > 2 > 1) normally observed for bridge-unsubstituted porphyrins; however, on such a classification basis isomer III must be adjudged marginal since its spectrum borders closely upon the "phyllo type." It is interesting to note that the extinction coefficients of bands 1 and 3 exhibit far greater percentage variation among these isomers than do the extinction coefficients of any of the other five absorption bands in the range 260–700 mμ.

Each porphyrin isomer has been found to give its own distinctly characteristic X-ray powder pattern, thus permitting easy differentiation.[10] Porphyrin II exhibits polymorphism.[10]

In comparative solubility experiments in three different organic solvents both at the boiling point and at room temperature, the four porphyrin isomers showed the same order of decreasing solubility in each solvent: III > IV >> I > II. The three solvents listed in order of decreasing effectiveness were chloroform,

TABLE II

Isomer[a]	% yield	Calcd, % C	Calcd, % H	Calcd, % N	Found, % C	Found, % H	Found, % N	Solvents[b]
I	7	66.04	5.85	8.56	66.00	6.02	8.43	A–D (1:1); A–B (2:3)
II	5				65.99	6.05	8.56	A–B–C (4:6:3)
III	13				65.92	5.81	8.42	B–C (1:5)
IV	17				65.70	5.88	8.46	B–C (1:3); B–C (1:2)

[a] Formula $C_{36}H_{38}N_4O_8$. [b] A = chloroform; B = ethylene dichloride; C = ethanol; D = methanol.

glacial acetic acid, and acetone. In a fourth solvent, methanol, all isomers proved virtually insoluble. All these data serve to substantiate the separate identity of each of these four synthetically obtained tetramethyltetracarbethoxyporphyrins.

Experimental Section

All melting points were determined on the Nalge-Axelrod hot-stage apparatus and are uncorrected.

2-[(3-Carboxy-5-chloro-4-methyl-2-pyrrolyl)methylene]-3,5-dimethyl-2H-pyrrolenine-4-carboxylic Acid Diethyl Ester (V).[24]—This dipyrrylmethene was prepared by the procedure of Corwin and Doak[25] to give a 58% yield of the once-recrystallized free base: mp 144.5°; lit.[25] mp 145–146°.

2,2′-Methylenebis(4-methyl-3-pyrrolecarboxylic acid) Diethyl Ester (VI).[12,26]—5,5′-Methylenebis(3-methyl-2,4-pyrroledicarboxylic acid) 4,4′-diethyl ester[12] (40 g) was heated under nitrogen with 40 g of triethanolamine at 190° for 12 min. While still hot, the reaction mixture was dissolved in 200 ml of ethanol, then poured into 1400 ml of cold water. The precipitated product was filtered, dried, then extracted three times with hot isooctane, 1300 ml of the solvent being used each time. Concentration of the combined extracts to a volume of 1000 ml gave a purified product, which after recrystallization from ethanol–water (7:4), gave 16 g or 51% of product: mp 174–177°; lit. mp 173°,[26] 188°.[12]

2-[(3-Carboxy-5-chloro-4-methyl-2-pyrrolyl)methylene]-5-chloro-4-methyl-2H-pyrrolenine-3-carboxylic Acid Diethyl Ester (VII).—A solution of 0.50 ml (3.5 moles) of freshly distilled sulfuryl chloride in 2 ml of ether was added all at once with stirring to a solution of 550 mg of dipyrrylmethane VI in 30 ml of absolute ether, which had been cooled previously to 10°. The reaction mixture was maintained at 10° for 30 min with constant stirring, then treated with 90 ml of hexane, and refrigerated. The product was filtered off, resuspended in 20 ml of absolute ether, filtered again, and washed with cold ether after chilling. The resulting purple hydrochloride was dissolved in chloroform, agitated with powdered calcium hydroxide. After filtration to remove the calcium salts, the crude free base was obtained by evaporation of the filtrate to dryness. Recrystallization from acetone yielded 410 mg or 62% of product, mp 173–174.5°. An analytically pure sample (from acetone) melted at 177.5–178°.

Anal. Calcd for $C_{17}H_{18}Cl_2N_2O_4$: C, 53.00; H, 4.71; N, 7.27. Found: C, 53.10; H, 4.70; N, 6.96.

2-[(3-Carboxy-4,5-dimethyl-2-pyrrolyl)methylene]-4,5-dimethyl-2H-pyrrolenine-3-carboxylic Acid Diethyl Ester (VIII).—This dipyrrylmethene was prepared by the method of Brunings and Corwin:[22] mp 160–165° dec; lit.[22] mp 164–165° dec.

2-[(4-Carboxy-3,5-dimethyl-2-pyrrolyl)methylene]-3,5-dimethyl-2H-pyrrolenine-4-carboxylic Acid Diethyl Ester (XIV).—The dipyrrylmethene hydrochloride was prepared as described by Fischer and Orth[27] and was converted to the free base as described above in the preparation of VII: mp 188–189.5° dec; lit.[27] mp 190°.

2[(4-Carboxy-3,5-dimethyl-2-pyrrolyl)methyl]-4,5-dimethyl-3-pyrrolecarboxylic Acid Diethyl Ester (XII).—The method employed by Corwin and Brunings[23] for the preparation of a mono-N-methyldipyrrylmethane was adapted as follows. Ethyl 2,4-dimethyl-3-pyrrolecarboxylate and ethyl 4,5-dimethyl-3-pyrrolecarboxylate (7 g each) were dissolved in 70 ml of alcohol and 9.8 ml of aqueous 37% formaldehyde solution was added. After warming the mixture to 45°, 3.5 ml of concentrated hydrochloric acid was added dropwise with stirring during 10 min, and stirring was continued for an additional 15 min at 55°. Refrigeration caused the separation of 13 g of crude product which after successive recrystallizations from benzene, chloroform, and acetone melted at 201–203°: wt 4.3 g or 30%. Admixture with either corresponding isomeric symmetrical dipyrrylmethane caused in each case a depression of the melting point below that of either component of the mixture.

Anal. Calcd for $C_{19}H_{26}N_2O_4$: C, 65.88; H, 7.57; N, 8.09. Found: C, 65.88; H, 7.66; N, 8.55.

2-[(3-Carboxy-4,5-dimethyl-2-pyrrolyl)methylene]-3,5-dimethyl-2H-pyrrolenine-4-carboxylic Acid Diethyl Ester (IX). A.—By Oxidation of Dipyrrylmethane (XII).—This methene was prepared from the corresponding methane, XII, by the brominative oxidation procedure of Brunings and Corwin.[22] Methane XII (1 g) gave after purification 190 mg of methene free base IX, mp 138.5–141.5° dec.[28]

B. By Condensation of Aldehyde (XIII) with α-Free Pyrrole (XI).—To a solution of 2.435 g of ethyl 2-formyl-4,5-dimethyl-3-pyrrolecarboxylate (XIII)[29,30] and 2.084 g of ethyl 2,4-dimethyl-3-pyrrolecarboxylate in 10 ml glacial acetic acid at 75–90° was added 2.5 ml of concentrated hydrochloric acid. After cooling to room temperature and adding more glacial acetic acid and some ether, the product was filtered off. This crude methene hydrochloride was converted to the free base as described in the case of methene VII. Recrystallization from acetone, then from benzene–hexane, gave 2.6 g of the methene base, mp 140–144° dec.[28] Mixture melting point[28] with methene base IX obtained from XII *via* procedure A above gave no depression. However, admixture with either isomeric dipyrrylmethene VIII or XIV produced a distinct melting point depression.[28]

Anal. Calcd for $C_{19}H_{24}N_2O_4$: C, 66.26; H, 7.02; N, 8.13. Found: C, 66.12; H, 6.88; N, 8.04.

Tetramethylporphyrintetracarboxylic Acids Tetraethyl Esters (I–IV).—The condensation procedure for obtaining each of the four isomeric porphyrins was essentially the same. The two appropriate dipyrrylmethenes (1 mmole each)[31] [2 mmoles of I], 730 mg (3.65 mmoles) of cupric acetate monohydrate, and 18.2 g of naphthalene were mixed intimately in a Pyrex container, which was then plunged into a hot oil bath at 180–210° and held at this temperature for 20–25 min. While still hot the reaction mixture was taken up in ethylene dichloride and poured onto a column of alumina (Fisher No. A-540). Ethylene dichloride eluted the naphthalene and other nonporphyrin impurities and was followed by chloroform which eluted the copper porphyrin complex. After evaporation of this porphyrin fraction to dryness, the residue was taken up in 36 ml of concentrated sulfuric acid by stirring for about 1.5 hr. Glacial acetic acid (73 ml) was then added cautiously and the mixture was then poured over 146 g of cracked ice, followed by the addition of 290 ml of pyridine with cooling. The mixture was transferred to a separatory funnel and shaken with 365 ml of chloroform. The pyridine–chloroform layer containing the porphyrin was washed with water

(24) H. Fischer, E. Sturm, and H. Friedrich, *Ann.*, **461**, 267 (1928).

(25) A. H. Corwin and K. W. Doak, *J. Am. Chem. Soc.*, **77**, 464 (1955).

(26) H. Fischer and P. Halbig, *Ann.*, **447**, 133 (1926).

(27) H. Fischer and H. Orth, "Die Chemie des Pyrrols," Vol. 1, Akademische Verlagsgesellschaft, M. B. H., Leipzig, 1937, p 39.

(28) Dipyrrylmethenes rarely return to the crystalline state after being melted; thus some decomposition is taking place. However, in the case of a low-melting dipyrrylmethene, this decomposition point may be a fairly characteristic constant for the compound.

(29) H. Fischer and H. Beller, *Ann.*, **444**, 238 (1925).

(30) G. G. Kleinspehn and A. H. Corwin, *J. Am. Chem. Soc.*, **76**, 5641 (1954).

(31) These methene condensations to give porphyrins have in some cases been carried out employing quantities of reactants (and naphthalene) ranging from one-eighth up to six times those cited in the present typical procedure. Indeed the porphyrin yields reported in the accompanying table were obtained in runs utilizing a total of from 8 to 12 mmoles of dipyrrylmethenes.

and then evaporated to dryness. The residue was washed with hot water, dried again, taken up in ethylene dichloride, and chromatographed on an alumina (Fisher No. A-540) column. The free porphyrin was eluted with chloroform. Evaporation of the chloroform fraction gave a residue which was washed with hot methanol, then recrystallized from a suitable solvent. In general it has been found advantageous to repeat the sulfuric acid treatment of the product a second time in order to ensure complete removal of the copper. The yields of analytically pure metal-free porphyrins thus obtained are given in Table II together with the analytical values and the solvents used for recrystallization. All isomers have decomposition points >360°.

Acknowledgment.—The authors wish to thank Dr. Ralph M. Deal for early determinations at room temperature of the ultraviolet and visible absorption spectra of the four isomeric porphyrins. It was these data which first pointed up the significant spectral differences among isomers. Thanks are also due to Susan Lauder whose spectral data under controlled temperature conditions appear in Table I. We are indebted to Drs. Ernst Klesper and Peter K. Iber for the X-ray powder pattern determinations.[10]

Formation of Perhydrophenalenes and Polyalkyladamantanes by Isomerization of Tricyclic Perhydroaromatics[1]

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The mixture of isomers from the perhydrogenation of phenanthrene rapidly isomerizes at 0° in the presence of aluminum bromide complex to the equilibrium mixture of *trans,syn,trans*-perhydroanthracene (I), *trans,anti,-trans*-perhydrophenanthrene, and *cis,syn,trans*-perhydroanthracene. In the absence of solvent during isomerization, extensive crystallization of I displaces the equilibrium forming additional I. Starting with either perhydrophenanthrenes or perhydroanthracenes at 27°, a series of consecutive reactions takes place giving rise in order of their appearance to the equilibrium mixture mentioned above, the equilibrium mixture of methylperhydrophenalenes, 1,3-dimethyl-5-ethyladamantane, and, finally, 1,3,5,7-tetramethyladamantane. Small concentrations of nonbridgehead, C_{14} adamantanes accompany the bridgehead adamantanes at equilibrium. At 0° the perhydrofluorenes rearrange rapidly to the equilibrium mixture of *cis*- and *trans*-perhydrophenalene, with the latter present in large preponderance, and further isomerization at ambient temperature causes the perhydrophenalenes to isomerize in high yield to 1-ethyl-3-methyladamantane and finally to 1,3,5-trimethyladamantane accompanied by a small amount of nonbridgehead C_{13} adamantane isomers. Perhydroacenaphthene isomerizes at ambient temperature completely and rapidly to 1-ethyladamantane which, in turn, converts more slowly to 1,3-dimethyladamantane and a small amount of nonbridgehead dimethyladamantanes. A detailed discussion is presented of the thermodynamics of these reactions.

In a study of aluminum chloride catalyzed isomerization of perhydroanthracenes Cook, *et al.*,[2] observed the sequence of rearrangements at ambient temperature: *cis, syn, cis* (mp 61°) → *cis, syn, trans* (mp 39°) → *trans, syn, trans* (mp 90°). The product of isomerization at 100° was an uncrystallizable, mobile liquid. Recently, Hill, *et al.*,[3] investigated the aluminum bromide catalyzed isomerization at 0° of *trans,syn,trans*-(I), *trans,anti,trans*-, and *cis,anti,cis*-perhydroanthracenes and found that each gave the equilibrium mixture after 169 hr consisting of 96% I and 4% *cis,syn,trans*-perhydroanthracene. It was noted that infrared bands not present in any of the perhydroanthracenes became significant after 312 hr of reaction. Prokopets,[4] established qualitatively that, at 100° in the presence of aluminum chloride, liquid mixtures of isomeric perhydrophenanthrenes as well as of perhydroanthracenes isomerized to I.

Tricyclic saturated hydrocarbons having from 10 to 12 carbon atoms have been found by Fort and Schleyer,[5] to undergo remarkable, aluminum halide catalyzed isomerizations to adamantane and its methyl and dimethyl homologs. In each case two of the rings in the starting material consisted of the [2.2.1]bicycloheptyl or the [2.2.2]bicyclooctyl systems and it was stated that "all strained tricyclic, saturated hydrocarbons having ten or more carbon atoms thus far investigated have rearranged at least in part to adamantane derivatives."

The fact that adamantane and its bridgehead-substituted methyl and dimethyl homologs are strainless molecules of a relatively high degree of branching[6] indicated to us that a thermodynamic driving force for conversion to this class of hydrocarbon exists even in the case of starting materials consisting of strainless, tricyclic saturated hydrocarbons, provided that the degree of branching in the latter is smaller than that of the corresponding bridgehead-substituted methyladamantanes. This implied that practically any tricyclic saturated hydrocarbon (excluding cyclopropanes), strained or unstrained, having ten carbon atoms or more will form adamantanes on equilibration with Lewis acids.

To test this hypothesis, mixtures of isomeric C_{14} perhydroanthracenes and perhydrophenanthrenes made by hydrogenation of the corresponding aromatics were treated at 0–25° with aluminum bromide complex, an active isomerization catalyst, and a series of rearrangements was observed leading finally to 1,3,5,7-tetramethyladamantane. The mixtures of relatively strained isomeric C_{12} and C_{13} tricyclic, saturated hydrocarbons formed by the perhydrogenation of acenaphthene and fluorene also rearranged quite readily at

(1) Preliminary communication: A. Schneider, R. W. Warren, and E. J. Janoski, *J. Am. Chem. Soc.*, **86**, 5365 (1964).

(2) J. W. Cook, N. A. McGinnis, and S. Mitchell, *J. Chem. Soc.*, 286 (1944).

(3) R. K. Hill, J. G. Martin, and W. H. Stouch, *ibid.*, **83**, 4006 (1961).

(4) E. I. Prokopets and S. M. Boguslavskaya, *J. Appl. Chem. USSR*, **11**, 1471 (1938); *Chem. Abstr.*, **33**, 5816[9] (1939).

(5) R. C. Fort, Jr., and P. von R. Schleyer, *Chem. Rev.*, **64**, 283 (1964).

(6) G. N. Lewis and M. Randall, "Thermodynamics," 2nd ed, revised by K. S. Pitzer and L. Brewer, McGraw-Hill Book Co., Inc., New York, N. Y., 1961, p 521.