dene bromide yielded ethylidene fluoride, and methylene iodide yielded methylene fluoride, both without stopping at the intermediate stage, CH_3CHFBr and CH_2IF, respectively; $CHBr_2CH_2Br$ yielded CHF_2CH_2Br and $CHFBrCH_2Br$ while acetylene tetrabromide yielded $CHFCHBr_2$ and $CHFBrCHBr_2$, with the difluorides predominant in both cases.

Finally experiments were undertaken to eliminate the use of iodine, which is expensive, cumbersome and causes rearrangements. Mercurous fluoride was treated with chlorine, quantitatively to yield mercuric fluorochloride. The operation is performed as follows.

Preparation of Mercuric Fluorochloride.—Mercurous fluoride is placed in a steel container equipped with a needle valve; this container can be made conveniently of pipe fittings. The container is evacuated, then connected to a chlorine tank; the valve is opened and chlorine admitted at the full pressure of the tank. The reaction is immediate and evolves a great deal of heat. After a few minutes, the chlorine pressure is released, the steel container opened, the mercury salt removed, crushed rapidly in a mortar and placed again in the container for a second chlorine treatment. This second treatment is needed because an appreciable amount of mercuric chloride is formed, which sublimes and builds a protective coat. The mercuric fluorochloride is a pale yellow, light powder, very distinct from the coarser mercurous fluoride. Its mercury content, which theoretically should be 78.65%, is generally found to be approximately 81% after the first chlorine treatment, and about 78.9% after the second treatment.

In its chemical effect, mercuric fluorochloride behaves as a mixture of mercuric fluoride and mercuric chloride. The reactions enumerated for the mixture of mercurous fluoride and iodine are performed with equal ease by this new salt. Some new side reactions are however apparent, as should be expected from the fact that the mixed salt acts like a mixture of salts; this is best illustrated by the fact that the reaction between ethylene dibromide and mercuric fluorochloride gives as main products ethylene fluoride and CH_2BrCH_2F, and as by-product CH_2ClCH_2Br, and consequently the residual mercury salt, after completion of the reaction, is almost pure mercuric bromide instead of mercuric chlorobromide.

Conclusion.—Mercurous fluoride is a good fluorinating agent when it acts on compounds possessing a relatively active bromine or iodine atom. When it is desired to fluorinate a substance with sluggish halogen atoms, the mercurous fluoride should be brought to the mercuric stage, which can be done by combining it with iodine or chlorine. These methods are only substitutes for the use of mercuric fluoride, which remains by far the most powerful and convenient fluorinating agent.

Summary

A preparation of mercurous fluoride is described; its uses and limitations as a fluorinating agent are discussed; its passage to the mercuric stage by means of chlorine or iodine is described. The advantages of a mercuric salt for fluorination purposes are again emphasized.

THE MIDGLEY FOUNDATION
COLUMBUS, OHIO

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Sterols. XXIX. Urane Derivatives

BY RUSSELL E. MARKER, OLIVER KAMM, THOMAS S. OAKWOOD, EUGENE L. WITTLE AND ELMER J. LAWSON

The preceding paper[1] in this series described the isolation, from pregnant mares' urine, of two triols. Both compounds form triacetates and these may be hydrolyzed to the original triols, which we designated as pregnanetriol-A and pregnanetriol-B. The latter compound is probably the pregnanetriol isolated by Haslewood, Marrian and Smith.[2]

We are now able to assign a tentative structure (I) to the triol-A. We have evidence that the parent hydrocarbon is an isomer of pregnane, probably differing from the latter only in respect to the configuration at C_9. For this new parent hydrocarbon we propose the name *urane*, thereby indicating its source, from urine. In the case of pregnanediol (II) the hydrogen atom at C_9 is considered to be *trans* to the methyl group at C_{10}, in accordance with the usual conventions regarding the configuration of the steroid nucleus.[3] Isomerism at C_9 has been found to occur in the case of sarmentogenin and digoxigenin[4] (formulas III and IV)

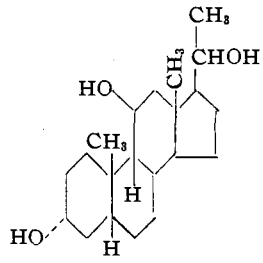
When uranetriol (triol-A) ($C_{21}H_{36}O_3$) is treated with chromic anhydride in acetic acid a derivative, $C_{21}H_{30}O_3$, is formed. This derivative does not form an acetate when heated with acetic anhydride; in fact, the original compound can

(1) Marker, Kamm, Crooks, Oakwood, Wittle and Lawson, THIS JOURNAL, **60**, 210 (1938).

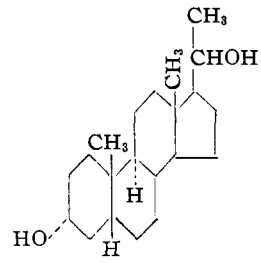
(2) Haslewood, Marrian and Smith, *Biochem. J.*, **28**, 1316 (1934).

(3) Strain, "The Sterols, Bile Acids, and Related Compounds," Chap. XV, p. 1255, in "Gilman, Treatise on Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1938, Vol. II.

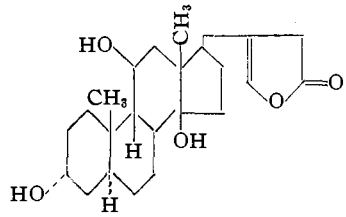
(4) Tschesche and Bohle, *Ber.*, **69**, 2497 (1936).



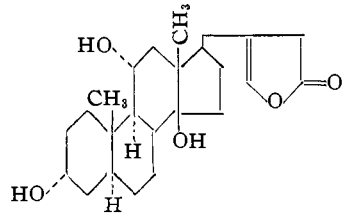
Uranetriol
(triol-A)
I



Pregnanediol
II



Sarmentogenin
III



Digoxigenin
IV

be recovered quantitatively from the acetic anhydride. The derivative, therefore, is a triketone. Uranetrione forms only a disemicarbazone and a *bis*-2,4-dinitrophenylhydrazone. This behavior suggests that the third ketone group is in a well-blocked position, and is comparable to the behavior of substances having a carbonyl group at C_{11}.[5-12] A similar lack of reactivity is not shown by ketone groups at any other known position in the steroid nucleus.[13-16]

(5) Fieser, "Chemistry of Natural Products Related to Phenanthrene," Reinhold Publishing Corp., New York, 1936, p. 283.

(6) Jacobs and Heidelberger, *J. Biol. Chem.*, **81**, 765 (1929).

(7) Although Jacobs and Heidelberger[6] assumed sarmentogenone to be a monoketone, Fieser, "Chemistry of Natural Products Related to Phenanthrene," 2nd Ed., 1936, p. 410, and Tschesche and Bohle[4] independently suggested that sarmentogenone was a diketone which formed only a monosemicarbazone.

(8) Smith, *J. Chem. Soc.*, 1305 (1935).

(9) Steiger and Reichstein, *Helv. Chim. Acta*, **20**, 817 (1937).

(10) Mason, Hoehn, McKenzie and Kendall, *J. Biol. Chem.*, **120**, 719 (1937).

(11) Reichstein, *Helv. Chim. Acta*, **19**, 29 (1937).

(12) Reichstein, *ibid.*, **19**, 402 (1936); Steiger and Reichstein, *ibid.*, **20**, 817 (1937).

(13) Wieland, Dane and Scholz, *Z. physiol. Chem.*, **211**, 261 (1932).

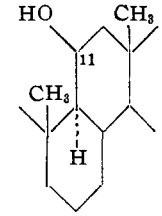
(14) Yamasaki and Kyogoku, *ibid.*, **233**, 29 (1935).

(15) Borsche and Hallwass, *Ber.*, **55**, 3324 (1922).

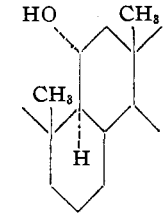
(16) Borsche and Hallwass, *ibid.*, **55**, 3318 (1922).

The formation of a triacetate from uranetriol raises an interesting point concerning the steric arrangement of the C_{11} —OH group in this and other natural products, and certain inferences may be presented based upon a study of models built to scale (Steiger's Organospheres). In the first place, comparison may be made between Reichstein's substance M (Δ^4-*allo*-pregnene-3,20-dione-11,17,21-triol), derived from the adrenal cortex[17-19] and digoxigenin.[8]

Reichstein's substance M has a C_{11} —OH group arranged in either the *cis* (A) or *trans* (B) position with respect to the two angular methyl groups at C_{10} and C_{13}, and this is true also of digoxigenin. Models show that a *cis* hydroxyl



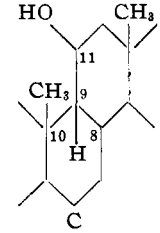
A
(Reichstein's M)



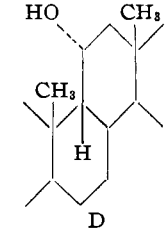
B
(Digoxigenin)

group should be considerably more hindered than a group *trans* to the angular methyl groups. A *trans* C_{11} —OH group appears to be only slightly more hindered than the C_{12} —OH group in cholic acid or desoxycholic acid, which is assumed to be *trans*. Since the C_{11} —OH group of Reichstein's M resists acylation while that of digoxigenin does not, Reichstein's M probably has the *cis* configuration (A) while digoxigenin is *trans* (B).

On the hypothesis advanced in the present paper, uranetriol has the same configuration at C_9 as sarmentogenin and, like this compound, has a C_{11} —OH group. The possible configurations are shown in C and D. The models show that the situation in this case is quite different



C
(Sarmentogenin,
Uranetriol)



D
(Dihydrodesoxysarmentogenin,
C_{11}-epimer of uranetriol)

(17) Reichstein, *Helv. Chim. Acta*, **20**, 978 (1937).

(18) Reichstein, *ibid.*, **19**, 979 (1936).

(19) Reichstein, *ibid.*, **20**, 953 (1937).

from the above, because of the bowing of the ring system about C_8–C_9. The C_{11} —OH group *cis* (C) to the angular methyl groups is less hindered than the hydroxyl in either A or B above, while the *trans* group (D) is greatly hindered. Since the C_{11} —OH group of sarmentogenin can be benzoylated, it probably has the *cis* configuration (C). Tschesche and Bohle[4] converted sarmentogenin into a desoxy ketone having a carbonyl group at C_{11} and converted this by catalytic hydrogenation with platinum oxide in acetic acid to a dihydrodesoxysarmentogenin (OH at C_{11}). The C_{11} —OH group in this compound resists benzoylation and therefore the configuration at C_{11} is probably epimeric to that of the natural compound and the hydroxyl group probably is *trans*, as in D.

Since the C_{11} —OH of uranetriol can be acetylated, this must be a *cis* group (C), comparable with that of sarmentogenin. However, catalytic reduction of uranetrione gives a new triol, epimeric in regard to the configuration of the hydroxyl groups at C_{11} and C_{20} with respect to triol-A. The formation of an epimeric C_{20} —OH group on hydrogenation of a ketone group at C_{20} has been observed before in the pregnane and *allo*-pregnane series,[20] and the formation of an epimeric C_{11} —OH group is comparable to the case of dihydrodesoxysarmentogenin.

We have found that when uranetrione is hydrogenated in acetic acid it readily adsorbs 2 moles of hydrogen and the third only slowly which is characteristic of C_{11} ketones. The new trihydroxy compound forms only a diacetate, when gently acetylated, as is shown by the fact that the latter is oxidized at room temperature by chromic anhydride to a mixture of keto acetates. This was converted to a mixture of products from which uranedione and 3,20-pregnanedione were isolated through steps which are shown in Fig. 3. Because insufficient material was at hand, no intermediates were isolated.

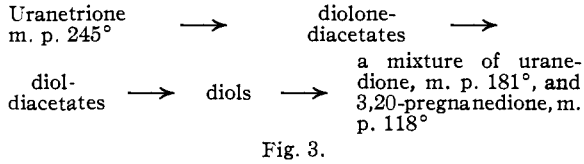


Fig. 3.

We do not know where the inversion of the urane nucleus into the pregnane nucleus occurred, but we feel that the uranedione, m. p. 181°, can hardly be a position isomer of pregnanedione, in view of the hindered position of the third ketone group of uranetrione, and in view of the fact that all the isomeric 3,20-pregnanediols do form diacetates.[21] The most likely step where the inversion may have occurred seems to be the Clemmensen reduction although it may also have occurred in the initial hydrogenation. This series of transformations indicates that two of the hydroxyl groups are located at C_3 and C_{20} in a ring system which differs from that of pregnane only in regard to the isomerism of an asymmetric center adjacent to a carbonyl group.

If the ketone group were at 4 or 6, *allo*-pregnane would be formed by the Clemmensen reduction, for 3,6-diketocholanic acid is very sensitive to acids and alkalies and gives *allo*-cholanic acid on reduction.[22] Isomerism at C_5 is excluded since then *allo*-pregnanedione would have been isolated.

Further evidence that the ring system is like that of pregnanedione in regard to C_5 is based on the ready formation of a urenetrione (a keto-progesterone). When uranetrione in acetic acid is treated at room temperature with bromine a bromo-uranetrione is formed. This readily loses hydrobromic acid on refluxing with pyridine to give a good yield of urenetrione. This behavior is comparable to that of other compounds of the coprostanone type, but is in sharp contrast to the behavior of compounds of the cholestanone type.[23] When uranetriol is boiled with sodium in xylene it yields a product giving very little precipitation with digitonin, thus supporting the coprostane configuration at C_5.

When uranetrione is reduced by the Clemmensen method, the parent hydrocarbon, urane, m. p. 128°, $C_{21}H_{36}$, is formed. This hydrocarbon is not identical with pregnane, m. p. 83.5°, nor with *allo*-pregnane, m. p. 84°. The latter, which has not been described before,[23a] depressed the melting point of pregnane. A small amount of

(20) Marker, Kamm, Wittle, Oakwood, Lawson and Laucius, THIS JOURNAL, **59**, 2291 (1937).

(21) This same dione also has been obtained by oxidizing the residue remaining after removing the triols from the original insoluble carbinol fraction, thus indicating that mares' pregnancy urine contains uranediol. Uranedione upon Clemmensen reduction gave the hydrocarbon urane which is identical with the hydrocarbon obtained from uranetrione.

(22) Windaus, *Ann.*, **447**, 233 (1926).

(23) Butenandt and Schmidt, *Ber.*, **67**, 1901 (1934); Butenandt and Mamoli, *ibid.*, **68**, 1850, 1854 (1935); Butenandt and Wolff, *ibid.*, **68**, 2091 (1935).

(23a) Quite recently *allo*-pregnane has been described also by Steiger and Reichstein [*Nature*, **141**, 202 (1938)].

another hydrocarbon, which we have been unable to obtain pure, was found in the mother liquors from the crystallization of urane. This may be pregnane, formed by isomerization of the uranetrione in the course of the reduction, just as the pregnanediol diacetate may have been formed in the course of the reduction of uranediolone diacetate. However, uranetrione, when boiled with an acetic acid–hydrochloric acid mixture, may be recovered unchanged. When uranetrione is boiled with alkali, only a portion of the uranetrione can be recovered. The reaction product is a mixture due to isomerization at asymmetric centers adjacent to carbonyl groups.

Summarizing these facts, the formation of a stereoisomer of pregnane by the reduction of uranetrione, the formation of a urenetrione, the action of alkali on uranetrione and the formation of two stereoisomeric diones (3,20-pregnanedione and uranedione) indicate that uranetriol is a 3,20-pregnanediol, isomerized at C_8, C_9, C_{14}, or C_{17}, and having a third hydroxyl group in the nucleus. Isomerization at C_{17} seems very unlikely since the known compounds of the iso series (isomeric at C_{17} to pregnane or *allo*-pregnane) melt much lower than the corresponding normal compounds. They are also very sensitive to acids; thus, iso-*allo*-pregnen-3-ol-20-one is largely isomerized to *allo*-pregnen-3-ol-20-one in the course of the formation of the acetate by refluxing with acetic anhydride.[24] We may conclude that the existence of urane compounds is not due to isomerism at C_{17}.

The third ketone group of uranetrione must be adjacent to an asymmetric carbon atom holding a hydrogen atom. Since this ketone group is also hindered, all positions except C_{11} for the ketone group seem eliminated on the basis of the arguments originally presented by Fieser[5] and recently summarized by Reichstein.[17-19] This eliminates isomerization with respect to C_8 and C_{14}. Therefore we feel that our experimental results can best be explained by placing the third hydroxyl group at C_{11}, and assuming that the configuration at C_9 is different from that found in pregnane. In accordance with the relative ease of acetate formation of the C_{11}—OH found in natural uranetriol as compared to the triol formed by the catalytic hydrogenation of uranetrione, we represent the former as *trans* to the methyl group at C_{10} and the latter as *cis* to this reference point.

Finally, we have found evidence that uranetriol occurs in human pregnancy urine. A neutral non-ketonic fraction from human pregnancy urine extracts was dissolved in ether, and some oil was precipitated by the addition of ligroin. This oil was oxidized with chromium trioxide in acetic acid at room temperature to give a mixture of ketones, isolated by the use of Girard's reagent. The solid ketonic mixture which precipitated when the Girard's reagent solution was acidified was fractionally distilled in a high vacuum to give *allo*-pregnanedione and uranetrione.

Experimental Part

Treatment of Uranetriol (Pregnanetriol-A) with Sodium in Xylene.—Uranetriol does not give a precipitate with alcoholic digitonin solution. Uranetriol (100 mg.) was refluxed with 1 g. of sodium in 50 cc. of xylene for eight hours. Amyl alcohol and water were added and the amyl alcohol–xylene layer was distilled. The residue gave only a slight precipitate with digitonin, thus indicating that uranetriol belongs to the coprostane series with regard to configuration at C_5.

Uranetrione.—One gram of uranetriol was dissolved in 25 cc. of acetic acid at room temperature and a solution of 1 g. of chromic trioxide in 10 cc. of 90% acetic acid was added. The mixture was allowed to stand for forty-five minutes, water was added, and the oxidation product was extracted with ether. (A liberal amount of ether must be used since the trione is sparingly soluble.) The ethereal solution was washed with sodium carbonate solution, the ether evaporated, and the residue crystallized from methanol and washed with a small amount of cold ether. After a final recrystallization from methanol it melted at 245° uncorr. When boiled with acetic anhydride no reaction occurs and the original trione is recovered unchanged.

Anal. Calcd. for $C_{21}H_{30}O_3$: C, 76.4; H, 9.1; mol. wt., 330. Found: C, 76.3; H, 9.2; mol. wt. (Rast), 319.

Uranetrione *bis*-2,4-Dinitrophenylhydrazone.—A mixture of 50 mg. of uranetrione, 120 mg. of 2,4-dinitrophenylhydrazine, and 10 cc. of alcohol was warmed for one minute, and 4 drops of hydrochloric acid added. The mixture was heated for forty minutes, cooled, and the precipitate filtered. The product was purified by leaching repeatedly with alcohol, and then melted at 236° with decomposition.

Anal. Calcd. for $C_{33}H_{38}O_9N_8$: C, 57.4; H, 5.5. Found: C, 57.5; H, 5.4.

Uranetrione Disemicarbazone.—A solution of 50 mg. of trione, 150 mg. of semicarbazide hydrochloride and 150 mg. of sodium acetate in 25 cc. of alcohol was refluxed for one hour, diluted with water and filtered. The solid was dissolved in alcohol, precipitated by the addition of water and cooling, and leached well with ether to give the disemicarbazone, which did not melt below 325°.

Anal. Calcd. for $C_{23}H_{36}O_3N_6$: C, 62.3; H, 8.2. Found: C, 62.5; H, 8.6.

(24) Butenandt and Fleischer, *Ber.*, **70**, 96 (1937). This article gives references to earlier papers on compounds of the iso series.

A solution of 100 mg. of uranetrione in 20 cc. of a mixture of equal volumes of glacial acetic acid and concd. hydrochloric acid was boiled gently under reflux for two hours. The solution turned pink. The solution was poured into a large volume of water and the solid was filtered and washed well with water; yield 90 mg.; m. p. 242–245°. A mixture of this product with uranetrione showed no depression in melting point.

A solution of 90 mg. of uranetrione in 50 cc. of 5% methyl alcoholic sodium hydroxide solution was boiled under reflux for two hours. Part of the alcohol was evaporated and the solution was then poured into a large volume of water and the solid was filtered and washed. No definite product could be obtained from the powder which remained.

Uranetrione from Human Pregnancy Urine.—The neutral fraction from an extract representing 3000 gallons of human pregnancy urine after removal of theelin, theelol, pregnanediols and *epi-allo*-pregnanolone was dissolved in a small amount of ether and 500 cc. of ligroin (b. p. 90°) was added. The ether was distilled and the product was allowed to stand overnight in a refrigerator. The ligroin layer was decanted from the oil which precipitated. The oil was dissolved in 600 cc. of acetic acid and over a one-hour period a solution of 50 g. of chromic trioxide in 200 cc. of 90% acetic acid was added at room temperature with stirring. It was stirred an additional hour, then water was added and the product was extracted with ether. The ethereal solution was washed with sodium carbonate solution, then evaporated to dryness. The residue was dissolved in 500 cc. of alcohol and refluxed for thirty minutes with 20 g. of Girard's reagent. Water was added and the product was extracted with ether. The aqueous layer was acidified with hydrochloric acid and heated on a steam-bath. The solid ketones which separated were filtered and distilled using a mercury pump. The fraction distilling from 120 to 150° consisted chiefly of *allo*-pregnanedione, m. p. 199°, which gave no depression in melting point when mixed with pure *allo*-pregnanedione. The fraction distilling from 170 to 200° was recrystallized from methanol several times and yielded a white crystalline product which melted at 241–244°. It gave no depression in melting point when mixed with an authentic sample of uranetrione (m. p. 242–245°).

Anal. Calcd. for $C_{21}H_{30}O_3$: C, 76.4; H, 9.1. Found: C, 76.5; H, 9.0.

Bromo-uranetrione.—A solution of 2 g. of uranetrione in 60 cc. of glacial acetic acid was cooled to 20° during the dropwise addition of 6.2 cc. of a 1.05 *M* solution of bromine in acetic acid. The bromine was decolorized immediately and hydrogen bromide was eliminated. After twenty minutes of standing, 200 cc. of water was added slowly to the acetic acid solution with shaking. A white precipitate appeared which was filtered and washed repeatedly with water. The substance was dried at 80° for four hours, after which treatment the weight was 2.3 g. and the melting point was 183°, dec. Crystallization from ethyl alcohol gave a melting point of 204°, dec.

Anal. Calcd. for $C_{21}H_{29}BrO_3$: C, 61.58; H, 7.13. Found: C, 61.98; H, 7.39.

Urenetrione.—A solution of 1.6 g. of bromo-uranetrione in 17 cc. of dry pyridine was boiled for three and one-half hours under a reflux condenser. At the end of this time, the solution was poured into an excess of dilute sulfuric acid and the solid which separated was extracted with ether. The ether solution was washed with water and evaporated to dryness. The brownish solid was taken up in alcohol, treated with boneblack, and recrystallized to a melting point of 196°.

Anal. Calcd. for $C_{21}H_{28}O_3$: C, 76.8; H, 8.6. Found: C, 76.9; H, 8.6.

This ketone exists in two forms, the second a hydrate which forms on crystallization from aqueous solvents, m. p. 219°.

Anal. Calcd. for $C_{21}H_{28}O_3 \cdot H_2O$: C, 72.9; H, 8.8. Found: C, 73.0; H, 9.0.

Pregnanedione and Uranedione from Uranetrione.—To a solution of 600 mg. of uranetrione in 100 cc. of glacial acetic acid was added 600 mg. of platinum oxide catalyst. The mixture was shaken with hydrogen under a pressure of 45 lb. (3 atm.) at 70° for two hours. The catalyst was filtered and the acetic acid evaporated. The solid remaining was refluxed for one-half hour with 25 cc. of acetic anhyride. The acetic anhydride was evaporated and the residue was dissolved in 10 cc. of acetic acid. To this was added a solution of 200 mg. of chromium trioxide in 5 cc. of 90% acetic acid. Oxidation took place immediately. After standing for one hour water was added and the product was extracted with ether. The ethereal solution was washed with sodium carbonate solution until free of acids. The ether was evaporated and the residue was boiled for two hours with amalgamated zinc and a mixture of hydrochloric and acetic acids. The product dissolved at once in this solution but upon boiling for five minutes came out as an oil, giving evidence of ketones being present and reduced. The product was extracted with ether and the ethereal solution washed with sodium carbonate solution. The ether was evaporated and the residue was refluxed for thirty minutes with an alcoholic potassium hydroxide solution. Water was added and the product was extracted with ether. The ether was evaporated and the residue was dissolved in 25 cc. of acetic acid. To this was added 500 mg. of chromium trioxide dissolved in 10 cc. of 90% acetic acid. It was let stand for thirty minutes and water was added. The product was extracted with ether, then distilled using a mercury vapor pump and collecting the fraction distilling from 120 to 150° (120 mg.). This was dissolved in acetone and a few drops of water was added. An oil separated which was recrystallized from methanol to give a product melting at 179°. This was a diketone and gave no depression in melting point when mixed with uranedione prepared by the oxidation of the residues of crystallization of the mixtures of crude triols. The major product (60 mg.) consisted of this diketone. Treated with acetic anhydride, it was recovered unchanged.

Anal. Calcd. for $C_{21}H_{32}O_2$: C, 79.7; H, 10.2. Found: C, 79.8; H, 10.2.

To the first acetone mother liquors was added a few drops more of water, precipitating an additional oil. This was removed and the filtrate was allowed to stand twenty-four hours in a refrigerator. Crystals appeared which were filtered off and recrystallized from 50% acetone.

This material melted at 118° and gave no depression when mixed with pregnanedione, m. p. 120°; yield 30 mg.

Anal. Calcd. for $C_{21}H_{32}O_2$: C, 79.7; H, 10.2. Found: C, 79.8; H, 10.1.

***allo*-Pregnane.**—Forty grams of 30-mesh C. P. zinc was covered with a 5% mercuric chloride solution and allowed to stand for fifteen minutes, and then the excess solution decanted, and the zinc washed twice with water. A solution of 1 g. of *allo*-pregnanedione in 100 cc. of acetic acid was added, then 100 cc. of C. P. hydrochloric acid and the mixture was refluxed gently. The hydrocarbon began to separate in about fifteen minutes. After the solution had been refluxed for three hours, it was cooled and extracted with pentane. The pentane extract was washed with sodium bicarbonate solution, and water, and evaporated. The residue was distilled in a high vacuum at 80–90°. The distillate was recrystallized from acetone. *allo*-Pregnane melts at 84°, and depresses the melting point of pregnane (m. p. 83.5°) to 52–60°.

Urane.—Urane was prepared from uranetrione by essentially the method used for the preparation of *allo*-pregnane from *allo*-pregnanedione. A mixture of 0.3 g. of uranetrione, 12 g. of amalgamated zinc, 30 cc. of acetic acid, and 30 cc. of hydrochloric acid was refluxed for five hours. The solution was cooled, extracted with pentane, and the pentane extract washed with sodium bicarbonate solution and water. After evaporating the pentane, the residue was crystallized repeatedly from acetone. There was obtained 60 mg. of pure urane, m. p. 128°, which depressed the melting point of *allo*-pregnane to 70°, and depressed the melting point of pregnane[25] to 55°. The mother liquors yielded 130 mg. of an impure crop, m. p. 95–112°. The mother liquors from this crop could not be crystallized. Urane gives no test for unsaturation with a solution of bromine in carbon tetrachloride.

Anal. Calcd. for $C_{21}H_{36}$: C, 87.4; H, 12.6. Found: C, 87.4; H, 12.5.

Uranedione.—When the filtrate from the crystallization of triols-A and -B was evaporated a yellow oil was obtained. This oil was dissolved in acetic acid, cooled to 20° and oxidized with an equal weight of chromium trioxide in 90% acetic acid by mixing the solutions at 20° and allowing them to stand at this temperature for one hour. The solution was then diluted with water, extracted with ether and the ethereal solution, after washing with water and sodium carbonate solution, was evaporated to dryness. The residue, after crystallization from ethyl alcohol, was found to be a mixture of uranetrione and uranedione which could be separated by crystallization from ethyl alcohol and methyl alcohol to yield uranedione, m. p. 182°.

This compound gave a depression in melting point when mixed with uranetrione (245°) and was recovered unchanged when refluxed with acetic anhydride. It gave a depression in melting point when mixed with *allo*-pregnanedione.

Anal. Calcd. for $C_{21}H_{32}O_2$: C, 79.4; H, 10.0. Found: C, 79.5; H, 10.2.

The Reduction of Uranedione.—To 4 g. of zinc previously amalgamated with a mercuric chloride solution was added a solution of 100 mg. of uranedione, 10 cc. of acetic acid and 10 cc. of concd. hydrochloric acid. The solution was refluxed gently for five hours and the solid which had separated was extracted with pentane and washed with water and sodium carbonate solution. Evaporation of the pentane and crystallization of the remaining solid gave 70 mg. of urane, m. p. 120–123°, which gave no depression on admixture with urane, m. p. 128°, from uranetrione. Recrystallization from acetone gave 40 mg., m. p. 127–128°.

We wish to acknowledge the assistance of Dr. George H. Fleming, who has performed all of the microanalyses reported in this paper.

Summary

A new sterol derivative, $C_{21}H_{36}O_3$, has been isolated from the neutral fraction of mares' pregnancy urine extract. It is a triol but differs from the compound previously reported by Haslewood, Marrian and Smith. Preliminary investigation indicates that the new compound possesses hydroxyl groups on carbon atoms 3, 11 and 20 and that the nuclear structure differs from pregnane probably due to asymmetry at C_9. The name urane is proposed for the new parent hydrocarbon and uranetriol for the new triol.

Uranetriol upon oxidation yields uranetrione which, however, possesses only two reactive carbonyl groups. Bromination of uranetrione followed by elimination of halogen acid yields urenetrione. Reduction of uranetrione by means of the Clemmensen reaction yields the hydrocarbon, urane.

Evidence has been obtained which indicates that mares' pregnancy urine contains a new diol belonging to the urane series and that uranetriol occurs also in human pregnancy urine. Reduction of the diketone by the Clemmensen method gave the same hydrocarbon as the trione.

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