tered, washed with pentane and recrystallized from acetone, m. p. 96–98°.

Anal. Calcd. for $C_{20}H_{40}O_2$: C, 76.8; H, 12.6; mol. wt., 312. Found: C, 76.5; H, 12.4; mol. wt., 324.

The non-carbinol fraction after removal of the above product was sublimed in a high vacuum; a fraction was collected at 100° and crystallized from acetone, m. p. 63°. When mixed with a hydrocarbon isolated from pregnancy urines, it gave no depression in melting point.

Anal. Calcd. for $C_{28}H_{58}$: C, 85.3; H, 14.8; mol. wt., 394. Found: C, 85.3; H, 14.9; mol. wt., 384 (Rast).

Summary

Anterior pituitary extract has been partially studied. 1. The only sterol isolated was cholesterol. 2. Sodium stearate was found. 3. A water-soluble nitrogenous product, $C_8H_{10}N_4O_4$ or $C_{10}H_{13}N_5O_5$ has been isolated. 4. The hydrocarbon found in pregnancy urines also was obtained.

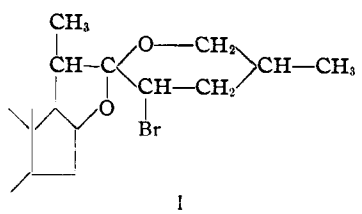
STATE COLLEGE, PENNA. RECEIVED JANUARY 24, 1941

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE]

Sterols. CXXI. Sapogenins. XLVIII. Bromosarsasapogenin and Bromodiosgenin[1]

BY RUSSELL E. MARKER, D. L. TURNER, ANTHONY C. SHABICA AND PAUL R. ULSHAFER

Marker and Rohrmann[1a] obtained tetrahydrosarsasapogenin by the Clemmensen reduction of bromosarsasapogenin, and sarsasapogenin by reduction with sodium in alcohol. This suggests that bromosarsasapogenin contains the ketal structure like sarsasapogenin. It seems probable that the bromine atom is adjacent to the potential carbonyl group at C-22 (I).



I

In order to determine the position of the bromine atom, we have oxidized the acetate of bromosarsasapogenin at 60° with chromic acid under the conditions employed for the oxidation of sarsasapogenin by Fieser and Jacobsen.[2] The only material in the neutral fraction from this oxidation was unchanged bromosarsasapogenin. The C-22 keto acid (3-hydroxy-16-keto-*bis-nor*-cholanic acid) of Marker and Rohrmann[3] was obtained in excellent yield from the acidic fraction. No intermediate oxidation products analogous to the C-22 lactone of Farmer and Kon[4] or to sarsasapogenoic acid and the C-27 neutral product of Fieser and Jacobsen,[2] were found. The isolation of the C-22 keto acid indicates that the bromine is at C-23 rather than at C-20, and the structure of the side-chain in the bromosapogenins may be represented by I.

Diosgenin acetate can be brominated at the double bond without affecting the side-chain.[5] We have found that it is also possible to brominate the side-chain; this gives 5,6,23-tribromodiosgenin acetate. When this is debrominated with potassium iodide in ethanol[6] the bromine in the side-chain is not affected and 23-bromodiosgenin acetate results.

Because of the relative stability of the brominated side-chain it is possible to carry out reactions depending on the presence of the nuclear double bond which fail with diosgenin acetate. Thus selenium dioxide, which attacks the sapogenin side-chain[1a] but does not react with bromosarsasapogenin,[1a] gives the reaction discovered by Rosenheim and Starling[7,8] in the case of bromodiosgenin acetate.

The oxidation of bromodiosgenin acetate under the conditions employed for the preparation of 7-keto compounds,[9] however, gives mostly acid products in addition to the expected 7-keto-bromodiosgenin acetate. The acid appears to be Δ^5-3-acetoxy-7,16-diketo-*bis-nor*-cholenic acid, although it gives only a monosemicarbazone instead of the expected disemicarbazone.

We wish to thank Parke, Davis and Company for their generous help.

(1) Original manuscript received August 12, 1940.
(1a) Marker and Rohrmann, THIS JOURNAL, 61, 846 (1939).
(2) Fieser and Jacobsen, *ibid.*, 60, 28, 2753 (1938).
(3) Marker and Rohrmann, *ibid.*, 61, 1285 (1939).
(4) Farmer and Kon, *J. Chem. Soc.*, 414 (1937).
(5) Tsukamoto, Ueno and Ohta, *J. Pharm. Soc., Japan*, 57, 9 (1937).
(6) Linnemann and von Zotta, *Ann.*, 192, 102 (1878).
(7) Rosenheim and Starling, *J. Chem. Soc.*, 377 (1937).
(8) Butenandt and Hausmann, *Ber.*, 70, 1154 (1937).
(9) Windaus, Lettré and Schenck, *Ann.*, 520, 98 (1935).

Experimental Part

3-Hydroxy-16-keto-*bis-nor*-cholanic Acid.—Bromosarsasapogenin acetate, 30 g., was oxidized at 60° as described by Fieser and Jacobsen.[9] The acidic fraction was taken up in ether and allowed to stand at room temperature for several days. The small white crystals were collected, washed with ether and finally crystallized from methanol to yield a product with m. p. 284–286° dec. This gave no depression in melting point when mixed with an authentic sample of 3-hydroxy-16-keto-*bis-nor*-cholanic acid of the same melting point, yield 6.4 g.

Anal. Calcd. for $C_{22}H_{34}O_4$: C, 72.9; H, 9.5. Found: C, 72.5; H, 9.4.

A solution of 100 mg. of the keto acid, 100 mg. of semicarbazide hydrochloride and 150 mg. of sodium acetate in 10 cc. of 95% ethanol and 2 cc. of water was refluxed on the steam-bath for one hour. The solution was then diluted with water and the white solid collected and crystallized from ether to give a product of m. p. 205–209° dec. which did not depress the m. p. of the semicarbazone of 3-hydroxy-16-keto-*bis-nor*-cholanic acid.

From the neutral fraction of the oxidation, 11.2 g. of unchanged bromosarsasapogenin was recovered.

Tribromodiosgenin Acetate.—A solution of bromine in acetic acid (2.19 cc. of 1.05 molar) was added at 20° to a solution of 1 g. of diosgenin acetate in 50 cc. of acetic acid. Then 1 drop of 48% hydrobromic acid was added and an additional 2.20 cc. of the bromine solution during ten minutes. The mixture was allowed to stand for thirty minutes; it was poured into water and filtered. The product was dried and recrystallized from acetone, m. p. 172° dec., yield 200 mg.

Anal. Calcd. for $C_{29}H_{43}O_4Br_3$: C, 50.1; H, 6.3. Found: C, 50.3; H, 6.2.

Bromodiosgenin Acetate.—A solution of 800 mg. of tribromodiosgenin acetate in 200 cc. of ethanol containing 350 mg. of potassium iodide was refluxed for two hours. The mixture was poured into water and extracted with ether. The ethereal solution was washed with sodium sulfite solution. Evaporation of the ether gave an oil which was crystallized from acetone, m. p. 177–179° dec.

Anal. Calcd. for $C_{29}H_{43}O_4Br$: C, 65.0; H, 8.1. Found: C, 64.9; H, 8.1.

Another preparation gave material of m. p. 197–198° dec. which did not depress the m. p. of the lower melting form.

Anal. Found: C, 65.1; H, 8.3.

To a solution of 500 mg. of bromodiosgenin acetate in 50 cc. of acetic acid was added 3 g. of zinc dust. The mixture was heated on a steam-bath overnight. The product was isolated in the usual manner and gave material, m. p. 199–200°, which did not depress the m. p. of diosgenin acetate (m. p. 199–200°). Hydrolysis gave material of m. p. 206–208° which did not depress the m. p. of diosgenin (m. p. 206–208°). Similar results were obtained by reduction with sodium in ethanol using the procedure previously described.[10]

Bromodiosgenin.—Bromodiosgenin acetate was hydrolyzed by heating on the steam-bath for ten minutes with 100 cc. of 1% ethanolic potassium hydroxide. The product was crystallized from pentane, m. p. 195° dec.

Anal. Calcd. for $C_{27}H_{41}O_3Br$: C, 65.7; H, 8.4. Found: C, 65.5; H, 8.6.

4-Hydroxybromodiosgenin.—Bromodiosgenin acetate (4 g.) was oxidized with selenious acid in exactly the same manner as was previously described for tetrahydrodiosgenin acetate.[11] The product was hydrolyzed with 1% ethanolic potassium hydroxide and crystallized from ether–pentane and then from acetone, m. p. 203 dec., yield 800 mg.

Anal. Calcd. for $C_{27}H_{41}O_4Br$: C, 63.6; H, 8.1. Found: C, 63.8; H, 8.2.

4-Dehydro-bromotigogenone.—Tribromodiosgenin acetate (1 g.) was hydrolyzed as described for the preparation of bromodiosgenin and the product which was noncrystalline was dissolved in 200 cc. of benzene and oxidized for forty minutes at 20° with a solution of 7 g. of chromic anhydride in 200 cc. of 85% acetic acid. The mixture was poured into water and the benzene layer was washed free of acetic acid and dried over magnesium sulfate. A solution of 5 g. of potassium iodide in 1 liter of ethanol was added and the mixture was refluxed for two hours. The product was isolated as described for bromodiosgenin acetate. It was recrystallized from ethyl acetate. It decomposes at 214° when heated rapidly.

Anal. Calcd. for $C_{27}H_{39}O_3Br$: C, 66.0; H, 8.0. Found: C, 65.5; H, 8.0.

7-Keto-bromodiosgenin Acetate.—To a solution of 15 g. of bromodiosgenin acetate in 750 cc. of acetic acid heated to 50° was added with stirring a solution of 12 g. of chromic anhydride in 200 cc. of 50% acetic acid, during five hours. The temperature was maintained at 50° for an additional five hours. Zinc dust was added to remove the excess chromic anhydride. The product was taken up in ether in the usual manner and washed free of acetic acid. Washing with sodium carbonate solution removed an acid fraction which was precipitated with dilute hydrochloric acid and taken up in ether. Evaporation of the ether gave an oil which was crystallized from ethyl acetate–pentane and then from ethyl acetate, m. p. 226–227°, yield 750 mg. It does not contain bromine.

Anal. Calcd. for $C_{24}H_{32}O_6$: C, 69.2; H, 7.8. Found: C, 69.0; H, 8.3.

When heated in aqueous ethanol with semicarbazide hydrochloride and potassium acetate it gave a monosemicarbazone which was crystallized from ethyl acetate and decomposes at 195° when heated rapidly.

Anal. Calcd. for $C_{25}H_{35}O_6N_3$: C, 63.4; H, 7.4. Found: C, 62.7; H, 7.5.

The neutral fraction from the oxidation of bromodiosgenin acetate remained an oil after evaporation of the ether. This was crystallized from ethyl acetate–methanol and then from pentane. It decomposes at 214° when heated rapidly. The yield of pure material was 400 mg.

Anal. Calcd. for $C_{29}H_{41}O_5Br$: C, 63.4; H, 7.5. Found: C, 63.2; H, 7.5.

Summary

1. The oxidation of bromosarsasapogenin ace-

(10) Marker and Rohrmann, THIS JOURNAL, **61**, 1921 (1939).

(11) Marker and Turner, *ibid.*, **63**, 767 (1941).

tate with chromic acid gave only the C-22 keto acid (3-hydroxy-16-keto-*bis-nor*-cholanic acid).

2. 23-Bromodiosgenin acetate has been prepared and various reaction products from this are described.

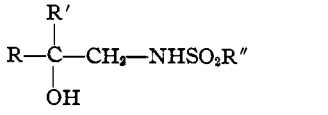
STATE COLLEGE, PENNA. RECEIVED JANUARY 27, 1941

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF ROCHESTER]

The Action of Acids on β-Hydroxysulfonamides

BY THEODORE L. CAIRNS AND JOHN H. FLETCHER

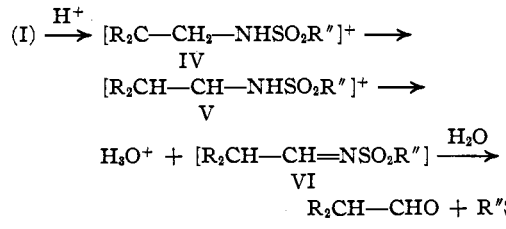
It is well known that prolonged treatment with acids will convert the benzenesulfonyl derivative of a primary amine to the corresponding amine.[1] However, it has been observed[2] that the sulfonamide of 1-amino-2-methyl-2-propanol (I) hydrolyzes in the presence of acid to give cleavage between the nitrogen and carbon atoms rather than between the nitrogen and sulfur. The products of this type of hydrolysis have been investigated, and a study has been made of the cleavage of the sulfonamides, (II) and (III), of 1-amino-2-propanol and ethanolamine.



(I) R, R′ = CH_3
(II) R = H, R′ = CH_3
(III) R, R′ = H
R″ = *p*-BrC_6H_4-

Treatment of (I) and (II) with sulfuric acid at 100° gave rise to *p*-bromobenzenesulfonamide, and isobutyraldehyde and propionaldehyde, respectively. The reaction took place with greater ease and in better yields in the case of the tertiary derivative (I) than with the secondary derivative (II). Under no conditions was it possible to bring about an analogous reaction with the primary derivative (III) which was always recovered unchanged. The reaction is evidently an acid catalyzed cleavage, since with other common dehydrating agents such as phosphorus pentoxide[2] and acetyl chloride entirely different products were obtained.

The cleavage to an aldehyde and the sulfonamide appears to be analogous to the pinacol rearrangement and the semi-pinacolinic deamination of 1,2-aminoalcohols.[3,4] A possible mechanism for the reaction is, as the first step, an acid catalyzed removal of the hydroxy group to give (IV), followed by a migration of hydrogen to (V). This compound then loses a proton from the nitrogen atom to produce (VI) which is hydrolyzed to give the aldehyde and the sulfonamide



It has also been observed that isobutylene oxide[5,6] and 1-amino-2-methyl-2-propanol give rise to isobutyraldehyde when treated with sulfuric acid at 100°.

Experimental[7]

1-Amino-2-methyl-2-propanol.[8]—To 567 g. of concd. aqueous ammonia was added 144 g. of isobutylene oxide and the mixture allowed to stand for two hours under a reflux condenser. Excess ammonia was removed by warming the homogeneous solution on a steam-bath. The mixture was then fractionated and the material coming over at 145–155° retained; yield, 52 g.

Methone Derivative of Isobutyraldehyde.[9,10]—To 50 cc. of water was added 2 cc. of isobutyraldehyde, a few drops of glacial acetic acid, and 50 cc. of alcohol containing 4 g. of methone (dimethyldihydroresorcinol). The mixture was shaken well and allowed to stand at room temperature for five days. The white crystals which were obtained were recrystallized from aqueous alcohol and dried at 65°, yield 3.2 g., m. p. 148–150°; the mixed melting point of this product with methone (m. p. 148–150°) was 128–138°.

Anal. Calcd. for $C_{20}H_{30}O_4$: C, 71.80; H, 9.05. Found: C, 71.95; H, 8.88.

Hydrolysis of 1-*p*-Bromobenzenesulfonamido-2-methyl-2-propanol.—This substance was prepared by the method of Adams and Cairns.[2]

(a) Five grams of 1-*p*-bromobenzenesulfonamido-2-methyl-2-propanol was added to 50 cc. of 50% sulfuric acid, and the mixture was steam distilled until 100 cc. of

(1) Shriner and Fuson, "Identification of Organic Compounds," John Wiley and Sons, New York, N. Y., 2nd ed., 1940, p. 49.
(2) Adams and Cairns, THIS JOURNAL, **61**, 2464 (1939).
(3) Gilman, "Organic Chemistry," John Wiley and Sons, New York, N. Y., Vol. I, 1938, p. 738-740.
(4) Cf. McKenzie, Roger and Wills, *J. Chem. Soc.*, 779 (1926).
(5) Breuer and Zincke, *Ann.*, **198**, 141 (1879).
(6) Tiffeneau, Orekhov and Levy, *Compt. rend.*, **179**, 977 (1924).
(7) Analyses by Mr. R. King.
(8) Krassuski, *Chem. Zentr.*, **79**, I, 1257 (1908).
(9) Vorländer, *Z. anal. Chem.*, **77**, 241 (1929).
(10) Weinberger, *Ind. Eng. Chem., Anal. Ed.*, **3**, 365 (1931).