lactone is assigned structure **4** (equatorial hydroxyl) and the minor product is its epimer **5**. These structural assignments are supported by the following observations. The infrared spectra (carbon tetrachloride solution) of both hydroxy lactones show carbonyl absorption at 1770 cm^{-1} and hydroxyl absorption. Their nmr spectra show a sharp peak at τ 8.8 ascribed to the methyl group and complex multiplets in the region of τ 6–7 ascribed to the carbinol proton. Oxidation[8] of the two hydroxy lactones gives the keto lactone **6** which exhibits carbonyl absorption at 1770 and 1720 cm^{-1} (chloroform solution). The 2,4-dinitrophenylhydrazone melts at 218–219°. Exposure of either hydroxy lactone to potassium *t*-butoxide in *t*-butyl alcohol affords a mixture containing about 85% of lactone **4** and 15% of **5**. A similar epimerization is observed for tetrahydrogibberellic acid,[9] and there is little doubt that the more stable hydroxy lactone has the equatorial hydroxyl group.[10]

(8) H. C. Brown and C. P. Garg, *J. Am. Chem. Soc.*, 83, 2952 (1961).
(9) B. E. Cross, J. F. Grove, and A. Morrison, *J. Chem. Soc.*, 2498 (1961).
(10) Satisfactory combustion analyses were obtained for all new compounds described in this communication.
(11) Alfred P. Sloan Research Fellow.

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Selective Reduction of Steroids by Homogeneous Catalytic Hydrogenation[1]

Sir:

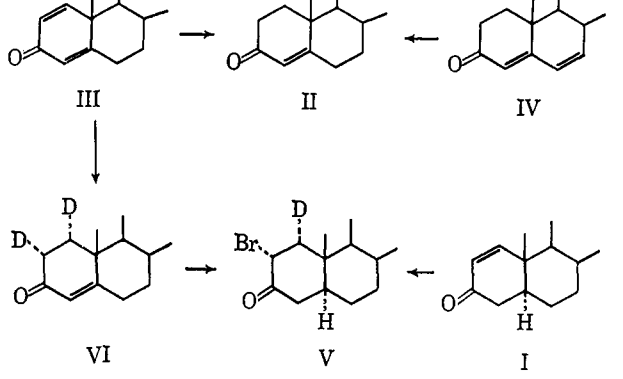
Homogeneous hydrogenation catalysis has recently been introduced by Wilkinson and collaborators[2] for the reduction of aliphatic olefins and acetylenes. Little is as yet known about the scope and limitation of this potentially powerful adjunct to organic chemical methodology, and it is for this reason that we examined the applicability of this technique in the steroid field. The present preliminary report indicates that the method has great promise for selective reductions and should also prove to be of utility in deuterium labeling.

Preparation of 0.005 *M* Catalyst Solution.[3] To a solution of 197 mg (0.75 mmole) of triphenylphosphine in 25 cc of benzene was added an equal volume of ethanol (or methanol) and 48 mg (0.125 mmole) of μ-dichloro-tetraethylenedirhodium.[4] The resulting yellow solution of tris(triphenylphosphine)chlororhodium[5] was filtered through cotton and used directly for the subsequent hydrogenation. The corresponding iodo catalyst (brownish black solution) was prepared by simply adding 1 equiv of sodium iodide to the solution of the chloro complex.

Typical Reduction Procedure. A 100-mg sample of steroid was dissolved in 20–50 cc of 0.005 *M* catalyst solution and stirred at room temperature and atmospheric pressure in a tightly stoppered flask which was first evacuated and filled with hydrogen (or deuterium) several times. After several hours, the solution was evaporated to dryness, and the residue was taken up in a mixture of petroleum ether and methylene chloride and filtered through alumina. Evaporation of the solvent yielded the product.

Results. Unhindered disubstituted olefins such as Δ^1-, Δ^2-, and Δ^3-cholestene were reduced by either the chloro or iodo catalyst to 5α-cholestane in nearly quantitative yield in 1.5–20 hr. More highly substituted olefins such as Δ^4-androstene, Δ^{14}-ergostene, and $\Delta^{8(14)}$-ergostene were recovered during this period of time. More hindered disubstituted olefins seem to react much more sluggishly as indicated in a single experiment with Δ^{11}-5β-pregnene-3,20-dione and the chloro catalyst in benzene–ethanol (1:1) solution (36 hr) which provided 83% of unreacted olefin and 13% of saturated diketone.

Of particular interest is the reduction of α,β-unsaturated ketones by this procedure.[6] In accord with the results on olefins, Δ^1-3-keto 5α-steroids (I) are readily reduced in 6–16 hr, while Δ^4-3-ketones (II) or Δ^5-7-keto 3β-acetates are recovered unchanged.[7] With this information as a background, the selective reduction of dienones was investigated and found to proceed extremely smoothly. Using the chloro catalyst and periods of 16–72 hr, $\Delta^{1,4}$-androstadiene-3,17-dione (III) and $\Delta^{4,6}$-androstadiene-3,17-dione (IV) are converted in 75–85% yield into the Δ^4-3-ketone (II), the remainder of the material being saturated diketone. More careful choice of reduction conditions will probably lead to nearly quantitative yields of Δ^4-3-ketone. This great separation in reactivity of different double bonds toward homogeneous catalytic hydrogenation conditions should be contrasted with the very poor yields of Δ^4-3-ketones, which are generally encountered[8–11] in all selective catalytic hydrogenations of $\Delta^{1,4}$-dien-3-ones (III), and the multiplicity of products that is often generated.



(1) Financial support (Grant No. CA-07195) from the National Institutes of Health of the U. S. Public Health Service is gratefully acknowledged.
(2) J. F. Young, J. A. Osborn, F. H. Jardine, and G. Wilkinson, *Chem. Commun.*, 131 (1965); F. H. Jardine, J. A. Osborn, G. Wilkinson, and J. F. Young, *Chem. Ind.* (London), 560 (1965).
(3) The helpful advice of Professor J. P. Collman of the University of North Carolina is gratefully acknowledged.
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(6) In the reduction of α,β-unsaturated ketones, a 1:1 ethanol–benzene solution is preferred over 1:1 methanol–benzene because the latter provides the dimethyl ketal of the saturated ketone. For certain synthetic purposes, ketal formation may be advantageous if simultaneous protection of the saturated carbonyl group is required.
(7) After 72-hr exposure to the chloro catalyst, 80% of the enone was still recovered and only 20% of the saturated ketone was formed.
(8) H. H. Inhoffen and Huang-Minlon, *Ber.*, 71, 1720 (1938).
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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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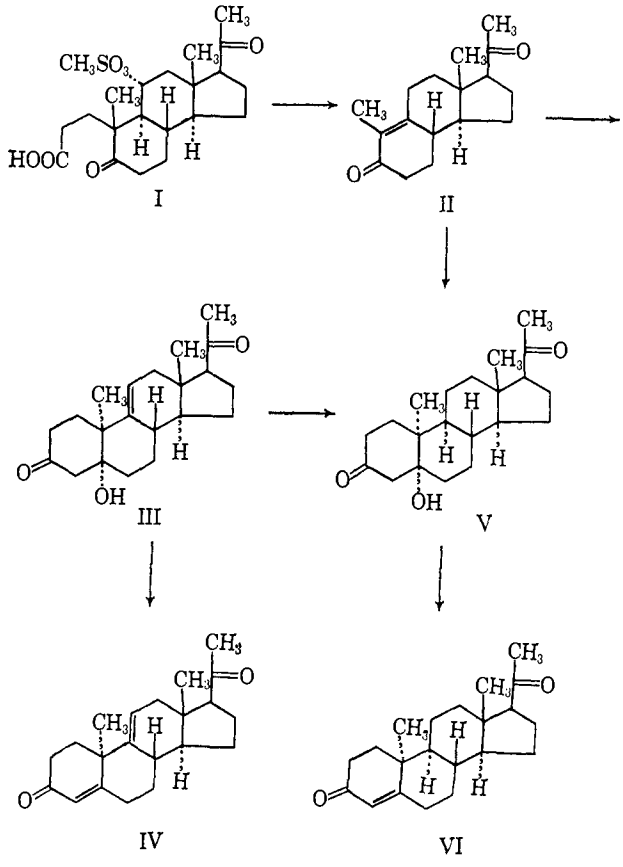
A Nonphotolytic Synthesis of 10α- and 9β,10α-Progesterone

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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(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).