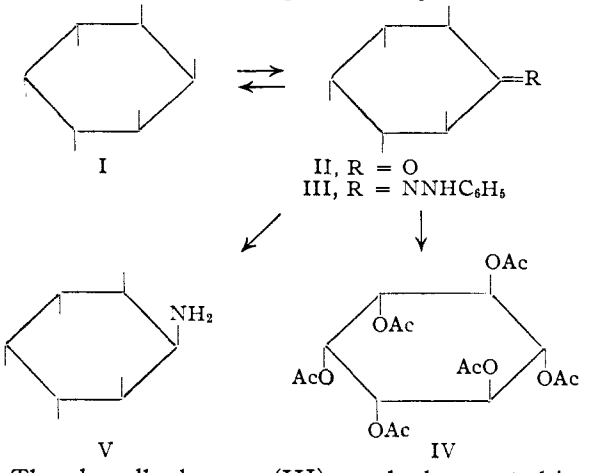
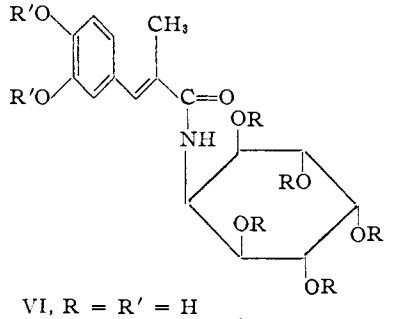
inositol hexaacetate,[8] m.p. 212–213°. (*Anal.* Calcd. for $C_{18}H_{24}O_{12}$: C, 50.00; H, 5.60. Found: C, 50.34; H, 5.69). Since *myo*-inositol and *neo*-inositol are formed by reduction of this inosose, the latter must be *neo*-inosose-2 (II); the phenylhydrazone derivative is represented by III.



I II, R = O III, R = $NNHC_6H_5$ V IV

The phenylhydrazone (III) was hydrogenated in the presence of a platinum catalyst to give in 53% yield an inosamine, m.p. 239–241° (dec.). (*Anal.* Calcd. for $C_6H_{13}NO_5$: C, 40.22; H, 7.31; N, 7.82. Found: C, 40.41; H, 7.73; N, 7.84). This inosamine gave a hexaacetate, m.p. 277–278°, (*Anal.* Calcd. for $C_{18}H_{25}NO_{11}$: C, 50.11; H, 5.84; N, 3.25. Found: C, 50.35; H, 6.02; N, 3.30), and an N-benzylidene derivative, m.p. 209–211° (dec.). (*Anal.* Calcd. for $C_{13}H_{17}NO_5$: C, 58.41; H, 6.41; N, 5.24. Found: C, 58.77; H, 6.49; N, 5.12). This synthetic inosamine was identical with the inosamine isolated from antibiotic 1703-18B and which has been shown to be *neo*-inosamine-2 (V).[3,9] Additionally, the hexaacetates[9] and the N-benzylidene derivatives[9] from the two sources were identical.

The 3,4-dihydroxy-α-methylcinnamic acid amide of *neo*-inosamine-2 (VI) has been postulated as the



VI, R = R′ = H
VII, R = CH_3CO–, R′ = C_2H_5CO–

$C_{16}H_{21}NO_8$ degradation product of the antibiotic 1703-18B,[10] and additionally, it appears to be at least isomeric, and possibly identical, with a portion of the antibiotic hygromycin.[11]

(8) M. Maquenne, *Ann. chim. phys.*, [6] **12**, 101 (1887).

(9) A sample of the material from the antibiotic was kindly furnished for comparison by Dr. J. B. Patrick.

(10) J. B. Patrick, private communication.

(11) (a) R. L. Mann, R. M. Gale, and F. R. van Abeele, *Antibiotics and Chemotherapy*, **3**, 1279 (1953); (b) R. L. Mann and D. O. Woolf, Abstracts of the 130th Meeting of the American Chemical Society, Atlantic City, p. 26-D.

The synthesis of VI was accomplished in the following manner. The N-benzylidene derivative of *neo*-inosamine-2 was acetylated to yield its penta-*O*-acetyl derivative (79% yield), m.p. 217–219°. (*Anal.* Calcd. for $C_{23}H_{27}NO_{10}$: C, 57.86; H, 5.70; N, 2.93. Found: C, 57.61; H, 6.09; N, 3.10). Selective hydrolysis of the latter with hydrochloric acid in tetrahydrofuran gave in 73% yield penta-*O*-acetyl-*neo*-inosamine-2 hydrochloride, m.p. 185–187°. (*Anal.* Calcd. for $C_{16}H_{23}NO_{10}\cdot HCl$: C, 45.13; H, 5.68; N, 3.29. Found: C, 45.39; H, 6.04; N, 3.40). Condensation of the latter material with α-methyl-3,4-dipropionoxycinnamoyl chloride gave in 69% yield 1,3,4,5,6-penta-*O*-acetyl-2-deoxy-2-(α-methyl-3,4-dipropionoxycinnamido)-*neo*-inositol (VII), m.p. 157–160°. (*Anal.* Calcd. for $C_{32}H_{39}NO_{15}$: C, 56.71; H, 5.80; N, 2.07. Found: C, 56.83; H, 5.60; N, 2.16). De-*O*-acylation of VII with triethylamine in methanol gave VI (71% yield), m.p. 256–259° (dec.). (*Anal.* Calcd. for $C_{16}H_{21}NO_8$: C, 54.08; H, 5.96; N, 3.94. Found: C, 53.71; H, 6.09; N, 4.06). This material was identical with the $C_{16}H_{21}NO_8$ degradation product[9,10] of the antibiotic 1703-18B.

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RECEIVED OCTOBER 1, 1956

PARTITION COEFFICIENTS FROM GAS-LIQUID PARTITION CHROMATOGRAPHY

Sir:

The evaluation of heats and entropies of solution from gas–liquid partition chromatography has not been attempted in a systematic manner.[1] The method[2] by which results are presented in terms of a "corrected retention volume" is satisfactory if only ΔH is to be obtained, but if ΔS is also required, the study of the temperature variation of the partition coefficient (K) is the more straightforward method; where

$$K = \frac{\text{concn. of solute in stationary liquid phase}}{\text{concn. of solute in gas phase}} \quad (1)$$

both concentrations in g./ml. The partition coefficient so defined may be calculated from the zero-flow retention volume v_R^0 by the relation

$$K = \left[\frac{v_R^0}{\alpha X} - 1\right]\frac{\alpha}{\gamma} \quad (2)$$

where α = gas-space volume fraction of the column, γ = stationary liquid phase volume fraction of the column, X = total volume of the column.

This equation may be obtained from the results of James and Martin[3] or more simply by the following procedure, the principle of which is due to Glueckauf.[4] Let $f(c)$ = amount of solute contained

(1) Since this note was submitted a paper by Porter, Deal and Stross (THIS JOURNAL, **78**, 2999 (1956)) has appeared in which thermodynamic data are obtained in a systematic manner from GLP chromatography by a method analogous to the one described in this note.

(2) A. B. Littlewood, C. S. G. Phillips and D. T. Price, *J. Chem. Soc.*, 1480 (1955).

(3) A. T. James and A. J. P. Martin, "Proceedings of the International Congress on Analytical Chemistry," Heffer and Sons, Oxford, 1952, p. 359.

(4) E. Glueckauf, *Trans. Faraday Soc.*, **51**, 34 (1955).

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.

(5) D. W. Simpson and R. M. Wheaton, *Chem. Eng. Progress*, **50**, 45 (1954).

(6) A. K. Wiebe, *J. Phys. Chem.*, **60**, 685 (1956).

(7) M. R. Hoare and J. H. Purnell, *Trans. Faraday Soc.*, **52**, 222 (1956).

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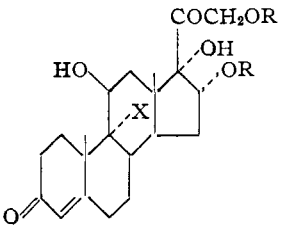
RECEIVED AUGUST 27, 1956

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

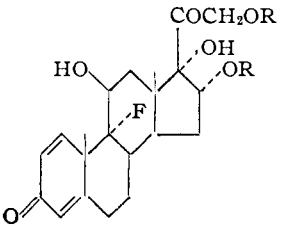
Sir:

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-

(1) Paper III, W. S. Allen and S. Bernstein, THIS JOURNAL, **78**, 1909 (1956).

(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.