for *t*-butyl groups in terms of steric requirements, is less comprehensible for methyl substituents. It is likewise not an obvious consequence of this mechanism that the preference for 1,2 shifts should be more marked in the vapor than in the liquid. The results are readily interpreted on the assumption that both types of mechanism operate concurrently to varying degrees. If, as seems reasonable, the three-dimensional Dewar structure represents a lower energy form than the tricyclohexene, it should be favored in solution to the extent that the solvent drains off excess excitation energy.[12a]

(12a) NOTE ADDED IN PROOF. While this work was in press, H. G. Viehe, R. Merényi, J. F. M. Oth, J. R. Senders, and P. Valange, *Angew. Chem. Intern. Ed. Engl.*, **3**, 755 (1964), reported the isolation of isomers having the Ladenburg, tricyclohexene, and Dewar structures from the trimerization of *t*-butylfluoroacetylene.

(13) Resident student associate, summer 1964.

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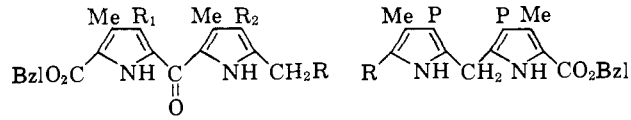
Received November 4, 1964

Two New Porphyrin Syntheses

Sir:

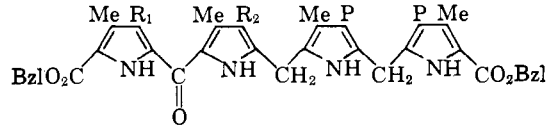
Hitherto porphyrin syntheses have generally depended on final coupling of two dipyrrolic units.[1] We now wish to describe two syntheses proceeding through crystalline tetrapyrrolic intermediates III and VI, each of which is stabilized by an internuclear carbonyl group. Potentially this approach offers great advantages in the synthesis of diversely substituted porphyrins, but here it is merely exemplified by syntheses of mesoporphyrin IX and similar compounds.

Chlorination of the pyrroketone Ia[2] (ν_{max} CO, 1582 cm.$^{-1}$; λ_{max} 250, 303, and 348 mμ (log ϵ 4.23, 4.08, and 4.33) in methylene chloride; λ_{max} 422 mμ (log ϵ 4.51) in methylene chloride–HCl, *cf.* urea and tropone!) by *t*-butyl hypochlorite in tetrahydrofuran–ether (1:1) at 3° yielded Id, which was coupled[3] as its pyridinium derivative with the lithium salt of IIb (prepared by semihydrogenation of IIa) to yield 44% of the tetrapyrrolic ketone IIIa, m.p. 143–144°, mol. wt. 870 (mass spectrum[4]). The carbonyl group in IIIa was reduced by diborane[5] in tetrahydrofuran–ethyl acetate (1:1) to a methylene group.[6] The bilane dicarboxylic acid resulting from hydrogenolysis was dehydrogenated to principally the bilene-b hydrochloride IV (λ_{max} 505 mμ (log ϵ *ca.* 4.60)) by *t*-butyl hypochlorite (1 mole) in ether; *if this step was omitted the synthesis could*

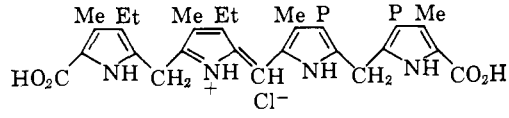


Ia, $R_1 = R_2 = C_2H_5$, R = H
b, $R_1 = CH_3$, $R_2 = C_2H_5$, R = H
c, $R_1 = C_2H_5$, $R_2 = CH_3$, R = H
d, $R_1 = R_2 = C_2H_5$, R = Cl

IIa, R = CO_2Bzl
b, R = CO_2H
c, R = H



IIIa, $R_1 = R_2 = C_2H_5$
b, $R_1 = CH_3$, $R_2 = C_2H_5$
c, $R_1 = C_2H_5$, $R_2 = CH_3$

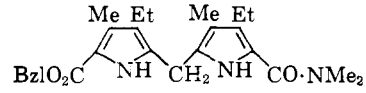


IV

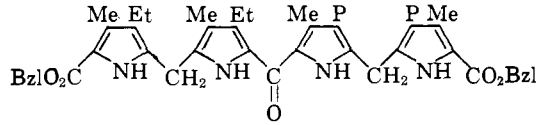
P = $CH_2CH_2CO_2CH_3$

still be carried through to porphyrins but the product was a mixture, arising from "jumbling" of the pyrrole nuclei.[7] Cyclization of IV with methyl orthoformate–trichloroacetic acid (1:3) in methylene chloride, followed by aeration, gave mesoporphyrin IX dimethyl ester as the only porphyrinic product in an over-all yield of 25% from IIIa. Analogous syntheses from Ib and Ic yielded tetrapyrrolic ketones IIIb, m.p. 142–143°, and IIIc, m.p. 153–154°, and thence 4-ethyl-1,2,3,5,8-pentamethyl-6,7-dimethoxycarbonylethylporphin, m.p. 255.5–256.5° (24% yield from IIIb), and 2-ethyl-1,3,4,5,8-pentamethyl-6,7-dimethoxycarbonylethylporphyrin, m.p. 295–296° (24% yield from IIIc).[8,9]

The second synthesis involves coupling of the pyrromethane amide V[3b] as its phosphoryl chloride complex (λ_{max} 390 mμ (log ϵ *ca.* 4.30)) with the pyrromethane IIc (derived from decarboxylation of IIb) in methylene chloride to an imine salt (λ_{max} 412 mμ (log ϵ *ca.* 4.23)). The latter was hydrolyzed by aqueous sodium carbonate to give the tetrapyrrolic ketone VI, m.p. 170° (38% yield from V and IIb). Hydrogenation of VI yielded the dicarboxylic acid, m.p. 178–179° dec.,



V



VI

which was decarboxylated at 185° to an oil (characterized by n.m.r.). The latter was cyclized with methyl orthoformate and boron trifluoride etherate in methylene chloride and, after aeration in the presence of triethylamine, the blue "β-hydroxyporphyrin" VII[10] (λ_{max}

(1) Exceptions with limited scope are described by A. H. Corwin and E. C. Coolidge, *J. Am. Chem. Soc.*, 74, 5196 (1952), and A. W. Johnson and I. T. Kay, *J. Chem. Soc.*, 2418 (1961). The classical synthesis of chlorophyll by R. B. Woodward, *et al.*, *J. Am. Chem. Soc.*, **82**, 3800 (1960), includes a fleeting open-chain tetrapyrrolic intermediate.

(2) J. A. Ballantine, unpublished work; *cf. Proc. Chem. Soc.*, 198 (1961).

(3) (a) A. Hayes, G. W. Kenner, and N. R. Williams, *J. Chem. Soc.*, 3779 (1958); (b) A. H. Jackson, G. W. Kenner, and D. Warburton, *ibid.*, in press.

(4) All crystalline compounds isolated were characterized by their mass, n.m.r., infrared, and ultraviolet spectra and by microanalyses.

(5) H. C. Brown and B. C. Subba Rao, *J. Am. Chem. Soc.*, **82**, 681 (1960).

(6) The intermediate pyrromethenes can be detected spectroscopically during reduction of pyrroketones: unpublished work by Mr. L. E. Houghton shows that diborane also reduced diaryl ketones containing electron-releasing substituents, such as Michler's ketone and dianisyl ketone, to diarylmethanes.

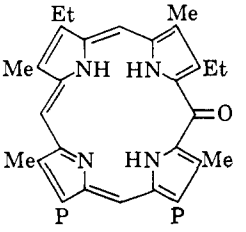
(7) D. Mauzerall, *J. Am. Chem. Soc.*, **82**, 2601 (1960).

(8) The good agreement with the published m.p. 255° and 290° [H. Fischer and E. Jordan, *Z. physiol. Chem.*, **191**, 38 (1930)] adds support to the accepted structure of chlorocruoroporphyrin.

(9) Mr. J. Wass has further extended the method to the syntheses of 2-ethyl-1,3,5,8-tetramethyl-4,6,7-trimethoxycarbonylethylporphin and of coproporphyrin III tetramethyl ester.

(10) A "hydroxyporphyrin" prepared from coproporphyrin I tetramethyl ester by H. Libowitsky and H. Fischer, *Z. physiol. Chem.*, **255**,

404, 585, and 635 mμ (log ϵ_{max} *ca.* 5.08, 4.30, and 4.48)) was formed. If the cyclization was carried out with methyl orthoformate–trichloroacetic acid, and followed by aeration without added base, a green compound (λ_{max} 404 and 700 mμ (log ϵ_{max} *ca.* 5.00 and 4.48)) was formed, which readily changed into VII or its salts (λ_{max} 416, 560, and 615 mμ (log ϵ_{max} *ca.* 5.40, 4.30, and 4.30)). This green compound is probably a tautomeric form of VII.



VII

Acetylation of VII gave β-acetoxymesoporphyrin IX dimethyl ester, m.p. 233.5–234.5° (λ_{max} 400, 498, 530, 568, and 620 mμ (log ϵ_{max} 5.30, 4.21, 3.80, 3.81, and 3.26[11])). Reduction of VII by sodium amalgam in methanol–acetic acid[12] gave *directly* mesoporphyrin IX dimethyl ester, which crystallized from the reaction mixture (24% yield from VI). *This work also opens a synthetic route to α-oxyporphyrins which have been postulated as intermediates in the catabolism of porphyrins leading to bile pigments.*[13]

Acknowledgment. We thank Dr. J. A. Ballantine for his pioneer studies of pyrroketones.

209 (1938), has very similar visible absorption. We favor the keto structure VII, which would gain aromaticity from dipolar character, but the tautomeric hydroxy structure is not excluded.

(11) *meso*-Monomethylaetioporphyrins likewise have, *e.g.*, λ_{max} 408, 505, 539, 579, and 630 mμ (log ε 5.14, 4.04, 3.63, 3.62, and 3.06): R. J. Abraham, A. H. Jackson, G. W. Kenner, and D. Warburton, *J. Chem. Soc.*, 861 (1963).

(12) H. Fischer and A. Treibs, *Ann.* 457, 209 (1927).

(13) R. Lemberg and J. W. Legge, "Haematin Compounds and Bile Pigments," Interscience Publishers, Inc., New York, N. Y., 1949, p. 458.

(14) C.S.I.R. South Africa overseas bursar.

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Received, November 30, 1964

Synthesis of 4-Acetamido-1,2,3,5-tetra-O-acetyl-4-deoxy-D-ribofuranose. A Pyrrolidine Sugar[1-3]

Sir:

In some work reported recently from these laboratories,[4] the synthesis of 4-thioribofuranose derivatives in which the ring hetero atom was sulfur rather than oxygen was described. The recent discoveries of the widespread occurrence in nature of various amino sugars such as the N-acetylnonulosaminic acids[5] which have an amine function δ to the reducing carbon made it of interest to attempt the preparation of 4-amino-4-deoxy-D-ribose derivatives with the idea of preparing a furanose sugar with nitrogen as the ring heterocycle.[6]

The synthesis of 4-acetamido-4-deoxy-D-ribofuranose derivatives was accomplished by two independent routes and is the subject of this communication.

Tosylation of methyl 2-O-benzoyl-β-L-arabinopyranoside (I)[7] yielded 46% of methyl 2-O-benzoyl-3,4-di-O-(*p*-tolylsulfonyl)-β-L-arabinopyranoside (II), m.p. 163–165° (from benzene, Skellysolve B).[8] Treatment of II with sodium azide in N,N-dimethylformamide (DMF) at 120° for 6 hr. gave a 74% yield of methyl 4-azido-2-O-benzoyl-4-deoxy-3-O-(*p*-tolylsulfonyl)-α-D-xylopyranoside (III), m.p. 100–101° (from 2-propanol). That the 4-tosylate of II had been displaced by the azide rather than the 3-tosylate was shown by the reaction of III with methanolic sodium methoxide. The resulting epoxide (VI) was obtained in 78% yield, m.p. 44.5–45.5°. Catalytic reduction of the azide III gave a 97% yield of crystalline amine (IV), m.p. 111–112°, which could be acetylated in 67% yield to the N-acetate (V), m.p. 150–151°.

The reaction of the N-acetate (V) with sodium acetate in aqueous DMF effected the displacement with inversion of the 3-tosylate by the neighboring 4-N-acetate[9] to give, after debenzoylation, a 63% yield of crystalline methyl 4-acetamido-4-deoxy-α-D-ribopyranoside (VII), m.p. 157.0–158.0° (from 2-propanol). The vicinal-*cis* relationship of the hydroxyl groups of VII was demonstrated by the preparation of the isopropylidene derivative (VIII), m.p. 114–115° (from benzene–cyclohexane).

Acetylation of VII gave the triacetate (IX) as an analytically pure oil. Acetolysis of either the N-acetate (VII) or triacetate (IX) gave an analytically pure sirup which was free of NH absorption at 6.5 μ in the infrared and which showed the presence of five acetyl groups between τ 7.88 and 8.02 by n.m.r. From these data, the pentaacetate was assigned the furanose structure (X). The isomeric pyranose N,N-diacetate (XI) would be expected to have N-acetate absorption at *ca.* τ 7.6 by n.m.r.[10]

Treatment of the acetolysis product X with 0.5% methanolic hydrogen chloride followed by reacetylation gave a 57% yield of a sirup which was essentially homogeneous on thin layer chromatography[8] and which showed the necessary four acetyl bands at τ 7.87–7.98 for the furanoside structure (XII). Deacetylation of XII with methanolic sodium methoxide gave the glycoside (XIII) as a sirup which was characterized as the tri-*p*-nitrobenzoate (XIV), m.p. 175.5–177.0° (from absolute ethanol).

Acetolysis of XIV gave the analytically pure anomers

(1) This work was carried out under the auspices of the Cancer Chemotherapy National Service Center, National Cancer Institute, National Institutes of Health, Public Health Service, Contract No. PH-43-64-500. The opinions expressed in this paper are those of the authors and not necessarily those of the Cancer Chemotherapy National Service Center.

(2) Portions of this work were described at the 148th National Meeting of the American Chemical Society, August 31, 1964. See Abstracts, p. 3D.

(3) Nomenclature used by *Chemical Abstracts*.

(4) E. J. Reist, D. E. Gueffroy, and L. Goodman, *J. Am. Chem. Soc.*, **85**, 3715 (1963); **86**, 5658 (1964).

(5) F. Zilliken and M. W. Whitehouse, *Advan. Carbohydrate Chem.*, **13**, 237 (1958).

(6) In a recent paper by W. A. Szarek and J. K. N. Jones, *Can. J. Chem.*, **42**, 20 (1964), the synthesis of a 4-acetamidotetrose, namely, methyl 4-acetamido-4-deoxy-L-erythrofuranoside, was described. It should be noted that this C_4 sugar cannot form a pyranoside, hence is forced into the furanoside configuration.

(7) M. A. Oldham and J. Honeyman, *J. Chem. Soc.*, 986 (1946).

(8) Melting points are corrected. All compounds analyzed satisfactorily and had infrared spectra which were compatible with the assigned structures. Thin layer chromatograms were run on silica gel G using ethyl acetate as the developing solvent.

(9) B. R. Baker and R. E. Schaub, *J. Org. Chem.*, **19**, 646 (1954).

(10) F. A. L. Anet, R. A. B. Bannard, and L. D. Hall, *Can. J. Chem.*, **41**, 2331 (1963).