A further difference between homogeneous rhodium and heterogeneous palladium catalysis manifests itself in the stereochemistry of hydrogen addition as demonstrated by appropriate deuteration experiments. Catalytic deuteration of Δ^1-cholesten-3-one (I) with tris(triphenylphosphine)chlororhodium proceeds from the α face, as does catalytic deuteration with palladium,[12,13] since subsequent back exchange with dilute methanolic alkali and monobromination led to 2α-bromocholestan-3-one-1α-d_1 (V) with the anticipated[12,13] nmr coupling constant (J = 6.5 cps) of the 2β-hydrogen signal (δ 4.75 in $CDCl_3$). Palladium-catalyzed tritiation[10] or deuteration[11] of $\Delta^{1,4}$-androstadiene-3,17-dione, however, proceeds from the β face to lead ultimately (after separation of other products) to *ca.* 15% of Δ^4-androstene-3,17-dione-1β-d_1. By contrast, homogeneous solution deuteration of this dienone (III) with the chloro catalyst occurred from the α side and gave nearly 85% of Δ^4-androstene-3,17-dione-1α,2α-d_2 (VI). The stereochemistry of the deuterium atoms was established by reduction of the Δ^4-double bond of VI with lithium in liquid ammonia, reoxidation of overreduced ketone by means of the Jones reagent, back exchange at C-2 with dilute methanolic alkali, and finally bromination at C-2. The resulting 2α-bromo 3-ketone V exhibited a splitting constant (J = 6.5 cps) for the nmr signal of the 2β hydrogen which is only consistent[12,13] with the 1α configuration of the remaining deuterium atom.

Further studies on the scope of such selective reductions, the determination of optimum reaction parameters, the requirements for simultaneous ketal production,[6] and especially the applicability of this technique to deuterium labeling in mass spectrometry are all under investigation in our laboratory.

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[12] F. J. Schmitz and W. S. Johnson, *Tetrahedron Letters*, 647 (1962).

[13] H. J. Ringold, M. Gut, M. Hayano, and A. Turner, *ibid.*, 835 (1962).

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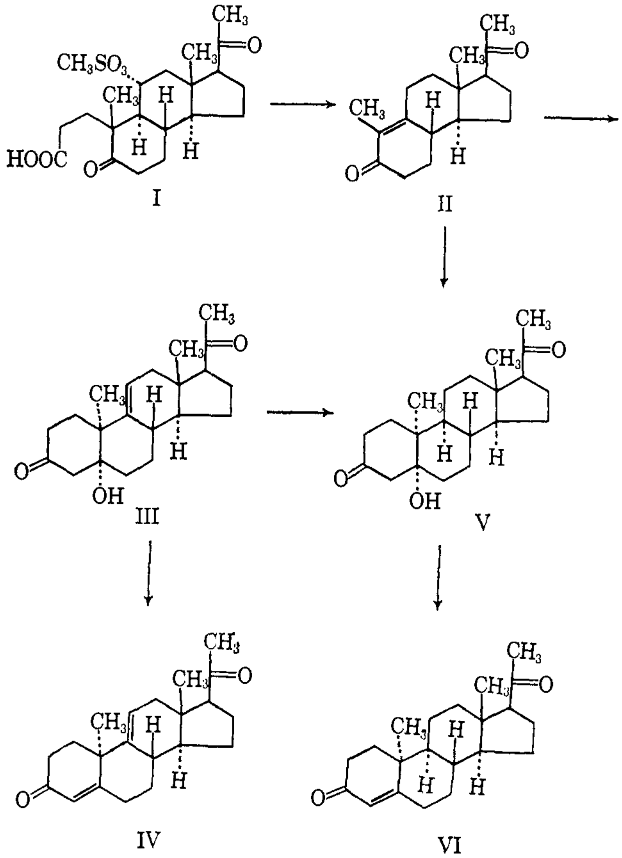
A Nonphotolytic Synthesis of 10α- and 9β,10α-Progesterone

Sir:

The original syntheses of 10α and 9β,10α steroids are based on the photolytic inversion of normal steroids.[1,2] We wish to report a novel synthesis which consists of the degradation of ring A of 11α-hydroxyprogesterone and the stereospecific rebuilding of 10α- (VI) and 9β,10α-progesterone (X) from the tricyclic intermediate (II).

Ozonization of 11α-mesyloxyprogesterone at $-70°$ gave 11α-mesyloxy-5,20-dioxo-3,5-seco-A-norpregnan-3-oic acid [I, mp 152–153°, $[\alpha]^{25}D$ $+47.9°$ (c 1, $CHCl_3$)] in a 60% yield. Retro-Michael degradation of the propionic acid moiety and elimination of methanesulfonic acid occurred simultaneously with concomitant migration of the resulting double bond when the sodium salt of I was heated in molten sodium phenylacetate, thus affording desA-pregn-9-ene-5,20-dione [II, mp 113–113.5°, $[\alpha]^{25}D$ $+54.1°$ (c 1, $CHCl_3$), λ_{max}^{EtOH} 248 mμ (ϵ 16,000), ν_{max} 109 (19-H), 48 (18-H), and 129 (21-H) cps[3]]. The yield of II was 40% and no other product could be isolated from the reaction mixture.



Condensation of II with methyl vinyl ketone in the presence of sodium ethoxide gave 5α-hydroxy-10α-pregn-9(11)-ene-3,20-dione (III, mp 197–198.5°, $[\alpha]^{25}D$ $+88°$ (c 1, $CHCl_3$), ν_{max} 33 (18-H), 85 (19-H), 128 (21-H), and 345 (11-H) cps]. Dehydration of III in boiling benzene catalyzed with p-toluenesulfonic acid proceeded smoothly to give the known 10α-pregna-4,9(11)-diene-3,20-dione[4] [IV, mp 162–167°, λ_{max}^{EtOH} 238 mμ (ϵ 14,700)]. Hydrogenation of III in acetic acid with platinum as catalyst furnished 9α-dihydro product V [mp 217–220°, $[\alpha]^{25}D$ $+86°$ (c 1, CH_3OH)]. The latter compound was also obtained by lithium in liquid ammonia reduction of II, followed by alkylation of the resulting enolate *in situ* with methyl vinyl ketone. Configurational assignment for the 5α-hydroxy group in III and V rests on the resistance to dehydration in ethanol in the presence of sodium ethoxide. Molecular models of III and V show that the 4β-hydrogen and the 5α-hydroxy groups cannot assume a *trans*-diaxial relationship favorable for E2 elimination under basic conditions. Dehydration of V in boiling benzene catalyzed with p-toluenesulfonic acid led to 10α-

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[1] J. Castells, E. R. H. Jones, G. D. Meakins, and S. Palmer, *J. Chem. Soc.*, 2907 (1962); R. Wenger, H. Dutler, H. Wehrli, K. Schaffner, and O. Jeger, *Helv. Chim. Acta*, **45**, 2420 (1962).

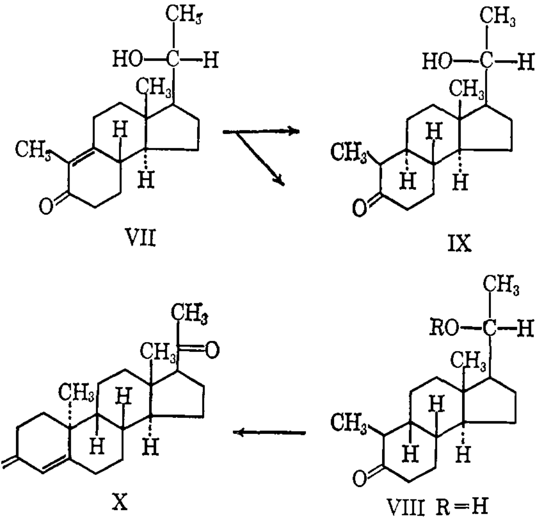
[2] P. Westerhof and E. H. Reerink, *Rec. Trav. Chim.*, **79**, 771 (1960).

[3] Melting points are corrected. The nmr spectra were recorded on a Varian A-60 spectrometer using deuteriochloroform as the solvent and tetramethylsilane as internal reference. Satisfactory analyses were obtained for all new crystalline compounds.

[4] G. Saucy, H. Els, F. Miksch, and A. Fürst, *Helv. Chim. Acta*, **49**, 1529 (1966).

progesterone[5] [VI, mp 193.5–195°, $[\alpha]^{25}\text{D}$ −125.6° (*c* 0.5, $CHCl_3$), $\lambda_{\max}^{\text{EtOH}}$ 244 mμ (ε 16,100); $\nu_{\max}$ 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°, $[\alpha]^{25}\text{D}$ −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°, $[\alpha]^{25}\text{D}$ +27.1° (*c* 0.5, EtOH), $\nu_{\max}$ 60.5 (19-H) cps, positive Cotton effect $[\alpha]_{300}$ + 440°].


VII

IX

X

VIII R=H

VIIIa R=CH$_3$CO

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°, $[\alpha]^{25}\text{D}$ −60° (*c* 0.5, $CHCl_3$); $\lambda_{\max}^{\text{EtOH}}$ 241 mμ (ε 16,200); $\nu_{\max}$ 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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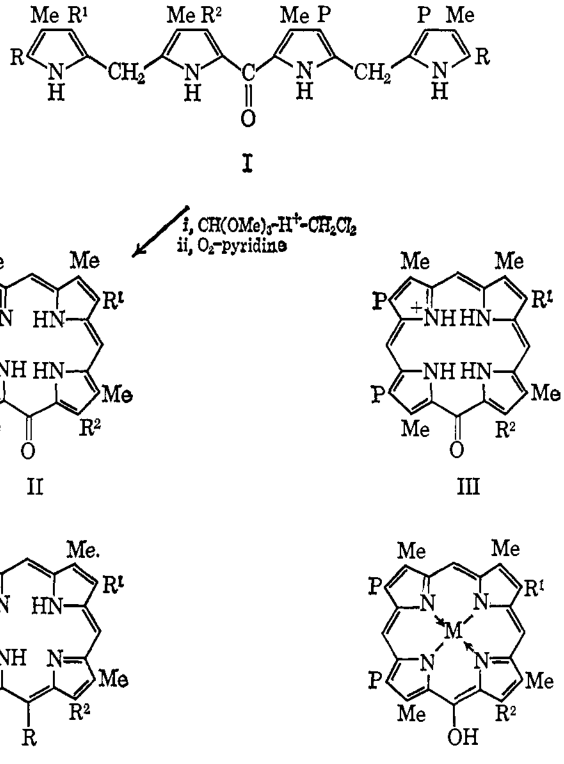
Oxyporphyrins

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

II

III

IV

V

P=CH$_2$CH$_2$CO$_2$Me
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

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[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)).