benzoic acid derivatives varied from a 120- to 200-fold as compared to plasma (see Table V).

The discrepancy in the relative potency of plasma and Cholase to hydrolyze ACh could be explained partly by loss of potency in storage and partly by the different methods used. It is more difficult, however, to explain the relatively lower activity of Cholase against *p*-aminobenzoic acid esters in general, and the considerable variation of its activity against various members of this group of compounds (see Table V).

The possibilities to be considered include: (1) That more than one enzyme capable of hydrolyzing ACh is present in human plasma and that the activity of these different enzymes toward other esters hydrolyzed by human plasma is variable. It is furthermore conceivable that with the method of purification used in the preparation of Cholase relatively less of the fraction primarily responsible for the hydrolysis of *p*-aminobenzoic acid esters is extracted. (2) That there is only one plasma cholinesterase but the activity of this one enzyme toward various substrates is affected to a variable degree by the extraction process and/or storage.

An answer to these questions would have considerable theoretical and practical importance. It might clarify whether the variation in activity toward ACh and I observed in certain mammalian plasmas as compared to human plasma[14] is due to marked species variation in the properties of a single enzyme or the uneven distribution of several enzymes in different mammalian plasmas.

Of the halogen substituted compounds included in this study, III, IV and VIII have proved to be excellent as local anesthetic agents under clinical circumstances. III[15] was found to be about twice and IV and VIII[16] about four times as potent as I. Their activity was characterized by rapid onset, great intensity, and excellent penetrating capacity. Because of their relatively fast enzymatic hydrolysis rate in human plasma, the possibility for the accumulation of toxic concentrations in the organism is limited. Indeed, no systemic absorption reactions have been encountered with the clinical use of these halogen substituted local anesthetic agents.

(14) M. H. Aven, A. Light and F. F. Foldes, *Federation Proc.*, **12**, 299 (1953).

(15) F. F. Foldes and P. G. McNall, *Anesthesiology*, **13**, 287 (1952).

(16) F. F. Foldes, J. W. Covalincenzo and J. H. Birch, *Anesthesia and Analgesia*, in press.

PITTSBURGH, PA.

[CONTRIBUTION FROM THE ROLLIN H. STEVENS MEMORIAL LABORATORY OF THE DETROIT INSTITUTE OF CANCER RESEARCH]

The Preparation of Four 3,17β-Dihydroxyestrenes[1]

BY JOHN A. HARTMAN

RECEIVED APRIL 26, 1955

Preparations of the unsaturated alcohols derived from $\Delta^{5(10)}$-estrene-3-one, 19-nortestoster-one and the enoldiacetate of the latter are described.

The catalytic hydrogenation of estrone, estradiol and estriol has yielded mixtures of mono-, di- and triols, along with some incompletely saturated material.[2-5] The stereochemistry of the newly formed asymmetric centers is unknown with the exception that both estrone and estradiol give the same dihydroxyestrane, reported to be identical with a naturally occurring steroid found in human pregnancy urine.[6]

The partial reduction of estradiol by the Birch[7] method provides a convenient synthesis of two 17β-hydroxyestrene-3-ones, *i.e.*, the $\Delta^{5(10)}$-(I) and Δ^{4}-(II). The latter has been assigned the "normal" or anti configuration at C_{10} by Wilds on the basis of molecular rotation.[7] Since it may be converted into a $\Delta^{3,5}$-enolacetate (III)[8] the formation of three estrene diol epimer pairs (3α- and 3β-hydroxy) is possible with unsaturation at carbon five common to all, and the stereochemistry at C_{17} and C_{10} known.

Since we were primarily interested in obtaining the 3β-epimers for biological testing, conditions were selected on the assumption that any hydrogen attached to C_{10} would have qualitatively, and perhaps quantitatively, the same effect as an angular methyl group on reduction with complex hydrides. Thus the ketones I and II were reduced with lithium aluminum hydride[9] and the enol diacetate III was reduced with sodium borohydride.[10]

None of the crude reduction mixtures formed an insoluble fraction when treated with a warm saturated 95% ethanol solution of digitonin. Negative results with this test are not indicative of the absence of the 3β-alcohols and previous work has indicated the lack of digiton in precipitates in the completely saturated compounds.[3,6] However, Dirscherl reported that two different "hexahydro" derivatives of estrone formed insoluble digitonides.[3]

(1) This work was supported by institutional grants to the Detroit Institute of Cancer Research from the American Cancer Society, Inc., The American Cancer Society, Southeastern Michigan Division, and The Kresge Foundation. We also wish to thank the Schering Corporation for a gift of estradiol used to prepare the starting materials.

(2) A. Butenandt and U. Westphal, *Z. physiol. Chem.*, **223**, 147 (1934).

(3) W. Dirscherl, *ibid.*, **239**, 49 (1936).

(4) J. F. Danielli, G. M. Marrian and G. A. D. Haslewood, *Biochem. J.*, **27**, 311 (1933).

(5) R. E. Marker and E. Rohrmann, THIS JOURNAL, **60**, 2927 (1938).

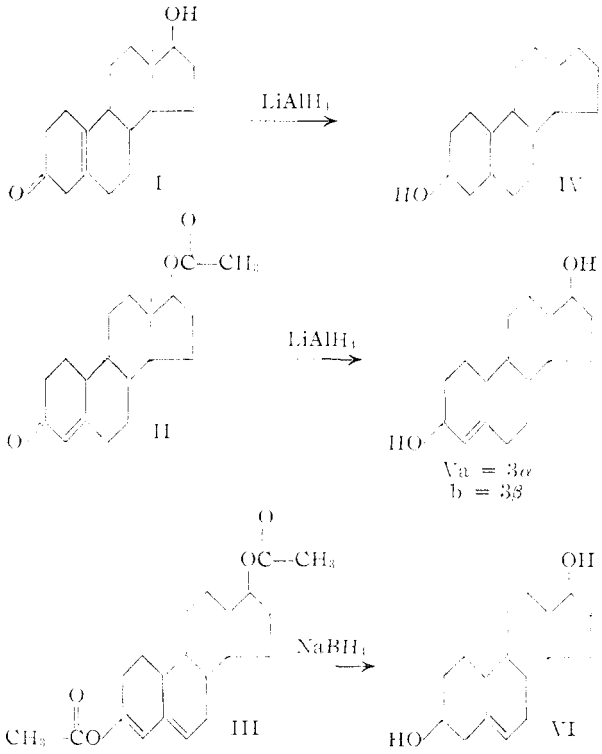
(6) R. E. Marker, E. Rohrmann, E. L. Wittle and E. J. Lawson, *ibid.*, **60**, 1901 (1938).

(7) A. J. Birch, *J. Chem. Soc.*, 2531 (1949); A. L. Wilds and N. A. Nelson, THIS JOURNAL, **75**, 5366 (1953); A superior preparation is described using the 3-methyl ether and lithium in liquid ammonia.

(8) A. S. Dreiding and J. A. Hartman, to be published.

(9) W. G. Dauben, R. A. Micheli and J. F. Eastham, THIS JOURNAL, **74**, 3852 (1952).

(10) B. Belleau and T. F. Gallagher, *ibid.*, **73**, 4458 (1951); W. G. Dauben and J. F. Eastham, *ibid.*, **73**, 4463 (1951).



The lithium aluminum hydride reduction of the β,γ-unsaturated ketone I produced a 77% yield of crystalline diol IV as well as some partially crystalline residue. In an attempt to determine whether or not this represented a single epimer or a 1:1 molecular compound of the 3α- and 3β-forms, it was converted into its diacetate and chromatographed on alumina. While it appeared that two different isomers were eluted when the solvent was changed, from petroleum ether–benzene (1:1) to benzene, the two samples had identical melting points and showed no depression on mixing. Further confirmation as to identity of the two was afforded by their equal optical rotations at identical concentrations. Retention of a high rotation and differences in melting points from the compounds derived from II indicated that isomerization of I → II did not precede reduction of the carbonyl group.

An attempted catalytic hydrogenation of the diol IV or its diacetate was unsuccessful, only starting material being recovered.

The α,β-unsaturated ketone II was reduced, as its 17-acetate, with lithium aluminum hydride and gave a crude crystalline diol V in 86% yield which could not be fractionally crystallized. On conversion to the diacetate and chromatography from alumina, the two epimers could be separated. The 3α-isomer was eluted first to the extent of 25% and the 3β-form followed closely in a 55% yield. Tentative configurational assignments were made on the basis of comparisons of the molecular rotations in the analogous compounds in the Δ^4-cholestene-3-ol series,[11] *i.e.*, the 3α-form having the higher positive specific rotation.

Catalytic hydrogenation of the $3\beta,17\beta$-diacetate gave mostly a product whose behavior on chromatography, elemental analysis and infrared spectrum indicated that one acetoxy group had been removed. Another product isolated was a saturated diacetate of unknown configuration at C_5 and whose melting point differs by 20° from those derived from human pregnancy urine.[5,12]

Saponification of the unsaturated diacetates gave the epimeric pair of diol V(a and b). The 3β-form Vb retained water of crystallization and after drying at 100° *in vacuo* partially decomposed giving both a broad melting point and an unsatisfactory analysis.

The sodium borohydride reduction of the enol diacetate III gave what appeared to be a single diol VI which could be directly crystallized to the extent of 69% as a monohydrate and is tentatively assigned the 3β-configuration. In one experiment the crude diol was acetylated and on chromatography it gave an 88% crude yield which was eluted like the diacetate of IV.

Acknowledgment.—This problem was suggested initially by Dr. Andre S. Dreiding and the author also wishes to thank Dr. Carl Djerassi for a consultation in the preparation of the manuscript.

Experimental[13]

$3\beta,17\beta$-Dihydroxy-$\Delta^{5(10)}$-estrene (IV).—A solution of 0.50 g. of 17β-hydroxy-$\Delta^{5(10)}$-estrene-3-one[7] (I) in 25 cc. of benzene was added dropwise, over a period of five minutes, to a stirred solution of 1.2 g. of lithium aluminum hydride in 100 cc. of dry ether. After one hour the excess hydride was decomposed with ethyl acetate and the alumina complexed with 75 cc. of 25% aqueous Rochelle salt. A light emulsion was broken with a few drops of 10% hydrochloric acid and after separation the aqueous layer was extracted with benzene and then ether. The combined organic solutions were washed with water, saturated sodium bicarbonate, saturated sodium chloride, dried over magnesium sulfate and concentrated. The colorless residual solid was boiled with methylene chloride which appeared to selectively dissolve one component. However, upon filtration the insoluble material, 0.11 g. (22%), m.p. 195–197°, showed no mixture melting point depression with the diol obtained from the chilled filtrate, m.p. 197–200°, wt. 0.22 g. (44%). A second crop weighed 0.057 g. (11%), m.p. 184–196°. Evaporation of the mother liquor to dryness gave a partially crystalline mixture, 0.15 g., which was used in an unsuccessful attempt to prepare the diene.

The three crystalline crops were combined and recrystallized from methylene chloride and then 95% ethanol to give cubes, m.p. 208–209°. An analytical sample was crystallized from methanol to give diamond shaped prisms, m.p. 208.0–209.4°, $[\alpha]^{26}D$ +122.5°, MD +348 (*c* 1.02, chf.).

Anal. Calcd. for $C_{18}H_{28}O_2$: C, 78.21; H, 10.21. Found: C, 77.82; H, 10.24.

An attempted catalytic hydrogenation at atmospheric pressure in methanol with Adams catalyst gave only starting material, m.p. 204–209°, alone and when mixed with the starting material.

The diacetate of IV was prepared from 60 mg. (m.p. 203–209°) with 1 cc. of acetic anhydride and 2 cc. of dry pyridine at room temperature. After three hours the volatile solvents were removed *in vacuo* and the tan gum taken up in *ca.* 1 cc. of benzene and chromatographed on 2.8 g. of

(11) L. F. Fieser and M. Fieser, "Natural Products Related to Phenanthrene," Reinhold Publishing Corp., New York, N. Y., Third Edition, 1949, p. 216.

(12) Under these conditions, Δ^4-cholestene-3-ol is reported to yield coprostanol, ref. 11, p. 239. It would not seem advisable to assign these reduction products the A/B *cis* configuration in the absence of other isomers for comparison of optical rotations.

(13) The melting points of the analytical samples were taken on uncalibrated Anschütz thermometers, all others are not corrected. The infrared spectra were recorded by a Perkin-Elmer model 21 instrument with a 5% solution in chloroform. Analyses by Micro Tech Laboratories, Skokie, Ill.

alumina prepared with petroleum ether. Elution with the same solvent (3 × 10 cc.) returned no material. Petroleum ether–benzene (1:1), three 10-cc. portions, gave 34 mg. of a colorless solid which after two crystallizations from petroleum ether gave **3β,17β-diacetoxy-Δ$^{5(10)}$-estrene** as long needles, m.p. 120.6–121.4°. Elution with benzene (three 10-cc. portions) gave an additional 32 mg. of a gum which on crystallization from petroleum ether gave plates, m.p. 120.4–121.6°. A mixed melting point was unchanged. Rotations of the two samples at equal concentrations showed no significant difference, $[\alpha]^{24}D$ +122.8°, M_D +442 (*c* 1.01, chf.); $\lambda_{max}^{CHCl_3}$ 3.44 (m), 5.80 (s), 6.95 (m), 7.32 (s), 7.98 (s), 8.64 (w), 8.93 (w), 9.05 (w), 9.16 (w), 9.60 (s), 9.72 (s), 10.02 (m), 10.70 (m), 11.02 (w), 11.56 (w) and 11.90 (w) μ.

Anal. Calcd. for $C_{22}H_{32}O_4$: C, 73.29; H, 8.95. Found: C, 72.93; H, 8.88.

An attempted hydrogenation, as with IV above, was unsuccessful.

Lithium Aluminum Hydride Reduction of 19-Nortestosterone 17-Acetate.—A solution containing 0.60 g. of II (m.p. 91–93°, λ_{max}^{alc} 240mμ ε 18,110)[8] in 25 cc. of dry ether was added dropwise with stirring over a period of five minutes to a refluxing solution of 1.5 g. of lithium aluminum hydride in 100 cc. of dry ether. After an additional 90 minutes of refluxing, the excess hydride was decomposed as described above. The colorless residual solid could not be crystallized from ethanol and crystallization from ether gave crops of needles with wide melting ranges indicating mixtures. A total of 0.455 g. (86%) was collected as crystalline material and an additional 0.035 g. (6%) remained as a gum.

All of the material was recombined and acetylated in 10 cc. of dry pyridine with 5 cc. of redistilled acetic anhydride for two hours at room temperature. After removal of the solvents *in vacuo* the acetylated product was taken up in 5 cc. of benzene and put onto a column of 22 g. of alumina prepared with petroleum ether. The first eleven fractions (25 cc. each) eluted with petroleum ether, petroleum ether–benzene (2:1) and (1:2) gave no material. Fractions 12–14, eluted with benzene gave colorless needles, 0.143 g. (20%), which after two recrystallizations from petroleum ether and then methanol gave **3α,17β-diacetoxy-Δ^4-estrene** as clusters of fine needles, m.p. 112–113.5°, $[\alpha]^{25}D$ +149.0°, M_D +535 (*c* 1.08, chf.); $\lambda_{max}^{CHCl_3}$ 3.42 (s), 3.50 (s), 5.80 (s), 6.02 (w), 6.88 (m), 6.96 (m), 7.28 (s), 8.00 (s), 8.58 (w), 8.68 (w), 8.92 (w), 9.60 (s), 9.80 (s), 10.56 (m), 10.92 (m), 11.16 (m), 11.40 (m), 11.56 (w) and 12.00 (w) μ.

Anal. Calcd. for $C_{22}H_{32}O_4$: C, 73.29; H, 8.95. Found: C, 73.19; H, 9.06.

Fraction 15, eluted with the same solvent, gave 0.038 g. (5.5%) of a gum which on crystallization from petroleum ether appeared to be a mixture of the 3α- and 3β-forms.

Fractions 16–20, eluted with benzene–ether (2:1), contained 0.376 g. (55%) of colorless needles. Recrystallization from ether–petroleum ether and then ether gave **3β,17β-diacetoxy-Δ^4-estrene** as short silky needles, m.p. 139.2–140.2°, $[\alpha]^{25}D$ −19.7, M_D −71.0 (*c* 1.045, chf.); $\lambda_{max}^{CHCl_3}$ 3.42 (s), 3.50 (m), 5.80 (s), 6.00 (w), 6.90 (m), 7.32 (s), 8.00 (s), 8.72 (w), 8.92 (w), 9.00 (w), 9.19 (w), 9.25 (w), 9.60 (s), 9.76 (s), 10.30 (m), 11.12 (m), 11.24 (m), 11.68 (w) and 12.00 (w) μ.

Anal. Calcd. for $C_{22}H_{32}O_4$: C, 73.29; H, 8.95. Found: C, 73.39; H, 8.95.

Further elution with ether gave no additional material.

3β,17β-Dihydroxy-Δ^4-estrene.—A mixture of 0.104 g. of the higher melting diacetate obtained in the preceding experiment in 5 cc. of methanol was saponified with 2 cc. of 10% potassium hydroxide under nitrogen for 16 hours at room temperature. Glacial acetic acid was added dropwise to *p*H 6 and dilution with water gave a non-filterable solid which was taken up in ether and upon concentration with acetone gave the diol Vb, as a monohydrate, as short needles, m.p. 168–170° with sintering at 145°, wt. 0.069 g. (81%). The analytical sample was recrystallized from ether to give a micro-crystalline monohydrate, m.p. 169.4–170.6° with sintering at 145° when immersed at 140°, $[\alpha]^{25}D$ +28.2, M_D +77.9 (*c* 1.06, chf.).

Anal. Calcd. for $C_{18}H_{28}O_2 \cdot H_2O$: C, 73.43; H, 10.27. Found: C, 73.29; H, 10.56. Calcd. for $C_{18}H_{28}O_2$: C, 78.21; H, 10.21. Found after drying at 110°: C, 77.13; H, 10.25.

3α,17β-Dihydroxy-Δ^4-estrene.—The 3α-form was obtained by the same procedure using the lower melting diacetate obtained above. The crude diol Va melted at 204–206°. The analytical sample was recrystallized from acetone to give fine silky needles, m.p. 206.0–207.8°, $[\alpha]^{24}D$ +124.2, M_D +343 (*c* 0.61, chf.).

Anal. Calcd. for $C_{18}H_{28}O_2$: C, 78.21; H, 10.21. Found: C, 78.34; H, 10.51.

The reaction was repeated on another 0.30-g. sample of II but the crude mixture of diols could not be separated using the pure epimers as seeds.

Hydrogenation of 3β,17β-Diacetoxy-Δ^4-estrene.—When 0.105 g. of the diacetate (m.p. 135–137°) in 5 cc. of methanol and 10 mg. of Adams catalyst was hydrogenated at atmospheric pressure the uptake ceased after six minutes. Separation from the catalyst by filtration and dilution with a few drops of water and chilling gave two crops of material having wide melting point ranges. After recombining in ether the material was taken to dryness and chromatographed on 4 g. of alumina prepared with petroleum ether. After 60 cc. of petroleum ether had been collected without material, one of the monoacetates was eluted with 20 cc. of petroleum ether–benzene (1:2), wt.. 43 mg. (49%), crystallization from petroleum ether gave one isomer of **17β-acetoxyestrane** as needles, m.p. 76.2–77.2°, $[\alpha]^{25}D$ +21°, M_D +63.8 (*c* 0.41 chf.); $\lambda_{max}^{CHCl_3}$ 3.44 (s), 3.52 (s), 5.80 (s), 6.92 (s), 7.30 (s), 7.96 (s), 8.92 (w), 9.62 (m), 9.76 (m), 10.22 (w) and 10.52 (w) μ.

Anal. Calcd. for $C_{20}H_{32}O_2$: C, 78.89; H, 10.60. Found: C, 78.89; H, 10.91.

Further elution with benzene (40 cc.), gave 23 mg. (22%) of a gum which on crystallization from petroleum ether gave one of the isomers of the **3β,17β-diacetoxyestrane**, as short needles, m.p. 140.2–141.8° (reported for two other isomers of unknown configuration[6] m.p. 160° and 170°), $[\alpha]^{25}D$ +4.4°, M_D +15.9 (*c* 0.45, chf.); $\lambda_{max}^{CHCl_3}$ 3.44 (s), 3.52 (s), 5.80 (s), 6.92 (m), 7.32 (s), 8.00 (s), 8.70 (w), 8.82 (w), 9.44 (m), 9.78 (s), 10.30 (m), 10.46 (m), 11.10 (w), 11.26 (w) and 12.02 (w) μ.

Anal. Calcd. for $C_{22}H_{34}O_4$: C, 72.89; H, 9.45. Found: C, 73.03; H, 9.61.

Sodium Borohydride Reduction of 3,17β-Diacetoxy-Δ^{3,5}-Estradiene (III) (Enol Diacetate of 19-Nortestosterone).—The reduction was carried out as described by Belleau and Gallagher[10] on 0.50 g. of III (m.p. 168–173°; λ_{max}^{alc} 234 mμ, ε 21,000)[8] and 1.1 g. of sodium borohydride in 25 cc. of 70% ethanol using 200 cc. of 95% ethanol to dissolve the steroid. After decomposition the material was extracted into ethyl acetate and then the organic layer washed with water, saturated sodium bicarbonate, saturated sodium chloride and dried over magnesium sulfate. Concentration to dryness gave 0.387 g. of a nearly colorless solid, m.p. 95–100°. Recrystallization from 95% ethanol gave **3β,17β-dihydroxy-Δ^5-estrene (VI)** as fine short needles, m.p. 152–157°, wt. 0.21 g. (55%). A second crop of the same melting point added 10% and the third crop, m.p. 117–130°, raised the crystalline yield to 69%.

In another experiment the crude diol from 0.50 g. of III was acetylated and chromatographed on 15 g. of alumina prepared with petroleum ether. Elution with the same solvent (4 25-cc. portions) and petroleum ether–benzene (1:1) gave no material. Benzene (six 25-cc. portions) slowly eluted 0.244 g. of a gum which gave fine short needles from petroleum ether, m.p. 130–131°. Further elution with benzene–ether (2:1) gave an additional 0.098 g. which on crystallization from petroleum ether gave short needles, m.p. 129–130°, alone and when mixed with the first eluted material. The analytical sample was crystallized from petroleum ether and a little ether to give **3β,17β-diacetoxy-Δ^5-estrene** as short needles, m.p. 136.2–137.0°, $[\alpha]^{26}D$ −18.7°, M_D −67.6 (*c* 0.96, chf.); $\lambda_{max}^{CHCl_3}$ 3.40 (s), 5.99 (s), 6.00 (w), 6.95 (m), 7.28 (m), 7.98 (s), 9.24 (m), 9.70 (s), 10.20 (w), 10.42 (w), 10.92 (w) and 12.10 (w) μ. Further elution with ether gave no additional material.

Anal. Calcd. for $C_{22}H_{32}O_4$: C, 73.29; H, 8.95. Found: C, 73.14; H, 9.07.

Saponification of the diacetate as above gave the crude diol VI, m.p. 161–162°, as a monohydrate. Crystalliza-

tion from ether gave the analytical sample of 3β,17β-dihydroxy-Δ⁵-estrene monohydrate as fine short needles, m.p. 165.0–165.8°, $[\alpha]^{25}D$ +11.7°, M_D +33.5 (*c* 1.0, chf.).

Anal. Calcd. for $C_{18}H_{28}O_2 \cdot H_2O$: C, 73.43; H, 10.27. Found: C, 73.29; H, 10.28.

DETROIT 1, MICHIGAN

[CONTRIBUTION FROM THE NATIONAL INSTITUTE OF ARTHRITIS AND METABOLIC DISEASES, NATIONAL INSTITUTES OF HEALTH]

1,5-Anhydro-D-altritol[1]

BY EMMANUEL ZISSIS AND NELSON K. RICHTMYER

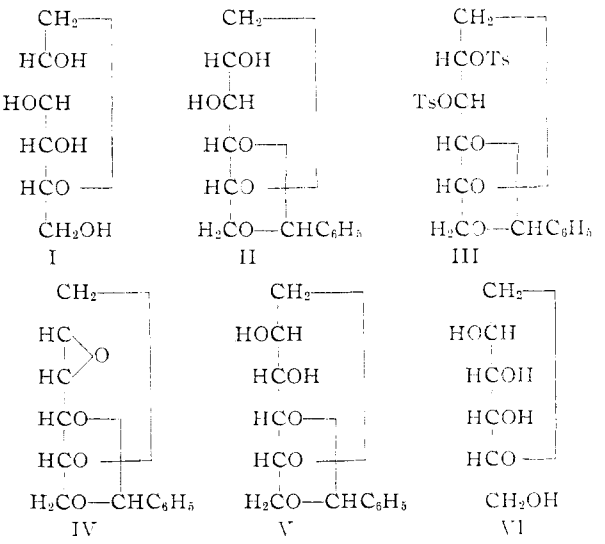
RECEIVED APRIL 29, 1955

1,5-Anhydro-D-glucitol (polygalitol) has been transformed, through a sequence of reactions involving carbon atoms 2 and 3, to the new 1,5-anhydro-D-altritol. The same anhydrohexitol has been obtained, though in very small yield, by lithium aluminum hydride reduction of the sirupy acetobromo compound prepared by the action of hydrogen bromide on α-D-altropyranose pentaacetate.

1,5-Anhydro-D-glucitol (polygalitol) and 1,5-anhydro-D-mannitol (styracitol) occur in nature and also have been synthesized by several methods in the laboratory; 1,5-anhydro-D-galactitol and 1,5-anhydro-D-talitol have been obtained synthetically.[2] Ness and Fletcher[3] have recently prepared both the 1,5-anhydro-D- and L-gulitols, the former by the lithium aluminum hydride reduction of sirupy tetra-*O*-acetyl-D-gulopyranosyl bromide and the latter by the similar reduction of tetra-*O*-benzoyl-β-D-fructopyranosyl bromide (with accompanying Walden inversion of configuration at carbon 2 of the fructose molecule).

We have synthesized the new 1,5-anhydro-D-altritol by application of the same sequence of reactions to 1,5-anhydro-D-glucitol (I) that had been effective earlier in the transformation of methyl α-D-glucopyranoside to methyl α-D-altropyranoside.[4] Thus, the first steps were the preparation of 1,5-anhydro-4,6-*O*-benzylidene-D-glucitol (II) and its 2,3-di-*O*-*p*-tolylsulfonyl derivative (III). Reaction of III with methanolic sodium methoxide in chloroform solution resulted in the elimination of both tosyl groups and the formation of an ethylene oxide ring; by analogy with the glycoside studies, the compound is presumed to have the D-allitol configuration IV. Hydrolytic opening of the ethylene oxide ring was accomplished by boiling with caustic potash and the resulting principal product was the desired 1,5-anhydro-4,6-*O*-benzylidene-D-altritol (V). Simple acid hydrolysis removed the benzylidene group and 1,5-anhydro-D-altritol (VI) was obtained as stout prisms melting at 127–129° and showing $[\alpha]^{20}D$ +28.4° in water.[5] The compound was characterized further through preparation of its crystalline tetraacetate and tetrabenzoate. Its reaction with periodate was in complete harmony with the 1,5-anhydro-D-hexitol structure.

We have synthesized 1,5-anhydro-D-altritol also by the procedure described by Ness, Fletcher and Hudson[2c,3]; the reaction of α-D-altropyranose pentaacetate[4c] with hydrogen bromide in glacial acetic acid, followed by reduction of the resulting sirup with lithium aluminum hydride, afforded the desired substance, which was identified through its crystalline tetrabenzoate. In contrast to the excellent yields of 1,5-anhydrohexitols obtained from the pentaacetates of D-glucose, D-mannose and L-rhamnose,[2c] our product was isolated in only a 1.5% over-all yield[6]; this was sufficient to confirm the structure assigned on the basis of its original synthesis, but hardly useful, without considerable improvement, for preparative work.



The rotations of the optically active polyhydric alcohols in water are relatively low; in ammonium molybdate and particularly in acidified molybdate solutions, however, these values may be greatly

(1) Presented in part before the Division of Carbohydrate Chemistry at the Cincinnati Meeting of the American Chemical Society, April 1, 1955.

(2) (a) See the review by L. F. Wiggins, *Advances in Carbohydrate Chem.*, **5**, 191 (1950); (b) H. G. Fletcher, Jr., L. H. Koehler and C. S. Hudson, THIS JOURNAL, **71**, 3679 (1949); (c) R. K. Ness, H. G. Fletcher, Jr., and C. S. Hudson, *ibid.*, **72**, 4547 (1950); (d) W. A. Bonner and J. E. Kahn, *ibid.*, **73**, 2241 (1951); W. A. Bonner, *ibid.*, **73**, 2659 (1951); (e) H. G. Fletcher, Jr., and H. W. Diehl, *ibid.*, **74**, 3175 (1952).

(3) R. K. Ness and H. G. Fletcher, Jr., *ibid.*, **75**, 2619 (1953).

(4) (a) G. J. Robertson and C. F. Griffith, *J. Chem. Soc.*, 1193 (1935); (b) G. J. Robertson and W. Whitehead, *ibid.*, 319 (1940); (c) N. K. Richtmyer and C. S. Hudson, THIS JOURNAL, **63**, 1727 (1941).

(5) In agreement with the generalization of H. G. Fletcher, Jr., and C. S. Hudson [THIS JOURNAL, **71**, 3682 (1949)], the molecular rotation of 1,5-anhydro-D-altritol (+4660) lies well between the molecular rotations of methyl α-D-altropyranoside (+24,430) [reference 4c] and methyl β-D-altropyranoside (−6410) [R.E. Reeves, THIS JOURNAL, **72**, 1499 (1950)]. See also ref. 3, footnote 14, for additional support of this generalization.

(6) *Cf.* ref. 3, in which 1,5-anhydro-4,6-*O*-benzylidene-D-gulitol was obtained in 10% yield from methyl α-D-gulopyranoside tetraacetate.