The dependence of the rate of exchange on the pressure (Table III) is explained readily with reaction (5) being the rate determining step. In the pressure range of the present experiments the concentration of ethylene in the adsorption layer does not increase proportionally to the pressure. Since the rate determining step is the dissociation of ethylene, the relative rate of exchange will decrease with increasing pressure.

Summary

The interaction of heavy hydrogen and ethylene has been investigated on platinized platinum foil at pressures of 10–100 mm. in the temperature range 0–236°. It is shown that two reactions occur: hydrogenation according to $C_2H_4 + D_2 = C_2H_4D_2$ and exchange according to $C_2H_4 + D_2 = C_2H_3D + HD$. In the temperature range 0–150° the hydrogenation has a temperature coefficient higher than unity corresponding to an energy of activation of 10 kcal. Above 150° the temperature coefficient is smaller than unity. A comparison of the hydrogenation with the ortho-para-conversion of H_2 and D_2 and with the reaction $H_2 + D_2 \rightleftarrows 2HD$ shows that in the lower temperature range the rate determining step is the activation of hydrogen molecules which involves the loosening of the bond between their two atoms.

The temperature coefficient of the exchange reaction is larger than that of the hydrogenation and corresponds to an energy of activation of 22 kcal. The rate-determining step of the exchange reaction is the reaction $C_2H_4 \longrightarrow C_2H_3 + H$. It is shown that the temperature coefficient of the hydrogenation above 150° is not due, as was hitherto assumed, to the desorption of ethylene, but to the shifting of the equilibrium $C_2H_4 \rightleftarrows C_2H_3 + H$ toward the right-hand side owing to the high temperature coefficient of the rate determining step.

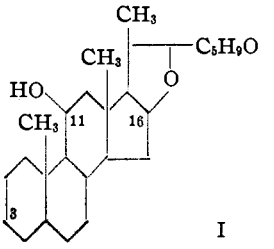
JERUSALEM, PALESTINE RECEIVED SEPTEMBER 22, 1937

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

Sarsasapogenin. I. An Investigation of the Side Chain

BY LOUIS F. FIESER AND ROBERT P. JACOBSEN[1]

This investigation of the comparatively readily available sapogenin from sarsaparilla root was undertaken partly in the hope of gaining a further insight into the nature of the terminal portion of the side chain characteristic of the steroid sapogenins and partly with the idea that it might be possible to degrade the compound into physiologically active substances of the sex hormone type. At the time the work was undertaken Jacobs and Simpson[2] had established the principal outlines of the structure of the aglycone and the tentative formula I,[3] or the alternate formula[2d] with the oxidic bridge extending to C_{15} instead of C_{16}, was uncertain only with respect to the point just mentioned and the location of the nuclear secondary hydroxyl group. Askew, Farmer and Kon[4] subsequently reported surface film measurements which could not be reconciled with the view[2c] that



I

the hydroxyl group is situated at C_{11} in ring C, and from their results, and from certain other inferences, they concluded that the group in question probably is located either at the characteristic sterol position (C_3) or at C_2. This gave further impetus to the degradative work which we had planned.

Our first line of attack was suggested by the observation of Jacobs and Simpson[2a] that on treatment with hydrochloric and acetic acids sarsasapogenin yields a volatile unsaturated ketone of the formula $C_8H_{14}O_3$. This ready elimination of the entire side chain in one step seemed to offer a promising route to a C_{19}-compound having a steroid ring system, but we were disappointed in

(1) Du Pont Research Fellow.

(2) (a) Jacobs and Simpson, *J. Biol. Chem.*, **105**, 501 (1934); (b) THIS JOURNAL, **56**, 1424 (1934); (c) Simpson and Jacobs, *J. Biol. Chem.*, **109**, 573 (1935); (d) *ibid.*, **110**, 565 (1935).

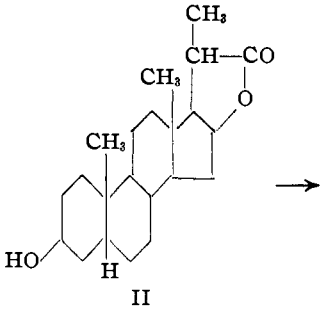
(3) Fieser, "Natural Products Related to Phenanthrene," 2d edition, Reinhold Publishing Corp., New York, 1937, pp. 336–337.

(4) Askew, Farmer and Kon, *J. Chem. Soc.*, 1399 (1936).

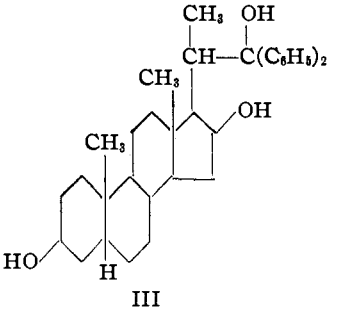
this expectation. The acid cleavage of sarsasapogenin acetate was investigated under a variety of conditions but the yield of the volatile ketone could not be raised above 17% of the theoretical amount and all attempts to isolate a nuclear fragment were unsuccessful. Uncrystallizable gums were encountered for the most part, and the small amounts of crystallizates isolated in some experiments seemed to have the original complement of carbon atoms and to be either identical or isomeric with the starting material. A slight improvement was noticed when sarsasapogenone was employed in place of the aglycone acetate, and the volatile ketone was obtained in 26% yield by refluxing this substance with acetic and hydrochloric acids. On treating sarsasapogenone with hydrobromic acid in chloroform at 100° for five hours, we isolated from the non-volatile fraction a crystalline product which was definitely characterized through the oxime as an isosarsasapogenone. Although the positive results are not very extensive, we are inclined to think that the action of acids on the steroid sapogenins consists in part in the cleavage of the side chain from the nucleus and in part in an isomerization, possibly by the opening of one or more oxidic rings which subsequent closure in a different manner.

We next investigated the controlled oxidation of sarsasapogenin acetate with chromic anhydride, hoping in this way to gain further information concerning the structure of the side chain and to find some more practical means of effecting its elimination. One oxidation product isolated from the mixture was characterized as the acetate of a hydroxylactone, $C_{22}H_{34}O_3$ (II, below). We had degraded this substance through the keto lactone to a desoxy lactone $C_{22}H_{34}O_2$, when our experiments in this direction were anticipated by Farmer and Kon.[5] These investigators had already prepared the desoxylactone and identified aetiobilianic acid as a product of its further degradation, thereby proving that sarsasapogenin belongs to the coprostane series and that the oxidic bridge is linked to ring D at position 16. Our experiments were therefore discontinued, and the report in the Experimental Part is limited to a record of the melting points observed for the compounds investigated; our results fully confirm those of Farmer and Kon.

A start was made on another degradation of the hydroxylactone. The free hydroxy compound, the probable structure of which is represented in formula II, on treatment in toluene solution with an excess of phenylmagnesium bromide gave a



II



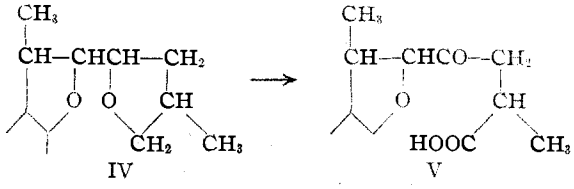
III

crystalline diphenyl carbinol derivative of the composition corresponding to III. On acetylation in cold pyridine this yielded a monoacetate without reëstablishment of an oxidic bridge, and consequently the compound offers promise of being convertible into perhydrocyclopentenophenanthrene derivatives of the type desired. This possibility is being investigated as supplies of the acetate lactone accumulate in the course of the preparation of a second oxidation product which presents certain points of special interest.

Farmer and Kon used a rather large amount of chromic anhydride in their oxidation experiments and obtained in addition to the acetate of the C_{22}-lactone (II) small amounts of a C_{27}-triketo acid and of a C_{20}-lactone. Using much less oxidizing agent, we obtained a mixture of unchanged sarsasapogenin acetate, the acetate of II, and a new substance melting at 190–191° and characterized as a hydroxy acid of the formula $C_{27}H_{42}O_5$, the acetyl group having been eliminated in the process of extracting the acidic fraction with alkali. In order to obtain a fair yield of this acid it seems necessary to operate in such a way that a considerable amount of the starting material remains unattacked. The C_{27}-acid forms an acetate, a methyl ester, and a methyl ester benzoate, and it is clearly analogous to the acid of the same composition (m. p. 221–222°) obtained by Tschesche

(5) Farmer and Kon, *J. Chem. Soc.*, 414 (1937).

and Hagedorn[6] as one of the oxidation products of tigogenin acetate. The acids probably differ only in the configuration at C_5, the one belonging to the coprostane and the other to the cholestane series, and we shall refer to them as sarsasapogenoic acid and tigogenoic acid. Tschesche and Hagedorn were inclined to the view that tigogenoic acid contains a γ-keto acid group (V) arising from the opening of a terminal five-membered oxidic ring in the side chain (IV), although the corresponding ester gave no nitrogen-containing reaction products with hydroxylamine or semicarbazide and failed to undergo catalytic hydrogenation.



From sarsasapogenoic acid we have obtained three reaction products of possible importance in determining the nature of the first recognized step in the oxidation of the acetylated sapogenins, and consequently in establishing the character of the sapogenin side chain. The results, however, are difficult of interpretation, and at the present time we wish merely to indicate the lines of investigation which are being followed in an effort to settle the points at issue. Most fully characterized is an acid obtained by heating sarsasapogenoic acid with alcoholic alkali and having the composition of the starting material less the elements of water. The substance forms a crystalline methyl ester acetate and it is unsaturated to permanganate. The new compound, which we designate anhydrosarsasapogenoic acid, has been converted into crystalline oxidation and hydrogenation products and other derivatives, but a description of these experiments will be deferred until further evidence is available concerning the structures. Sarsasapogenoic acid also has been converted by reaction with hydroxylamine in methyl alcoholic solution at 135° into a compound (m. p. 247°, dec.) of the composition $C_{27}H_{44}O_5N_2$, and a hydrogenation of the free acid in either acetic acid or alcohol has been accomplished with the production of an acidic substance (m. p. 174–180°) of the composition $C_{27}H_{42}O_4$. The further investigation of these compounds is in progress.

(6) Tschesche and Hagedorn, *Ber.*, **68**, 1412 (1935); **68**, 2247 (1935).

Experimental Part[7]

Sarsasapogenin.—The material used in this investigation was obtained from Mexican (sarsaparilla) root. This was kindly ground and extracted for us by E. R. Squibb and Sons under the supervision of Dr. J. M. Ort. 200 lb. of root giving 40.5 lb. of sirupy alcoholic extract. After some experience with the procedure described by Jacobs and Simpson[2a] for the isolation of sarsasapogenin from similar material, it was found expedient to modify their procedure in the following respects.

The sirup was put through the de-fatting operation in 2.3-kg. portions, each batch being dissolved in 2.5 liters of alcohol, agitated at 60° (steam-bath) with a Hershberg wire stirrer,[8] and extracted with two 2-liter portions of ligroin. The gummy glycoside subsequently precipitated from the alcoholic solution with ether, and separated by decanting the solvent, was dissolved in 2-kg. portions in water (4 liters per portion) and the solution was heated and stirred until the balance of the ether had been evaporated. Concentrated hydrochloric acid was then added to the aqueous solution at 80° as specified,[2a] and the remainder of the process, including crystallization of the crude aglycone from ammoniacal alcohol, was conducted according to Jacobs and Simpson. At this point we employed with advantage the method of purification introduced by Askew, Farmer and Kon[4]; the somewhat brown crude product was taken into benzene and the solution was filtered from suspended material and passed through a tower of activated alumina, which removed nearly all of the color. One crystallization from acetone or benzene–alcohol gave colorless sarsasapogenin melting at 194–197°; the yield from 200 lb. of root was 220 g. This material was sufficiently pure for conversion to the acetate, the product melting at 143–145° after one crystallization from chloroform–acetone. Satisfactory sarsasapogenone, m. p. 221–223°, was also obtained in 63% yield from the nearly pure sapogenin.

Acid Cleavage of the Side Chain.—In one series of experiments 2.5-g. portions of sarsasapogenin acetate in 50–150 cc. of a mixture of equal volumes of glacial acetic acid and concentrated hydrochloric acid were heated for one to two hours either at the boiling point or at 90°. The fragrant ketone ($C_8H_{14}O_3$) was separated from the mixture by steam distillation and converted into the semicarbazone as described by Jacobs and Simpson,[2a] the maximum yield of purified semicarbazone being 0.15 g. (13%). Under similar conditions Jacobs and Simpson[2a] obtained somewhat more of the same semicarbazone from gitogenin. Our crystallized material melted at 118–120° (J. and S., 119.5–120°). The residue from the steam distillation invariably contained halogen and consisted of a gum. After refluxing the residue with sodium butylate in butanol in one experiment, and with alcoholic potassium hydroxide in another, crystalline products, m. p. 175–176.5° and 189–193°, eventually were isolated. The melting point of the first crystallizate was depressed slightly by admixture of sarsasapogenin, while no depression was noted in the case of the higher melting product. In another experiment treatment of the residue with

(7) All melting points are corrected. Analyses by Mrs. G. M. Wellwood and Mrs. Verna R. Keevil.

(8) Hershberg, *Ind. Eng. Chem., Anal. Ed.*, **8**, 313 (1936).

acetone–methanol gave a crystalline product which when further purified melted constantly at 125–126.7° and had the composition of sarsasapogenin acetate (m. p. 143–145°) or an isomer.

Anal. Calcd. for $C_{29}H_{46}O_4$: C, 75.94; H, 10.11. Found: C, 75.85, 75.76; H, 10.05, 10.47.

While the melting point could not be raised to that of sarsasapogenin acetate, mixtures of the two substances melted at intermediate temperatures and the individuality of the substance is uncertain.

The results were similar using glacial acetic acid–48% hydrobromic acid. No fragrant ketone was produced when the acetate was heated with glacial acetic acid–15% sulfuric acid, in a chloroform solution saturated with hydrogen bromide, or with acetic anhydride–acetic acid saturated with dry hydrogen chloride. Treatment of sarsasapogenin acetate in boiling glacial acetic acid with a stream of dry hydrogen chloride gave a poor yield (3%) of the semicarbazone, as in the similar experiment of Jacobs and Simpson,[2a] and the addition of concentrated hydrochloric acid to the above mixture increased the yield to 17%. The further addition to the mixture of either amalgamated zinc or fused zinc chloride did not improve the result, although some volatile ketone was formed in each case. Treatment of the acetate with zinc chloride in glacial acetic acid solution without the use of hydrogen chloride led to a succession of color changes, but the acetate was largely recovered unchanged.

Sarsasapogenone seems to be attacked by acids somewhat more readily than the sapogenin acetate. On refluxing 1 g. of the ketone with 40 cc. of glacial acetic acid and 10 cc. of concentrated hydrochloric acid for two hours, we obtained 0.15 g. (26%) of the semicarbazone, m. p. 115–116°. In other experiments the sapogenone (1 g.) was heated with 48% hydrobromic acid (10–15 cc.) and chloroform (5 cc.) in a sealed tube at 100° for five to seven hours, and the product was worked up for the recovery of the nuclear fragment and without steam distillation. The washed chloroform extract deposited on evaporation a brown, crystalline product, about a third of which remained undissolved when triturated with ether–petroleum ether. The undissolved material after repeated crystallization from ether–petroleum ether and from acetone melted at 175.5–178°, and a sample obtained in a later experiment melted at 182–185°. The composition is that of the starting material, but there was a definite depression in the melting point of a mixture of the samples.

Anal. Calcd. for $C_{27}H_{42}O_3$: C, 78.21; H, 10.21. Found: C, 78.26; H, 10.00.

The purer sample of this **isosarsasapogenone** gave an **oxime** which crystallized from dilute methanol as needles, m. p. 176–179°, dec.

Anal. Calcd. for $C_{27}H_{43}O_3N$: C, 75.48; H, 10.39; N, 3.26. Found: C, 75.14; H, 9.80; N, 3.48.

The melting point is quite distinct from that (125–126°) of sarsasapogenone oxime. Isosarsasapogenone (0.2 g.) was refluxed for one hour with acetic acid (20 cc.) and concentrated hydrochloric acid (5 cc.) and on steam distillation of the mixture the presence of the ketone $C_8H_{14}O_3$ was apparent from the odor.

An attempt was made in the above experiment to isolate a pure product from the material readily extracted by ether–petroleum ether, but repeated crystallization from dilute propyl alcohol gave a substance, m. p. 166–170°, which did not appear to be entirely homogeneous.

Oxidation of Sarsasapogenin Acetate.—To 20 g. of the acetate in 400 cc. of glacial acetic acid (distilled over chromic anhydride) at 60–65° there was added dropwise with constant stirring a solution of 12 g. of chromic anhydride in 200 cc. of 80% acetic acid. The addition was conducted at a regular rate over a period of three and one-half to four hours, and after a total of five hours the mixture was allowed to cool and 5 cc. of alcohol was added to reduce the excess oxidizing agent. After removing most of the solvent by concentration at diminished pressure, water was added and the gummy reaction product was extracted with ether. The well washed ethereal solution was extracted with 3% sodium hydroxide and the alkaline extract, after being washed with ether, was warmed on the steam-bath for several minutes to expel ether and to complete the saponification of the acetate acid. On acidifying the cooled solution the crude **sarsasapogenoic acid** separated as a reddish solid, and crystallization from dilute acetone gave nearly colorless flat needles or leaves melting at 188–189°. The yields in four experiments conducted under very nearly identical conditions were 7.1 g., 4.4 g., 4.9 g. and 5.5 g. (or 28%). When the acid was extracted from the ethereal solution with sodium bicarbonate solution, or when the dilute alkaline extract was not heated prior to acidification, the crude acid separated from dilute acetone as an oil.

The ethereal solution remaining from the alkali extraction was washed with water and with saturated sodium chloride solution and the bulk of the ether was distilled. On adding acetone to the residual solution and cooling, a quantity of solid crystallized in the form of flat needles, m. p. 141–145°. This consisted principally of unchanged **sarsasapogenin acetate,** and the amount varied from 2.2–6.1 g., the larger amount referring to the experiment giving the best yield of the C_{27}-acid.

The acetate lactone ($C_{24}H_{36}O_4$) was obtained by concentrating the acetone–ether mother liquor and carefully diluting the solution with water. The material separated as fine colorless needles, m. p. 150–165°, in amounts varying from 0.5–1.5 g. A single crystallization from ether–hexane gave thin rectangular leaves melting at 184.5–185.5° (Farmer and Kon,[5] 184.5°). The analysis and saponification equivalent confirmed the formula assigned to the compound by Farmer and Kon. The remaining residue from the mother liquor consisted of a clear gum.

Reactions of the Hydroxy Lactone $C_{22}H_{34}O_3$(II).—Our sample of the hydroxylactone, obtained from the above acetate, melted at 193–196° (F. and K., 202°). In experiments paralleling those of Farmer and Kon, this was converted into the corresponding keto lactone, m. p. 182–185° (F. and K., 184.5°), and the desoxylactone $C_{22}H_{32}O_2$, m. p. 129.3–130.5° (F. and K., 133.5°, remelting at 128°). Analyses confirmed the formulas assigned.[5]

The diphenyl carbinol, III, was prepared by adding 900 mg. of the hydroxylactone in 20 cc. of toluene to the stirred Grignard reagent from 1.12 g. of magnesium and

7.3 g. of bromobenzene. About half of the ether was distilled and the remaining solution was refluxed on the steam-bath for three and one-half hours. After adding iced acid and removing the solvent with steam, the residual solid was precipitated twice from a small volume of ether with petroleum ether and a solution of the resulting material in ether–petroleum ether then slowly deposited 650 mg. of crystalline solid, m. p. 155–163°. By repeated crystallization from acetone–ether–hexane this was obtained in the form of monoclinic prisms, m. p. 162–164° (after drying in vacuum at 100°).

Anal. Calcd. for $C_{34}H_{46}O_3$: C, 81.23; H, 9.22. Found: C, 80.98; H, 9.23.

The **monoacetate of the diphenyl carbinol III** was prepared by allowing a solution of 200 mg. of the carbinol and 0.5 cc. of acetic anhydride in 3 cc. of pyridine to stand at 25–30° for three hours, adding 0.5 cc. more anhydride and allowing the mixture to stand overnight. The gummy solid which precipitated on dilution with water was taken up in ether–acetone. After concentrating the solution and adding hexane, there was obtained 135 mg. of long flat needles, m. p. 189–190°. Repeated crystallization from ether–hexane brought the melting point (of well dried material) to 192.5–193.5°.

Anal. Calcd. for $C_{36}H_{48}O_4$: C, 79.37; H, 8.88; sapon. equiv., 545. Found: C, 79.67; H, 9.00; sapon. equiv., 565.

Sarsasapogenoic Acid.—By further crystallization of the oxidation product (m. p. 188–189°, crude) from dilute acetone or from ether–hexane the melting point was raised to 190–191° (well dried). The acid is very soluble in acetone or alcohol, only moderately soluble in ether, and practically insoluble in hexane.

Anal. Calcd. for $C_{27}H_{42}O_5$: C, 72.61; H, 9.48; neut. equiv., 446. Found: C, 72.51; H, 9.45; neut. equiv., 452, 450.

The **acetate** was prepared by warming a mixture of the acid (0.2 g.), potassium acetate (0.07 g.) and acetic anhydride (4 cc.) for one-half hour. The product separated on adding water to the cooled solution, and the dried solid was crystallized from ether–hexane, using Norite. It crystallized as rectangular tablets (0.19 g.) melting at 155.5–156.5°, and the melting point was not raised on recrystallization.

Anal. Calcd. for $C_{29}H_{44}O_6$: C, 71.28; H, 9.08. Found: C, 71.51; H, 9.23.

The **methyl ester,** prepared by the action of diazomethane on a suspension of sarsasapogenoic acid (0.5 g.) in ether, crystallized from ether–hexane in the form of very fine needles, m. p. 130–131° (0.47 g.).

Anal. Calcd. for $C_{28}H_{44}O_5$: C, 73.00; H, 9.63. Found: C, 73.27; H, 9.64.

The **methyl ester benzoate** was obtained by heating a solution of the methyl ester (0.1 g.) and benzoyl chloride (1 cc.) in pyridine (5 cc.) for one-half hour on the steam-bath. After decomposing the excess acid chloride the product was extracted with ether, and after thorough washing with bicarbonate solution the solvent was evaporated. Crystallization from ether–hexane gave fine needles, m. p. 128.8–129.3°, or heavy prisms, m. p. 125.5–126.5°. A mixture of the two forms melted at 128.5–129.3°.

Anal. Calcd. for $C_{35}H_{48}O_6$: C, 74.43; H, 8.57. Found: C, 74.38; H, 8.47.

Anhydrosarsasapogenoic Acid.—Five grams of sarsasapogenoic acid (m. p. 188–189°) was boiled under reflux for two hours with a solution of 2 g. of sodium hydroxide in a mixture of 50 cc. of alcohol and 20 cc. of water. The solution was diluted with an equal volume of water, cooled, and made acid to Congo Red with dilute sulfuric acid. A yellow solid separated, which was collected, washed with water, dried in vacuum over sulfuric acid, powdered and triturated with ether. The ether-insoluble material amounted to 2.9–3.3 g. and melted in the range 210–220°. This was dissolved in hot chloroform, the solution was clarified with Norite, concentrated to a small volume and diluted with acetone. On cooling, the substance separated as a crusty deposit consisting of clusters of small, colorless prisms (1.5–1.9 g.), m. p. 239–243°, dec. One further crystallization from chloroform–acetone brought the melting point to 244–246°, dec., with slight preliminary sintering at 239°. The acid is nearly insoluble in ether or acetone, and more readily soluble in chloroform or alcohol. It rapidly decolorizes alkaline permanganate solution.

Anal. Calcd. for $C_{27}H_{40}O_4$: C, 75.66; H, 9.41; neut. equiv., 429. Found: C, 75.88; H, 9.50; neut. equiv., 437, 434.

Methyl Ester Acetate of Anhydrosarsasapogenoic Acid.—On adding excess diazomethane in ether to a suspension of 100 mg. of anhydrosarsasapogenoic acid in ether at 4° the solid gradually dissolved, and evaporation of the solution left a clear resin which could not be induced to crystallize. It was therefore taken up in 3 cc. of acetic anhydride containing 20 mg. of potassium acetate and the solution was refluxed for one-half hour. On decomposing the excess anhydride with water, a solid product was obtained, and on crystallization from aqueous methanol 75 mg. of fine needles, m. p. 145–146.5°, was obtained. After two further crystallizations the well-dried material melted at 147–148°. The substance is very soluble in alcohol or methanol and rapidly decolorizes alkaline permanganate.

Anal. Calcd. for $C_{30}H_{44}O_5$: C, 74.34; H, 9.15. Found: C, 74.17; H, 9.25.

Summary

In a first attempt to degrade sarsasapogenin to compounds of the sex hormone series the acid cleavage of the sapogenin acetate and of sarsasapogenone was investigated, but the yield of volatile C_8-ketone first isolated by Jacobs and Simpson was invariably low and it was found that the reaction consists in part in an isomerization, rather than cleavage.

The oxidation of sarsasapogenin acetate under very mild conditions has been found to yield, in addition to the acetate of a C_{22}-hydroxylactone already described by Farmer and Kon, an acid of

the composition $C_{27}H_{42}O_5$. This substance has yielded certain transformation products of an interesting and new type, and a partial report of the results is made in order to indicate the lines of further investigation which are being pursued in an effort to determine the character of the terminal part of the sapogenin side chain and to effect the degradation envisioned.

CONVERSE MEMORIAL LABORATORY
CAMBRIDGE, MASS. RECEIVED NOVEMBER 20, 1937

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING OF THE UNIVERSITY OF PENNSYLVANIA]

α-Sulfonyl and α,α-Disulfonyl Amides[1]

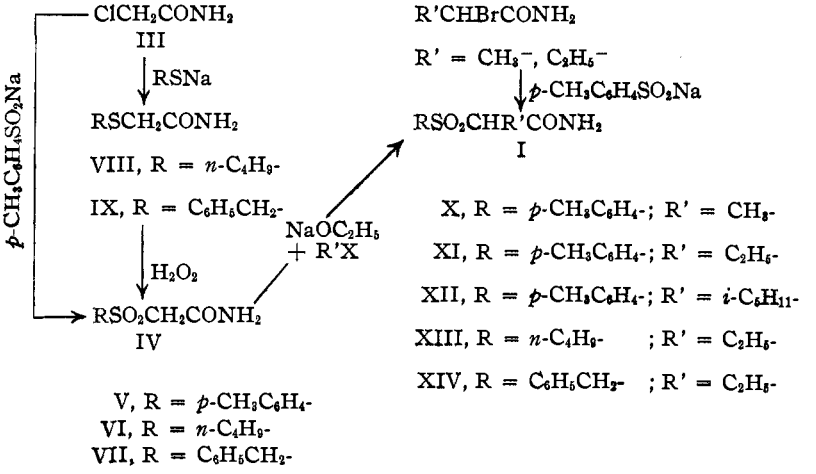
BY EDMOND L. D'OUVILLE[2] AND RALPH CONNOR

A study[3] of the lability of the methylene group in benzyl *p*-tolyl sulfone aroused our interest in other active methylene compounds containing sulfone groupings. The investigation reported here was undertaken in order to make available α-sulfonyl amides (I) and α,α-disulfonyl amides (II). In view of the fact that sulfone[4] and amide[5]

$RSO_2CHRCONH_2$ (I) $\qquad (RSO_2)_2CHCONH_2$ (II)

groups are present in certain hypnotics, the possibility that the presence of these two functions in the same molecule might give an enhanced physiological activity was the source of additional interest in these derivatives.

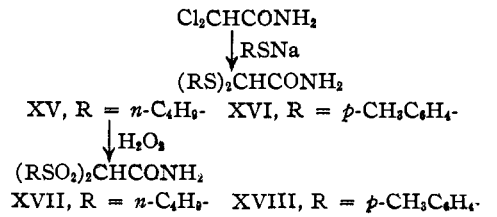
The α-sulfonyl amides (I) were prepared by the reaction of an α-halogenated amide with sodium *p*-toluenesulfinate or by the alkylation of α-sulfonylacetamides (IV). The latter were prepared from chloroacetamide and sodium *p*-toluenesulfinate[6] or from chloroacetamide and a sodium mercaptide, followed by oxidation. These reactions are summarized in the flow-sheet.



The products (I) were insoluble in cold alkali and in cold water. When the metathesis reactions were carried out under the optimum conditions described below, the different methods of synthesis of I were equally successful; the availability of the starting materials seemed to be the most important factor to be considered in selecting the method of synthesis of a given compound of this type.

The preparation of α,α-disulfonyl amides was accomplished by the reaction of dichloroacetamide with the appropriate sodium mercaptide, followed by oxidation.

The disulfonyl amides dissolved in a saturated solution of sodium carbonate and were reprecipitated by mineral acids. The alkaline hydrolysis of α,α-di-*p*-tolylsulfonylacetamide (XVIII) to give bis-*p*-tolylsulfonylmethane confirms the structure of the products and also suggests a possible practical method for the synthesis of disulfones.



(1) This communication is abstracted from a thesis submitted by Edmond L. d'Ouville in partial fulfilment of the requirements for the degree of Doctor of Philosophy at the University of Pennsylvania in June, 1937.

(2) Chemical Foundation Fellow.

(3) Connor, Fleming and Clayton, THIS JOURNAL, **58**, 1386 (1936).

(4) Baumann and Kast, *Z. physiol. Chem.*, **14**, 52 (1890).

(5) Volwiler and Tabern, THIS JOURNAL, **58**, 1352 (1936).

(6) Tröger and Hille, *J. prakt. Chem.*, [2] **71**, 201 (1905).