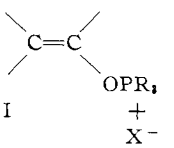
reactions of halocarbonyl compounds with tertiary phosphines and phosphites.



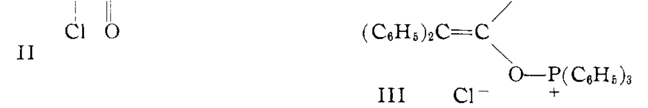
I

R = alkyl, aryl, or alkoxy

The formation of this intermediate can occur by attack of trivalent phosphorus on carbonyl carbon,[1,2] carbonyl oxygen,[1,5] or on halogen.[1,6] Although the position of attack has not yet been unequivocally determined, halogen attack seems the most likely at this time.[1]

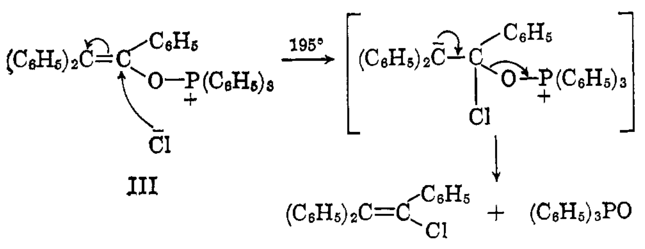
In two instances[5,6] the isolation of an enol phosphonium salt was reported, but essentially no physical data were given in support.

We now wish to report the isolation and characterization of an enol phosphonium salt; that derived by the action of triphenylphosphine on the haloketone II. The salt III was obtained in good yield (68%). It is an extremely hygroscopic white solid, insoluble in refluxing xylene and having the correct elemental analysis for III. *Anal.* Calcd.: C, 80.28; H, 5.28; P, 5.46; Cl, 6.16. Found: C, 80.85; H, 5.49; P, 5.48; Cl, 6.18; ionic Cl, 6.16. The infrared spectrum [($CHCl_3$): 3.01 μ (w), 3.40 (m), 4.16 (w), 6.30 (m), 6.74 (w), 9.96 (m), 8.58 (m), 8.94 (s), 9.63 (m), 9.86 (s), 10.05 (s), 10.34 (s)] showed no carbonyl absorption. Proton magnetic resonance analysis showed a multiplet centered at 2.6 τ. The P^{31} n.m.r. spectrum exhibited a chemical shift of −63 p.p.m. relative to 85% phosphoric acid.



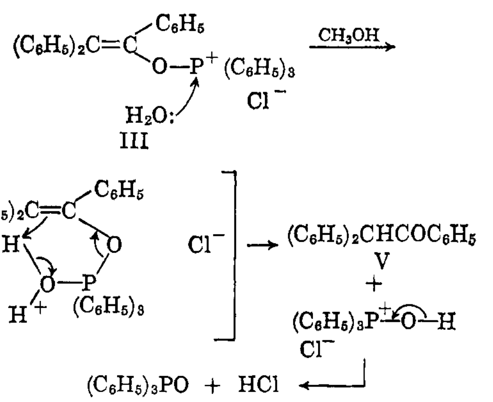
Recrystallization of III from ethylene dichloride afforded white needles, which analyzed for a 1:1 adduct of III and ethylene dichloride. *Anal.* Calcd.: C, 71.86; H, 5.09; P, 4.64; Cl, 15.94; ionic Cl, 5.31. Found: C, 71.92; H, 5.20; P, 4.76; Cl, 15.90; ionic Cl, 5.68. The n.m.r. spectrum exhibited a multiplet at 2.6 τ and a singlet at 6.24 τ. The ratio of the peak areas was 8.2:1. Ethylene dichloride alone exhibits a singlet at 6.26 τ.

Pyrolysis of III was carried out at 195° (0.2 mm.) in a sublimation apparatus. The products of the pyrolysis were triphenylphosphine oxide and the expected product of the halogen migration reaction, triphenylchloroethylene (IV). The melting point of IV was not depressed upon admixture of authentic material prepared by the route of van de Kamp.[7] The infrared spectra were superimposable.



IV

Hydrolysis of III led to triphenylphosphine oxide and the dehalogenated ketone V. Again the melting point was not depressed upon admixture of authentic material, and the infrared spectra were superimposable.



The elucidation of the mechanism of the decomposition of these salts *via* the Perkow and halogen migration reactions is now continuing.

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(5) S. Trippett, *J. Chem. Soc.*, 2337 (1962).

(6) H. Hoffmann and H. J. Diehr, *Tetrahedron Letters*, 583 (1962).

(7) J. van de Kamp and M. Sletzinger, *J. Am. Chem. Soc.*, **63**, 1879 (1941).

Steroids. CCXLIII.[1] Steroids of Unnatural Configuration. The Synthesis of $9\beta,10\alpha$-19-Nor Steroids

Sir:

Retro ($9\beta,10\alpha$) steroids have so far been obtained only by photochemical reactions.[2] We wish to report a chemical synthesis of two 19-nor steroids with the *anti-cis-anti-trans* stereochemical arrangement depicted in IVa,b. It is well known[3] that Birch reduction of estrone methyl ether (9α-H) and subsequent acid treatment leads to 19-nortestosterone ($9\alpha,10\beta$ stereochemistry). However, conformational considerations indicated that an analogous reduction of a ring A aromatic (9β-H) steroid should lead to a 19-nor-Δ^4-3-ketone with $9\beta,10\alpha$-stereochemistry.

An approach to 9β-ring A aromatic steroids arose from studies with 11-keto ring A aromatic pregnanes.[4] Alkaline hydrolysis (1% sodium hydroxide in methanol) of 3-hydroxy-19-norpregna-1,3,5(10)-triene-11,20-dione benzoate (Ib)[4] afforded a phenol Id [m.p. 202–204°; $[\alpha]_D$ +248° (dioxan); $\lambda_{\max}^{\text{EtOH}}$ 282 mμ (log ε 3.31). *Anal.* Found: C, 76.65; H, 7.45; O, 15.47] which was isomeric with but different from the expected product Ia.[4] The phenol Id was characterized as its benzoate Ie [m.p. 179–181°; $[\alpha]_D$ +204° ($CHCl_3$); $\lambda_{\max}^{\text{EtOH}}$ 231 mμ (log ε 4.34). *Anal.* Found: C, 78.19; H, 6.84] and methyl ether If [m.p. 157–159°; $[\alpha]_D$ +274° ($CHCl_3$); $\lambda_{\max}^{\text{EtOH}}$ 280 mμ (log ε 3.31). *Anal.* Found: C, 77.74; H, 8.34; O, 14.29]. The optical rotatory dispersion curves of the six compounds Ia–If clearly demonstrated that the pregnane side chain was β-

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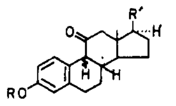
(1) Part CCXLII: A. D. Cross and P. Crabbé, *Tetrahedron* (submitted for publication).

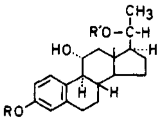
(2) (a) The classical work of Windaus, Heilbron, and their schools on the irradiation of ergosterol is summarized by L. F. Fieser and M. Fieser, "Steroids," Reinhold Publishing Corp., New York, N. Y., 1959, p. 136; (b) J. Castells, E. R. H. Jones, G. D. Meakins, and R. W. J. Williams, *J. Chem. Soc.*, 1159 (1959), and related papers; (c) W. G. Dauben and G. J. Fonken, *J. Am. Chem. Soc.*, **81**, 4060 (1959); (d) E. H. Reerink, H. F. L. Schöler, P. Westerhof, A. Querido, A. A. H. Kassenaar, E. Diczfalusy, and K. C. Tillinger, *Nature*, **186**, 168 (1960); P. Westerhof and E. H. Reerink, *Rec. trav. chim.*, **79**, 771, 795, 1118 (1960); (e) R. Van Moorselaar, Ph.D. Thesis, University of Leiden (Holland), 1962.

(3) A. J. Birch, *J. Chem. Soc.*, 367 (1950); C. Djerassi, R. Riniker, and B. Riniker, *J. Am. Chem. Soc.*, **78**, 6362 (1956).

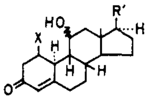
(4) A. Bowers, J. S. Mills, C. Casas-Campillo, and C. Djerassi, *J. Org. Chem.*, **27**, 361 (1962).



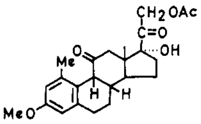
I a, R = H; R' = $COCH_3$; 9α-H
b, R = Bz; R' = $COCH_3$; 9α-H
c, R = Me; R' = $COCH_3$; 9α-H
d, R = H; R' = $COCH_3$; 9β-H
e, R = Bz; R' = $COCH_3$; 9β-H
f, R = Me; R' = $COCH_3$; 9β-H
g, R = Bz; R' = $CH(OCOOEt)CH_3$; 9α-H
h, R = H; R' = $CH(OH)CH_3$; 9β-H
i, R = CH_3CO; R' = $CH(OAc)CH_3$; 9β-H
j, R = Me; R' = $CH(OH)CH_3$; 9β-H
k, R = Me; R' = $CH(OAc)CH_3$; 9β-H



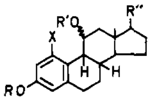
III a, R = R' = H
b, R = Bz; R' = H
c, R = Bz; R' = COOEt



IV a, $X = <^{H}_{H}$; R' = $CH(OH)CH_3$
b, $X = <^{H}_{CH_3}$; R' = OH



V



VI a, R = R' = X = H; R'' = $<^{CH(OH)CH_3}_{H}$
b, R = Me; R' = X = H; R'' = $<^{CH(OH)CH_3}_{H}$
c, R = Me; R' = Ac; X = H; R'' = $<^{CH(OAc)CH_3}_{H}$
d, R = X = Me; R' = H; R'' = O

orientated in every case.[5] It was concluded therefore that Id, Ie, and If differed from their isomers Ia, Ib, and Ic[7] by the configuration at the only other epimerizable center C-9.[8] Other examples have recently been reported of the alkaline isomerization of 9α-11-keto-ring A-aromatic steroids to their 9β-epimers.[9] The way to 9β-ring A aromatic steroids was now clear and a convenient route in the pregnane series utilized 3-hydroxy-19-norpregna-1,3,5(10),9(11)-tetraen-20-one (II)[10] as starting material. Hydroboration[4,11] of II afforded the triol IIIa [m.p. 249–250°; [α]D −66° (dioxan); λ_{max}^{EtOH} 279 mμ (log ε 3.43). *Anal.* Found: C, 76.56; H, 8.90; O, 14.68] which was converted to the benzoate IIIb [m.p. 180–183°; [α]D −68° ($CHCl_3$); λ_{max}^{EtOH} 231 mμ (log ε 4.29). *Anal.* Found: C, 76.87; H, 7.27] by the Schotten–Baumann procedure.[12] Selective esterification of the latter compound at C-20 with ethyl chloroformate[13] (15 min. at 0° in pyridine) provided the cathylate IIIc [m.p. 136–138°; [α]D −57° ($CHCl_3$); λ_{max}^{EtOH} 230 mμ (log ε 4.25). *Anal.* Found: C, 72.89; H, 7.36; O, 20.03] which was oxidized with 8 *N* chromic acid to the ketone Ig [m.p. 191–193°; [α]D +168° ($CHCl_3$); λ_{max}^{EtOH} 231 mμ (log ε 4.31). *Anal.* Found: C, 73.93; H, 7.01]. Base treatment (1.5% sodium hydroxide in methanol) of Ig led to hydrolysis of the ester groupings at C-3 and C-20 and epimerization at C-9 to afford the 9β-dihydroxy ketone Ih which was characterized as its 3,20-diacetate Ii [m.p. 131–132°; [α]D +185° ($CHCl_3$); λ_{max}^{EtOH} 269 and 275 mμ (log ε 2.78 and 2.73). *Anal.* Found: C, 72.66; H, 7.82]. Dimethyl sulfate in acetone containing potassium carbonate converted Ih to the amorphous methyl ether Ij which gave a crystalline acetate Ik [m.p. 117–119°; [α]D +221°; λ_{max}^{EtOH} 280 mμ (log ε 3.29). *Anal.* Found: C, 74.62; H, 8.26; O, 17.29]. Oxidation of Ij afforded the 9β-11,20-diketone If. Lithium aluminum hydride reduction of Ij gave 3-methoxy-9β-19-norpregna-1,3,5(10)-triene-11ξ,20β-diol (VIb) characterized as its diacetate VIc [m.p. 45–47°; [α]D +100° ($CHCl_3$); λ_{max}^{EtOH} 278 mμ (log ε 3.32). *Anal.* Found: C, 72.21; H, 8.08; O, 19.14]. Birch reduction of VIb followed by mild acid treatment gave 11ξ,20β-dihydroxy-9β,10α-19-norpregn-4-en-3-one (IVa) [m.p. 228–232°; [α]D −31° (pyridine); λ_{max}^{EtOH} 243 mμ (log ε 4.22). *Anal.* Found: C, 75.65; H, 9.52].

The optical rotatory dispersion curve of IVa was very similar to the curves of lumist-4-en-3-one[14,15] and 17β-hydroxy-9β,10α-androst-4-en-3-one[2e] and had a Cotton effect opposite in sign to that of 19-nortestosterone. These data are compatible with IVa having 9β,10α-orientated hydrogen atoms.

Similar studies in the androstane series led to 11ξ,17β-dihydroxy-1ξ-methyl-9β,10α-19-norandrost-4-en-3-one (IVb) [m.p. 203–204°; [α]D −33°; λ_{max}^{EtOH} 244–246 mμ; (log ε 4.11). *Anal.* Found: C, 74.94; H, 9.73] *via* the Birch reduction of 3,11ξ-dihydroxy-1-methyl-9β-estra-1,3,5(10)-trien-17-one 3-methyl ether (VId)[16] [m.p. 139–141°; [α]D +18° ($CHCl_3$); λ_{max}^{EtOH} 283 mμ (log ε 3.23). *Anal.* Found: C, 76.33; H, 8.10].

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(5) The compounds Ia–If all displayed positive Cotton effect curves. The peak intensities for Id–If were essentially double the intensities of the isomers Ia–Ic. This excludes a 17α-oriented side chain since the 20-carbonyl group in the 17-isopregnane series exhibits a negative rotatory dispersion curve.[6]

(6) See C. Djerassi, "Optical Rotatory Dispersion," McGraw-Hill Book Co., Inc., New York, N. Y., 1960, Chapter 4.

(7) This substance exhibited m.p. 190–193°; [α]D +332° ($CHCl_3$); λ_{max}^{EtOH} 277 and 285 mμ (log ε 3.22 and 3.21). *Anal.* Found: C, 77.45; H, 8.11.

(8) The n.m.r. data are in full accord with the 9β-stereochemistry of Id, Ie, and If. Private communication from Dr. A. D. Cross of these Laboratories.

(9) See (a) E. J. Bailey, J. Elks, J. F. Oughton, and L. S. Stephenson, *J. Chem. Soc.*, 4535 (1961); (b) E. Caspi, E. Cullen, and P. K. Grover, *ibid.*, 212 (1963).

(10) J. S. Mills, J. Barrera, E. Olivares, and H. Garcia, *J. Am. Chem. Soc.*, **82**, 5882 (1960).

(11) H. C. Brown and B. C. Subba Rao, *ibid.*, **78**, 5694 (1956).

(12) See L. F. Fieser and M. Fieser, "Advanced Organic Chemistry," Reinhold Publishing Corp., New York, N. Y., 1961, p. 290.

(13) L. F. Fieser, J. E. Herz, M. W. Klohs, M. A. Romero, and T. Utne *J. Am. Chem. Soc.*, **74**, 3309 (1952).

(14) The rotatory dispersion curve of lumist-4-en-3-one was obtained through the kindness of Prof. C. Djerassi and Prof. E. R. H. Jones.[15]

(15) J. Castells, G. A. Fletcher, E. R. H. Jones, G. D. Meakins, and R. Swindells, *J. Chem. Soc.*, 2627 (1960).

(16) Base treatment of 3,17α,21-trihydroxy-1-methyl-19-norpregna-1,3,5-(10)-triene-11,20-dione 3,21-diacetate[9a] followed by methylation and acetylation afforded 3,17α,21-trihydroxy-1-methyl-9β-19-norpregna-1,3,5(10)-triene-11,20-dione 3-methyl ether 21-acetate (V) [m.p. 124–127 and 173–174°; [α]D +126°; λ_{max}^{EtOH} 278 mμ (log ε 3.13). *Anal.* Found: C, 69.64; H, 7.34; O, 23.14] which underwent reduction with diborane and subsequent side chain degradation with sodium periodate to give VId.

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