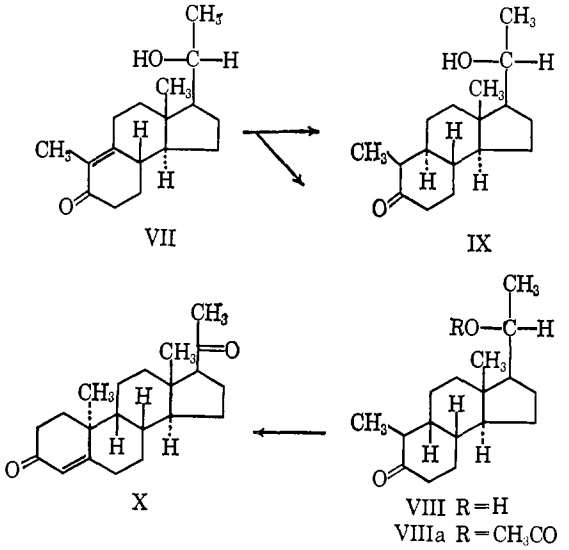
progesterone[5] [VI, mp 193.5–195°, $[\alpha]^{25}D$ −125.6° (*c* 0.5, $CHCl_3$), λ_{max}^{EtOH} 244 mμ (ε 16,100); ν_{max} 35 (18-H), 75.5 (19-H), 128 (21-H), and 347 (4-H) cps; ΔMD: progesterone *vs.* VI = −1030.2°; testosterone *vs.* 10α-testosterone[1] = −940.3°].

Reduction of II with sodium borohydride, followed by manganese dioxide oxidation of the allylic 5-hydroxy group of the resulting epimeric diols, afforded 20β-hydroxy-desA-pregn-9-en-5-one [VII, mp 122–123°, $[\alpha]^{25}D$ −33° (*c* 0.5, EtOH)] in a 79% yield. The minor product (5%) was the 20α analog. Hydrogenation of VII in ethanolic hydrochloric acid in the presence of rhodium on alumina catalyst resulted in 85% yield of a 6:1 mixture of 20β-hydroxy-desA-9β,10β-pregnan-5-one (VIII) and 20β-hydroxy-desA-9α,10α-pregnan-5-one (IX). The desired VIII was separated and characterized as the corresponding acetate [VIIIa, mp 100–100.5°, $[\alpha]^{25}D$ +27.1° (*c* 0.5, EtOH), ν_{max} 60.5 (19-H) cps, positive Cotton effect $[\alpha]_{300}$ + 440°].



VII IX X

VIII R=H
VIIIa R=CH_3CO

Condensation of VIII with methyl vinyl ketone in the presence of sodium *t*-amylate or Triton B, or with 4-diethylaminobutan-2-one in the presence of sodium ethoxide, led to crude 20β-hydroxy-9β,10α-pregn-4-en-3-one. The latter compound without purification was oxidized with chromic acid to give 9β,10α-progesterone [X, mp 163–164°, $[\alpha]^{25}D$ −60° (*c* 0.5, $CHCl_3$); λ_{max}^{EtOH} 241 mμ (ε 16,200); ν_{max} 82.5 (19-H), 41 (18-H), 128 (21-H), and 343 (4-H) cps]. The yield of X varied between 2 and 8% with an 80% recovery of the starting VIII. The product was found to be identical with an authentic sample of the same compound[6] by determination of the mixture melting point, by comparison of the ultraviolet, infrared, nmr, and mass spectra, and by thin layer chromatography.

Acknowledgment. We thank Dr. F. Vane, Mr. S. Traiman, and Dr. V. Toome for the nmr, mass, infrared, and ultraviolet spectra and Dr. Al Steyermark and his staff for the elemental analyses.

(5) In Belgian Patent 634,693 (1964), CIBA, 10α-progesterone was reported to be a progestational agent. However, no physical data were given for this compound.

(6) Obtained from Philips Duphar Co., Holland.

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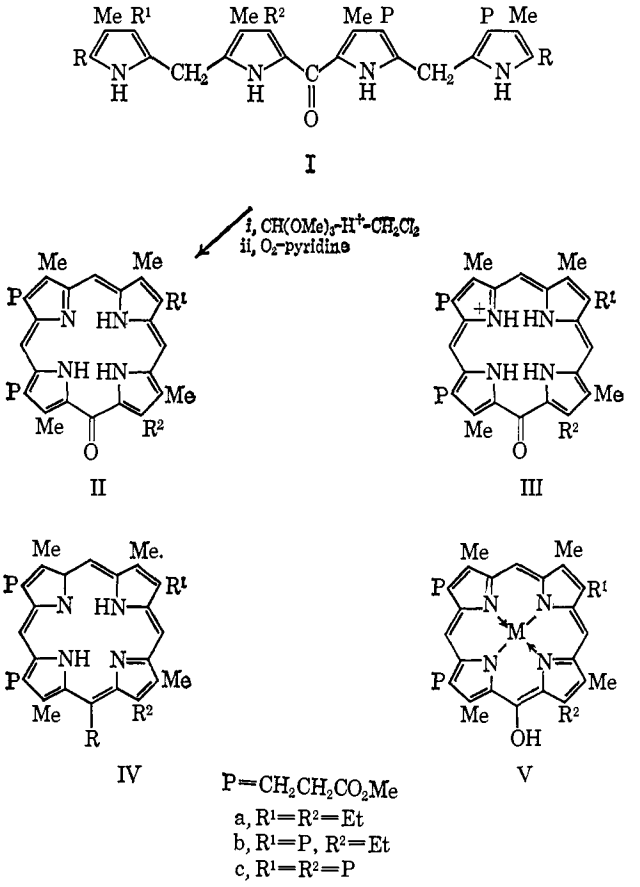
Received August 1, 1966

Oxyporphyrins

Sir:

Oxyporphyrins have been postulated as intermediates in the catabolism of porphyrins leading to bile pigments,[1] and in a previous communication[2] we briefly described the synthesis of the oxyprophyrin IIa by cyclization of the crystalline *b*-oxobilane (Ia; R = H) with methyl orthoformate followed by aeration. This work has now been improved[3] and extended to the synthesis of other oxyporphyrins,[4] *e.g.*, IIb and IIc; the conversion of oxyporphyrins to porphyrins has also been greatly improved by proceeding *via* catalytic hydrogenation of the acetoxyporphyrins (IV; R = OAc) followed by reoxidation (with air or iodine) rather than by direct sodium amalgam reduction of the oxyporphyrins.[2,5]



I

i, $CH(OMe)_3$-H^+-CH_2Cl_2
ii, O_2-pyridine

II III IV V

P=$CH_2CH_2CO_2Me$
a, R^1=R^2=Et
b, R^1=P, R^2=Et
c, R^1=R^2=P

In the present communication we wish to describe some of our recent observations on the structure and reactivity of oxyporphyrins, especially as this may be of direct relevance to porphyrin catabolism. They have

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

(2) A. H. Jackson, G. W. Kenner, G. McGillivray, and G. S. Sach, *J. Am. Chem. Soc.*, **87**, 676 (1965).

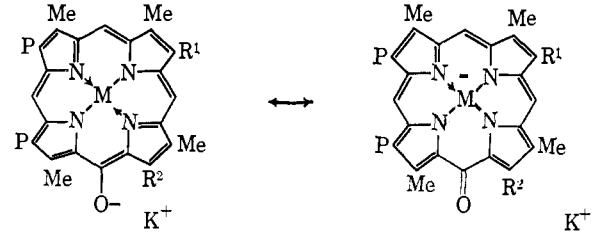
(3) The *b*-oxobilanes (I; R = CO_2CH_2Ph) may be conveniently purified by chromatography of the intermediate imine salts[2] and have now been obtained in up to 50% yield. We have also found that the corresponding dicarboxylic acids (I; R = CO_2H) may be cyclized directly to oxyporphyrins; the yields (60–70%) are as good as the earlier method involving a separate decarboxylation step.

(4) Other oxyporphyrins have recently been described by P. S. Clezy and A. W. Nichol (*Australian J. Chem.*, **11**, 1835 (1965)) and by J.-H. Fuhrhop, and H. H. Inhoffen (J.-H. Fuhrhop, Dissertation, Braunschweig, 1966).

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

now been obtained in crystalline form, *e.g.*, IIa,[6] deep blue needles, mp 186–187° (λ_{max} in CH_2Cl_2 401, 588, 635 mμ (log ϵ_{max} 5.07, 4.01, 4.21)), and the green form (λ_{max} 407, 500, 537, 584, 706 mμ (log ϵ_{max} 4.99, 3.35, 3.56, 3.56, 4.20)), has been shown to be the monoprotonated species IIIa. We had previously thought[2] that the latter might be a tautomer of the blue oxyporphyrin because it was recovered almost unchanged from chromatography on neutral alumina. However it is now clear that the oxyporphyrins are much stronger bases[7] than normal porphyrins, and that protonation takes place in two discrete stages to give first the green monocation and then the violet-red dication (*e.g.*, the dication corresponding to IVa, R = OH, λ_{max} 420, 523, 565, 619 mμ (log ϵ_{max} 5.49, 3.75, 4.08, 4.12)).

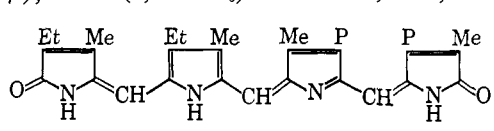
We assign the "oxo" structure[8] II, with contributions from mesomeric dipolar forms, to these oxyporphyrins rather than the tautomeric structure IV (R = OH), and the structure III (and mesomeric tripolar forms) to the monocations for the following reasons. (i) The blue oxyporphyrins and their green monocations exhibit strong peaks in their infrared spectra ($CHCl_3$) at *ca.* 1560 cm^{-1}, which are closely similar to the values observed for the carbonyl groups of simple pyrro ketones.[11] On the other hand the violet-red dications which must have the hydroxy structure IV (R = OH, with all four nitrogen atoms protonated) do not show any intense peaks between 1470 and 1670 cm^{-1}. (ii) The visible spectra of the blue and green compounds are quite unlike those of the corresponding porphyrins[12] (IV; R = H), or of the *meso*-acetoxy-[2,6] (IV; R = OAc) or *meso*-ethoxy-[6,13] (IV; R = OEt) porphyrins, but they are very similar to those of the blue free bases, and green salts of bilatrienes[14] (*e.g.*, biliverdin), and of phlorin free bases and salts.[15] The spectrum of the violet-red dication is however quite similar to that of octaalkylporphyrin dications.[12] (iii) The blue oxyporphyrins readily form red metallic complexes (V) (*e.g.*, Zn complex of Va,[6] mp >300°, λ_{max} (CH_2Cl_2) 409, 430, 536, 572 mμ (log ϵ_{max} 5.26, 4.70, 3.98, 3.77), the visible spectra of which are rather similar to those of other porphyrin–metal complexes. However, mild base treatment (*e.g.*, K_2CO_3 in acetone, or tetrahydrofuran containing a little methanol) of these metal derivatives gives a green monoanion (VI) (*e.g.*, VIa, λ_{max} 421, 466, 528, 625 (infl), 674 mμ (log ϵ_{max} 4.84, 3.67, 3.65, 3.52, 4.08)) which can be readily methylated or tosylated to give the corresponding red methoxy-[6] or tosyloxyporphyrin[6]–metal complexes. These monoanions also exhibit a strong peak at *ca.* 1580 cm^{-1} in their infrared spectra (tetrahydrofuran–methanol) and accordingly may be assigned the mesomeric structure VId ⟷ VIe in which there is a major contribution from the oxo form (VIe).



(iv) The nmr spectra[16] of the blue oxyporphyrin free bases (in $CDCl_3$) indicate a relatively small ring current compared with the corresponding porphyrins, because at −30° the β-methyl groups of IIb appear at τ 7.13 and 7.28, and a very broad band *ca.* τ 3 could be assigned to the methine protons (*cf.* the glaucobilin below and the range τ 3.0–3.5 for the methine protons of pyrromethenes). The spectra are poorly resolved even at this temperature, and at 78° all these resonances disappeared while those of the ester methoxyl groups (at τ 6.30 and 6.35) remained sharp; the causes of this unusual behavior will be the subject of further study.[17] The spectrum of the corresponding monocation (produced by addition of trifluoroacetic acid to the $CDCl_3$ solution) was normal but again indicated a much reduced ring current (*e.g.*, β-methyl resonances at τ 7.14 and 7.22, methine H at τ 1.34, 1.45, and 2.17) compared with the cation produced by further addition of trifluoroacetic acid (β-methyls at τ 6.55, 6.58, and 6.70 and methine H at τ −0.31, −0.18, and 0.23).[18]

Thus the carbonyl group in the oxyporphyrin free base and in the monocation largely blocks complete conjugation of the macrocycle (like the *meso*-dialkyl group in phlorins[15]), although dipolar structures with a negative charge on oxygen and a positive charge on nitrogen (as we have suggested in the case of simple pyrro ketones[11]) probably contribute to the resonance hybrid.

Aerial oxidation of the ferric chloride complex of the oxyporphyrin IIa in pyridine, followed by brief treatment with alkali and then with methanolic hydrogen chloride,[9] afforded the ring-opened bile pigment, glaucobilin-IXβ[6] (VII), mp 220–221° (λ_{max} in CH_2Cl_2 643 mμ); nmr (τ, $CDCl_3$) methine H, 3.35, 4.01, 4.12;



VII

(6) All compounds described in this paper (with the exception of the oxyporphyrin mono- and dications) have been obtained in crystalline form, and have given satisfactory elemental analyses.

(7) In CH_2Cl_2 or $CHCl_3$ the monocations are only partially converted into free base even by the addition of large excesses of bases such as cyclohexylamine, pyrrolidine, etc.

(8) R. Lemberg, B. Cortis-Jones, and M. Norrie (*Biochem. J.*, **32**, 177 (1938)) first suggested that "In the free state the oxyporphyrin is probably present in the keto-form"; see also the papers quoted in ref 4, 9, and 10.

(9) H. Fischer and H. Libowitzky, *Z. Physiol. Chem.*, **251**, 198 (1938); H. Libowitzky, *ibid.*, **265**, 191 (1940); E. Stier, *ibid.*, **272**, 239 (1942); **273**, 47 (1942).

(10) R. Lemberg, *Biochem. J.*, **29**, 1322 (1935); *Rev. Pure Appl. Chem.*, **6**, 1 (1956).

(11) J. M. Osgerby and S. F. MacDonald, *Can. J. Chem.*, **40**, 1585 (1962); J. A. Ballantine, A. H. Jackson, G. W. Kenner, and G. McGillivray, *Tetrahedron*, **22**, Suppl. I, 241 (1966).

(12) *Cf.* J. E. Falk, "Porphyrins and Metalloporphyrins," Elsevier Publishing Co., Amsterdam, 1964.

(13) Prepared by direct treatment of the oxyporphyrin with Meerwein's reagent, triethyloxonium tetrafluoroborate.

(14) *Cf.* D. Dolphin, A. W. Johnson, J. Leng, and P. Van den Broek, *J. Chem. Soc., Sect. C*, 881 (1966).

(15) R. B. Woodward, *Ind. Chim. Belge*, 1293 (1962).

(16) The −30° spectrum was determined by Dr. J. K. Becconsall.

(17) Preliminary esr measurements indicate the presence of a low concentration of free radicals.

(18) E. D. Becker, R. B. Bradley, and C. J. Watson, *J. Am. Chem. Soc.*, **83**, 3743 (1961); R. J. Abraham, A. H. Jackson, and G. W. Kenner, *J. Chem. Soc.*, 3468 (1961); R. J. Abraham, *Mol. Phys.*, **4**, 145 (1961); W. S. Caughey and W. S. Koski, *Biochemistry*, **1**, 923 (1962).

OCH_3, 6.29, 6.34; β-CH_3, 7.82 (2), 7.92, 8.16; $-CH_2-$, 7.0–7.5 multiplet; $(-CH_2)CH_3$, 8.84, 8.93). The spectral changes in the foregoing conversion correspond very closely with those observed by earlier workers[9,10] who employed oxyporphyrins prepared by direct oxidation of porphyrins. These compounds, like those prepared by our rational syntheses, must have the general structure exemplified in II and its mesomeric dipolar forms.

(19) Parke, Davis Studentship.

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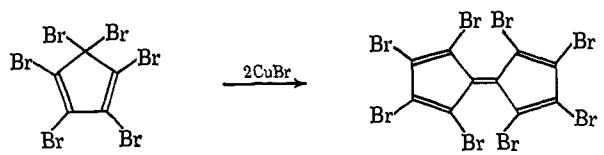
Received July 29, 1966

Octabromofulvalene[1]

Sir:

Other than fused-ring species, only three fulvalenes have been described as pure substances.[2-6] This communication reports the synthesis and characterization of the fourth such compound, octabromofulvalene (I), by the reductive coupling of hexabromocyclopentadiene[7] with copper(I) bromide.



I

In a typical experiment 10.90 g (0.020 moles) of hexabromocyclopentadiene in 27 ml of 90% 1,2-dimethoxyethane–10% water was chilled to −80°, and 5.75 g (0.040 mole) of copper(I) bromide was added. The reaction mixture was allowed to warm to 0° with stirring. Reaction took place as the water melted and within 3 min at 0° the copper(I) bromide was consumed. The reaction mixture was immediately filtered through sintered glass to separate the crude violet solid product. This solid was dissolved in chloroform–hexane and chromatographed on silicic acid yielding 0.50 g (6.6%) of pure I as dark blue crystals, mp 170° dec. *Anal.* Calcd for $C_{10}Br_8$: C, 15.93; Br, 84.1; H, nil. Found: C, 15.95; Br, 82.9; H, nil.

Octabromofulvalene is strikingly similar in its spectral properties to the known compound octachlorofulvalene.[4,5] The electronic absorption bands for the two compounds are listed in Table I. The three bands observed for the octachloro compound also appear in the spectrum of I, all with about the same intensity but shifted to lower energy. The highest energy infrared absorption, presumably a C=C stretching mode, appears at unusually low frequency in octachlorofulvalene as a sharp doublet (1525 and 1540 cm^{-1}). A similar doublet appears in the spectrum of of I at 1490 and 1505 cm^{-1}.

Table I. Electronic Spectra of Octahalofulvanes

$C_{10}Cl_8$[5]		$C_{10}Br_8$ (I)	
λ_{max}, cm^{-1} (A)	log ϵ	λ_{max}, cm^{-1} (A)	log ϵ
48,100 (2080)	4.45	45,300 (2210)	4.32
25,600 (3900)	4.61	24,200 (4140)	4.67
16,400 (6100)	2.40	15,700 (6375)	2.37

A two-dimensional X-ray diffraction study of octachlorofulvalene has shown that two five-membered rings are twisted out of plane, forming a dihedral angle of 41° at the central C–C bond.[8] The nonplanarity is presumed to result from steric interactions of the chlorine atoms at the 1, 4, 5, and 8 positions. Because the corresponding interactions should be even greater in octabromofulvalene, the structural and electronic properties of this compound will be of especial interest. Chemically, I is more reactive than octachlorofulvalene, and it is doubtless for this reason that methods of synthesis which are successful for the chloro analog[4,5,9] do not yield I. Detailed studies of the chemistry of both I and octachlorofulvalene are in progress.

(1) This work was supported by a grant from the National Science Foundation.
(2) E. C. Schreiber and E. I. Becker, *J. Am. Chem. Soc.*, 76, 3354, 6125 (1954).
(3) P. L. Pauson and B. J. Williams, *J. Chem. Soc.*, 4153 (1961).
(4) V. Mark, *Tetrahedron Letters*, 333 (1961).
(5) A. E. Ginsberg, R. Pautz, and F. Korte, *ibid.*, 779 (1962).
(6) The parent compound, fulvalene, has been prepared by several methods but is unstable and has never been obtained pure. See K. V. Scherer, Jr., *J. Am. Chem. Soc.*, 85, 1550 (1963), and references therein.
(7) F. Straus, L. Kollek, and W. Heyn, *Ber.*, 63B, 1868 (1930). The hexabromocyclopentadiene used in the present study was prepared from hexachlorocyclopentadiene and boron tribromide by a new method which will be fully described in a forthcoming paper.
(8) P. J. Wheatley, *J. Chem. Soc.*, 4936 (1961).
(9) C. F. Law, Thesis, University of Wisconsin, 1966.

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Received July 20, 1966

The Stereochemistry of the Thermal Decomposition of Vinylic Copper(I) and Silver(I) Organometallic Compounds[1]

Sir:

The thermal decomposition of organometallic compounds of copper(I) and silver(I) is important in the oxidative coupling of aryl Grignard reagents by copper(I) and silver(I) halides,[2] and is probably involved in the Ullman and related reactions.[3,4] These thermal decomposition reactions have been variously suggested to proceed by a bimolecular or concerted mechanism, in which dimer formation occurs within an aggregate of the organometallic compound,[3a,4] or by a radical mechanism, in which dimers arise from free radicals generated by homolytic cleavage of the carbon–metal bonds.[2,5]

We have explored the question of the intermediacy of free radicals in the thermal decomposition of vinylic copper(I) and silver(I) organometallic compounds by

(1) Supported in part by the National Science Foundation under Grant GP-2018.
(2) H. Hashimoto and T. Nakano, *J. Org. Chem.*, 31, 891 (1966), and references therein.
(3) (a) A. H. Lewin and T. Cohen, *Tetrahedron Letters*, 4531 (1965); (b) H. C. Brown and C. H. Snyder, *J. Am. Chem. Soc.*, 83, 1002 (1961).
(4) E. A. Bickley and J. H. Gardner, *J. Org. Chem.*, 5, 126 (1940).
(5) F. Glockling and D. Kingston, *J. Chem. Soc.*, 3001 (1959); C. E. H. Bawn and F. J. Whitby, *ibid.*, 3923 (1960).