in 1 ml. of column at equilibrium with mobile phase of concentration c; $f^*(c)$ = amount of solute in 1 ml. of solvent (stationary liquid phase) at equilibrium; then

$$f(c)/c = [f^*(c)/c]\ \gamma + \alpha$$

but

$$f^*(c)/c = K$$
$$f(c)/c = V_R^0/X$$

from which eqn. (2) is obtained on substitution.

Provided the correct substitutions are made eqn. (2) is identical with the result of Simpson and Wheaton[5] for an ion-exchange bed but the equation suggested by Wiebe[6] supposedly based on the results of Simpson and Wheaton is, in my opinion, incorrect. The equation quoted by Hoare and Purnell[7] is identical with (2) provided that their "column efficiency factor" X is identified with αX.

If $v_R^0/\alpha X \gg 1$, eqn. (2) reduces to

$$K = v_R^0/v_L \qquad (3)$$

where v_L is the total volume of stationary liquid phase on the column. The unknowns, γ, X and v_L are easily obtained with precision; α may be estimated with rather greater possible error by a number of methods, probably the most convenient being calibration of the column with a sample of inert gas. Fortunately, in most cases K is not strongly dependent on the value of α.

Provided K is very large only the assumption of any direct proportionality between K and v_R^0 is required to evaluate ΔH (*cf.* ref. 7). However, an adequate test of the theory requires a comparison of values of K obtained from eqn. (2) (preferably for cases where K is fairly small) and from static solubility measurements. Such experiments have been made (in collaboration with Mr. K. H. Napier) in this laboratory for benzene and over a stationary phase of polyethylene glycol cresyl ether. For instance, at 132° for benzene the chromatographic method gave K = 23.5, to be compared with K = 22.0 for the static method. The results will shortly be published in full.

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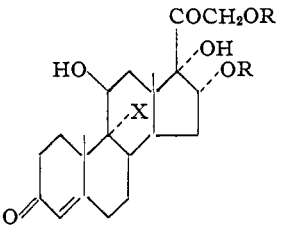
16-HYDROXYLATED STEROIDS. IV.[1] THE SYNTHESIS OF THE 16α-HYDROXY DERIVATIVES OF 9α-HALO-STEROIDS

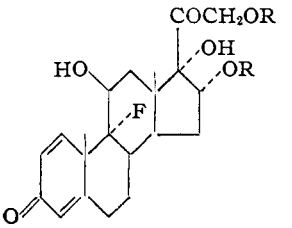
Sir:

We wish to report on the influence of 16α-hydroxylation on the biological activities of 9α-fluoro-corticoids.[2]

Treatment of 21-acetoxy-4,9(11),16-pregnatriene-3,20-dione (I)[3] with osmium tetroxide in benzene and pyridine afforded 21-acetoxy-16α,17α-dihydroxy-4,9(11)-pregnadiene-3,20-dione (II), m.p. 195–197.5°, λ_{max} 238.5 mμ (ε 16,700)[4], $[\alpha]^{25}D$ +93° ($CHCl_3$); (*Anal.* Calcd. for $C_{23}H_{30}O_6$: C, 68.63; H, 7.51. Found: C, 68.72; H, 7.79). Acetylation gave the 16α,21-diacetate III, m.p. 194–195°, $[\alpha]^{25}D$ +43° ($CHCl_3$); (*Anal.* Calcd. for $C_{25}H_{32}O_7$: C, 67.55; H, 7.26. Found: C, 67.31; H, 7.49).



IV, X = Br, R = Ac
VIa, X = Cl, R = H
VIb, X = Cl, R = Ac
VIIa, X = F, R = H
VIIb, X = F, R = Ac



VIIIa, R = H
VIIIb, R = Ac

The diene diacetate III in dioxane and water was treated with N-bromoacetamide and 10% perchloric acid to yield 16α,21-diacetoxy-9α-bromo-11β,17α-dihydroxy-4-pregnene-3,20-dione (IV), m.p. 125–126° dec. with previous browning; λ_{max} 243 mμ (ε 14,100), ν_{max} 3546, 1751, 1715, 1675, 1626 and 1236 cm.$^{-1}$; $[\alpha]^{25}D$ +76° ($CHCl_3$); (*Anal.* Calcd. for $C_{25}H_{33}BrO_8$: C, 55.45; H, 6.14; Br, 14.76. Found: C, 55.73; H, 6.54; Br, 14.51). Compound IV in absolute alcohol was refluxed with anhydrous potassium acetate to give 16α,21-diacetoxy-17α-hydroxy-9β,11β-oxido-4-pregnene-3,20-dione (V), m.p. 191.5–193.5°, λ_{max} 243–243.5 mμ (ε 15,000), ν_{max} 3571, 3436, 1757, 1745 (shoulder), 1673, 1626 and 1239 cm.$^{-1}$, $[\alpha]^{25}D$ −48° ($CHCl_3$); (*Anal.* Calcd. for $C_{25}H_{32}O_8$: C, 65.20; H, 7.00, Found: C, 65.00; H, 7.32).

A solution of the oxide V in chloroform (alcohol free) on reaction with chloroform saturated with hydrogen chloride (0°, 4.5 hrs.) gave 16α,21-diacetoxy-9α-chloro-11β,17α-dihydroxy-4-pregnene-3,-20-dione (VIb), m.p. 214.5–215.5°; λ_{max} 240.5 mμ (ε 15,800); ν_{max} 3604, 3521 (shoulder), 1767, 1751 (shoulder), 1727 (shoulder), 1684, 1637, 1252 and 1242 cm.$^{-1}$; $[\alpha]^{25}D$ +76° ($CHCl_3$); (*Anal.* Calcd. for $C_{25}H_{33}ClO_8$: C, 60.42; H, 6.69; Cl, 7.14. Found: C, 60.65; H, 6.80; Cl, 7.34). Treatment with sodium methoxide in methanol gave the free chlorohydrin VIa, m.p. unmelted at 400° (darkening began at 190°); λ_{max} 240–240.5 mμ (ε 15,900), ν_{max} 3425, 1709, 1661 and 1626 cm.$^{-1}$; (*Anal.* Calcd. for $C_{21}H_{29}ClO_6$: C, 61.08; H, 7.08; Cl, 8.59. Found: C, 61.48; H, 7.22; Cl, 8.29).

Opening of the oxide V in chloroform with anhydrous hydrogen fluoride gave 16α,21-diacetoxy-9α-fluoro-11β,17α-dihydroxy-4-pregnene-3,20-dione (VIIb), m.p. 237–239°; λ_{max} 237.5–238.5 mμ (ε 17,600), ν_{max} 3675, 3495, 1750, 1680, 1640 (shoul-

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(2) (a) J. Fried and E. F. Sabo, *ibid.*, **75**, 2273 (1953); **76**, 1455 (1954); (b) J. Fried, J. E. Herz, E. F. Sabo, A. Borman, F. M. Singer and P. Numerof, *ibid.*, **77**, 1069 (1955); (c) J. Fried, K. Florey, E. F. Sabo, J. E. Herz, A. R. Restivo, A. Borman and F. M. Singer, *ibid.*, **77**, 4181 (1955); (d) R. F. Hirschmann, R. Miller, R. E. Beyler, L. H. Sarett and M. Tishler, *ibid.*, **77**, 3166 (1955); (e) A. Nobile, W. Charney, P. L. Perlman, H. L. Herzog, C. C. Payne, M. E. Tully, M. A. Jevnik and E. B. Hershberg, *ibid.*, **77**, 4184 (1955); (f) J. A. Hogg, F. H. Lincoln, A. H. Nathan, A. R. Hanze, W. P. Schneider, P. F. Beal and J. Korman, *ibid.*, **77**, 4438 (1955); (g) E. Vischer, Ch. Meystre and A. Wettstein, *Helv. Chim. Acta*, **38**, 1502 (1955).

(3) W. S. Allen and S. Bernstein, THIS JOURNAL, **77**, 1028 (1955).

(4) The ultraviolet spectra were determined in absolute alcohol solutions. The infrared spectra are for pressed potassium bromide discs.

der) and 1245 cm.$^{-1}$; $[\alpha]^{24}D$ +70° ($CHCl_3$); (*Anal.* Calcd. for $C_{25}H_{33}FO_8$: C, 62.49; H, 6.92; F, 3.95. Found: C, 62.71; H, 7.06; F, 3.63). Saponification of VIIb with sodium methoxide in methanol gave 9α-fluoro-11β,16α,17α,21-tetrahydroxy-4-pregnene-3,20-dione (VIIa), m.p. 257–260° d. (previous softening and browning); λ_{max} 238.5 mμ (ε 16,300; ν_{max} 3635, 3440, 1720, 1674 and 1630 cm.$^{-1}$; $[\alpha]^{25}D$ +91° (pyridine); *Anal.* Calcd. for $C_{21}H_{29}FO_6$: C, 63.62; H, 7.37; F, 4.79. Found: C, 63.47; H, 7.51; F, 4.49).

Microbiological dehydrogenation of VIIb with *Cornyebacterium simplex*[2e] gave after acetylation of the crude fermentation mixture 16α,21-diacetoxy-9α-fluoro-11β,17α-dihydroxy-1,4-pregnadiene-3,20-dione (VIIIb), m.p. 158–235°[5]; λ_{max} 239 mμ (ε 15,200); ν_{max} 3390, 1740 (shoulder), 1730, 1660, 1610, 1608 (inflection) and 1235 cm.$^{-1}$; $[\alpha]^{25}D$ +22° ($CHCl_3$); (*Anal.* Calcd. for $C_{25}H_{31}FO_8$: C, 62.75; H, 6.53; F, 3.97. Found: C, 63.45; H, 7.44; F, 4.39). Saponification afforded the free steroid VIIIa, m.p. 260–262.5°,[6] λ_{max} 238 mμ (ε 15,800); ν_{max} 3388, 1705, 1660, 1620 and 1604 cm.$^{-1}$; $[\alpha]^{25}D$ +75° (acetone); (*Anal.* Calcd. for $C_{21}H_{27}FO_6$: C, 63.94; H, 6.90; F, 4.82. Found: C, 64.19; H, 7.17; F, 4.90).

Bio-assays:[7] In the rat liver glycogen assay (subcutaneous method) 16α,21-diacetoxy-9α-fluoro-11β,17α-dihydroxy-4-pregnene-3,20-dione (VIIb) possessed an activity 4–8 times that of hydrocortisone; whereas, the free steroid VIIa had a 3–5 fold activity. In the same assay, 16α,21-diacetoxy-9α-fluoro-11β,17α-dihydroxy-1,4-pregnadiene-3,20-dione (VIIIb) and its free steroid VIIIa were found to be, respectively, 15–36 and about 13 time more active than hydrocortisone.

In the rat electrolyte assay the 16α-hydroxy-fluorohydrins (VIIa,b) and 16α-hydroxy-1-dehydro-fluorohydrins (VIIIa,b) exhibited *no sodium retention properties.*

It is concluded that 16α-hydroxylation abolishes the sodium-retaining property of 9α-fluoro-steroids without destroying their glucocorticoid activity.

9α-Fluoro-11β,16α,17α,21-tetrahydroxy-1,4-pregnadiene-3,20-dione (VIIIa) and its diacetate VIIIb are the most active glucocorticoids hitherto reported which are devoid of sodium-retaining properties.

(5) The compound was apparently solvated, and the m.p. was difficult to determine. On many occasions the m.p. was about 186–188° with gas evolution.

(6) In a later run, the m.p. was 269–271°.

(7) The electrolyte assays on compounds VIIa, b were done by E. Rosenberg and R. I. Dorfman at the Worcester Foundation for Experimental Biology. These results were confirmed by P. H. Bell and F. I. Dessau and their associates (Experimental Therapeutics Research Section of these Laboratories) who also supplied the electrolyte data on compounds VIIIa,b, as well as all the glycogen data. These groups will report on their work elsewhere.

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RECEIVED OCTOBER 4, 1956

A NEW TECHNIQUE FOR THE CONVERSION OF OLEFINS INTO ORGANOBORANES AND RELATED ALCOHOLS

Sir:

In the presence of aluminum chloride the reducing powers of sodium borohydride are greatly enhanced.[1] We now wish to report that this reagent readily reacts with simple olefins, such as ethylene, 1- and 2-pentene, cyclohexene, and styrene, at temperatures of 25°, to form the corresponding trialkylboranes in yields of 90%.

Trialkylboranes are readily oxidized to the borate esters[2] which can be hydrolyzed to the corresponding alcohols. The reaction can be carried out without isolation of any of the intermediates. In this way cyclohexene has been converted into cyclohexanol, 1-hexene into 1-hexanol, styrene into 2-phenylethanol and 1,1-diphenylethylene into 2,2-diphenylethanol. Tne yields based on olefin are good, in the range of 70–90%. The following procedures are representative.

To a stirred solution of 0.25 mole of sodium borohydride and 0.084 mole of aluminum chloride in 250 ml. of diglyme[1] was slowly added 0.5 mole of 1-pentene. After 3 hours at room temperature, the reaction mixture was heated for 1 hour on a steam cone to complete the reaction. A nitrogen atmosphere was maintained. The flask was cooled, the diglyme removed under vacuum (<40° at 1 mm.) and the tri-*n*-pentylborane was collected at 94–95° at 2 mm. The yield was 33.0 g., 88%.

Anal. Calcd. for $C_{15}H_{33}B$: B, 4.83. Found: B, 4.55.

Oxidation by the procedure described below gave 1-pentanol of at least 95% purity, as indicated by infrared analysis. This and similar experiments indicate that in the reaction with 1-olefins, the boron becomes preferentially attached to the terminal carbon.

1,1-Diphenylethylene, 0.5 mole, was converted into the corresponding borane as described above for 1-pentene. Approximately 50% of the diglyme was removed under vacuum 1 (< 40°, 1 mm.), and the remaining solvent washed out with dilute hydrochloric acid and water. The crude product was treated with 0.2 mole of sodium hydroxide in 100 ml. of ethanol, followed by 68 g. of 30% hydrogen peroxide (20% excess) added at such a rate as to maintain a gentle reflux. The product was taken up in ether, washed and dried. Distillation gave 86.4 g. of 2,2-diphenylethanol, b.p. 192–194° at 20-mm. (87% yield). Recrystallization from petroleum ether gave a product, m.p. 64–65°, in 71% yield.

The reaction of olefins with aluminum borohydride at 140° has been reported.[3] For reasons presented earlier[1] aluminum borohydride cannot be present in the reagent in more than trace amounts. The great ease in preparing and handling the reagent as compared to aluminum borohydride should make the present procedure a highly convenient laboratory method for preparing organoboranes and for hydrating olefins. We have preliminary

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(2) J. R. Johnson and M. G. Van Campen, Jr., *ibid.*, **60**, 121 (1938).

(3) R. S. Brokaw and R. N. Pease, *ibid.*, **72**, 3237 (1950).