Anal. Calcd. for $C_{21}H_{25}O_4N_3$: C, 65.78; H, 6.57. Found: C, 66.23; H, 6.75.

Prednisolone-21-azide (IX). Reaction of prednisolone mesylate (650 mg.) and sodium azide (500 mg.) in 25 ml. of refluxing acetone for 3.5 hr. gave 441 mg. of product, after quenching in water. Recrystallization from acetone-water and finally methanol gave a sample with a decomposition point of 230–235°; $[\alpha]_D^{25}$ +214° (*c*, 0.4 in acetone). The infrared spectrum showed bands at 3.1–3.15, (shoulder 2.95–3.0), 4.82 (strong), 5.82, 6.07, 6.28 μ.

Anal. Calcd.: N, 10.90. Found: N, 10.76.

9α-Fluorohydrocortisone-21-mesylate (X). Methanesulfonyl chloride (1 ml.) was added to a stirred, cooled (5°) suspension of 3.4 g. (0.0089 mole) of 9α-fluorohydrocortisone in 40 ml. of pyridine. After 1.5 hr. of cooling and stirring, the mixture was poured into water. The mesylate was collected by filtration; washed with water, dried, and recrystallized from ethyl acetate; yield, 1.6 g., m.p. 212° dec.

9α-Fluoro-4-pregnene-11β,17α-diol-3,20-dione-21-azide (XI). A mixture of 1.39 g. (0.0030 mole) of 9α-fluorohydrocortisone-21-mesylate and 3.3 g. of sodium azide in 150 ml. of acetone was heated under reflux for 2 hr. The reaction mixture was cooled, poured into cold water, and aged 30 min. The azide was collected by filtration, washed with water, dried, and recrystallized from ethyl acetate as needles, m.p. 220–227° dec.; $[\alpha]_D^{26}$ +193° (*c*, 1.025 in acetone); yield, 1.08 g. (88%).

Anal. Calcd. for $C_{21}H_{28}N_3O_4F$: C, 62.20; H, 6.69; N, 10.36. Found: C, 62.25; H, 6.79; N, 10.56.

Acknowledgment. The authors are grateful to Mr. Robert Walker for the infrared spectra, to Mr. R. N. Boos for the microanalytical determinations, to Dr. C. A. Winter and his associates for the biological assays, and to Dr. Karl Folkers for his helpful suggestions.

RAHWAY, N. J.

[CONTRIBUTION FROM THE EASTERN REGIONAL RESEARCH LABORATORY[1]]

Steroidal Sapogenins. LXVII.[2] Preparation and Stereochemistry of 20α-Hydroxycyclopseudoneosapogenins[3a,b,c]

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Peracid oxidation of pseudotigogenin or pseudosmilagenin (I) gave the known 20α-hydroxycyclopseudoisosapogenins. Similar treatment of pseudosarsasapogenin (V) yielded a mixture of two 20α-hydroxy compounds (VIa and VIb) which differed in configuration at C-22. From the transformations occurring with VIa and VIb a mechanism can be formulated for the reactions of all pseudosapogenins with acids or peracids.

In previous publications we have shown that 20α-hydroxycyclopseudoisosapogenins along with side chain cleavage products could be obtained by chromium trioxide–acetic acid oxidation of the corresponding cyclopseudoisosapogenins[5a,b] whereas similar oxidation of cyclopseudoneosapogenins gave only side chain cleavage products.[5a,6] A more general route to 20α-hydroxy sapogenins involving peracid oxidation of pseudosapogenins seemed possible from the work of Callow and James[7] who obtained a 20α-hydroxy sapogenin by peracid treatment of pseudohecogenin. We first studied the oxidation of pseudotitogenin with peracids, since the structure of the expected product, 20α-hy-

(1) Eastern Utilization Research and Development Division, Agricultural Research Service, United States Department of Agriculture.

(2) Previous paper in this series, *Appl. Microbiol.*, 8, 345 (1960).

(3)(a) Trivial nomenclature used in this paper is in accordance with that recommended by L. F. and M. Fieser, *Steroids*, Reinhold Publishing Co., New York, 1959, p. 825; (b) Formal nomenclature for steroidal sapogenins is still unsettled. The recommendations for steroid sapogenins in Nomenclature Reports, *J. Am. Chem. Soc.*, November 5, 1960 are obsolete. We have adopted the Tentative Recommendations of the Steroid Nomenclature Sub-Committee, Appendix B, Information Bulletin No. 11, IUPAC (1960) using the system which designates the position of the oxygen atom of ring F with reference to the general plane of the ring, *i.e.* 22α-*O* or 22β-*O*; asymmetry at C-20 is then also designated by reference to the main ring system, *i.e.* 20αH or 20βH while that at C-25 utilizes the α_F, β_F system, 25α_F or 25β_F; (c) Abstracted from a dissertation by Henry A. Walens to be submitted to the Temple University Graduate Council in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

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(5)(a) M. E. Wall and H. A. Walens, *J. Am. Chem. Soc.*, 77, 5661 (1955); (b) M. E. Wall and H. A. Walens, *J. Am. Chem. Soc.*, 80, 1984 (1958).

(6) The side chain cleavage products undoubtedly arise from the chromic acid oxidation of the corresponding pseudosapogenins. R. K. Callow and co-workers, *J. Chem. Soc.*, 1966 (1955), have shown that in acidic media, cyclopseudosapogenins and pseudosapogenins exist in an equilibrium mixture. Since Wall and Serota, *J. Am. Chem. Soc.*, 79, 648 (1957) have demonstrated that cyclopseudoisosapogenins form pseudosapogenins more rapidly than the corresponding cyclopseudoneosapogenins, one would expect that the former should give more side chain cleavage products and less 20α-hydroxylation than the latter. Experimentally, the reverse situation is found. The Fiesers, ref. 3a, p. 828 have attempted to rationalize this situation by suggesting that the 20αH in cyclopseudoneosapogenins is shielded from chromic acid attack by the C-23 methylene group whereas the 20αH in cyclopseudoisosapogenins is in a less hindered environment.

(7) R. K. Callow and V. H. T. James, *Chem. & Ind. (London)*, 112 (1956).

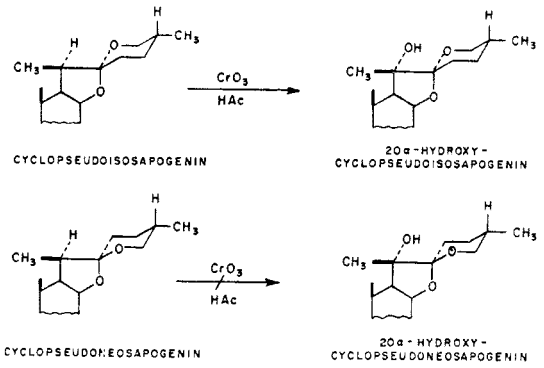

Figure 1

droxycyclopseudotigogenin acetate, was well established.[5b] Treatment of pseudotigogenin suspended in benzene with perbenzoic or peracetic acids at room temperature and for short time periods followed by acetylation gave 20α-hydroxycyclopseudotigogenin acetate in excellent yield. Similar peracetic oxidation of pseudosilagenin (I) followed by acetylation gave 80% yield of 20α-hydroxycyclopseudosmilagenin acetate (II). The structure and conformation of rings E and F in II

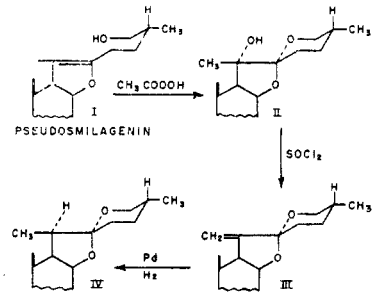

Figure 2A

should be identical with the spiroketal side chain of I since Marker demonstrated that tigogenin and smilagenin have identical spiroketal side chains and differ only in ring A/B fusion.[8] In addition, the infrared spectrum of II showed a strong band at 3520 cm.$^{-1}$ attributed to hydrogen bonding of the C_{20} α-hydroxyl group with the 22α-*O* atom,[5a,b] and the optical rotation was typically negative ($[\alpha]_D^{24}$ −72°) in accordance with values previously found for sapogenins with the 22α-*O* configuration.[9] Treatment of II with thionyl chloride in pyridine[5b] gave $\Delta^{20(21)}$-smilagenin acetate, III, in about 50% yield; characterized by analogy with the dehydration of 20α-hydroxycyclopseudotigogenin acetate and by the fact that the infrared spectrum of III shows absence of hydroxyl and presence of typical $=CH_2$ bands at 3077 and 1670 cm.$^{-1}$ [10] Hydrogenation of III in ether in the presence of palladium-carbon catalyst and absence of added acid gave a 75% yield of the known cyclopseudosmilagenin acetate, IV.[11]

Peracetic acid oxidation was then applied in a similar manner to pseudosarsasapogenin, (V), which differs only at C-25 from pseudosmilagenin, the former belonging to the $C_{25}\alpha_F H$ = 25L = neo-series, the latter to the $C_{25}\beta_F H$ = 25D = iso-series. In this case, application of the standard peracid treatment and acetylation gave a crystalline, hydroxylated cyclization product, which was a mixture, in approximately 70% yield. The infrared spectrum of the mixture showed presence of both nonbonded and hydrogen bonded OH bands at 3605 and 3520 cm.$^{-1}$, respectively. Chromatography cleanly separated this mixture into two nearly equal components. The first fraction eluted from the column, VIa, showed only hydrogen bonded hydroxyl and exhibited the negative optical rotation ($[\alpha]_D^{25}$ −82.5°) which we have previously associated with the 22α-*O* configuration.[9] The hydrogen bonding of the 20α-hydroxyl group with the 22α-*O* atom is in complete accord with the assigned structure of VIa which may be designated as 20α-hydroxy-22α-*O*-cyclopseudosarsasapogenin acetate. The structure of VIa was further confirmed as follows. Dehydration of VIa with thionyl chloride in pyridine gave $\Delta^{20,(21)}$-22α-*O*-sarsasapogenin acetate, VIIa, characterized by typical bands at 3080, 1670, and 895 cm.$^{-1}$ attributed to the vinyl grouping and by negative optical rotation. The unsaturated derivative VIIa was then converted to the starting material VIa by the route previously used in the tigogenin series.[5b] Treatment of VIIa with osmium textroxide gave a 20,21-dihydroxy sapogenin which on reaction with *p*-toluenesulfonyl chloride formed a 21-monotosylate. Reduction of the latter with lithium aluminum hydride and acetylation gave VIa in 25% over-all yield.[12]

The spiroketal side chain represented by formulation VIa is unique. Not only is VIa the first representative of a 20α-hydroxy sapogenin in the $25\alpha_F H$ series (25L) but the side chain is of a new type, as the combination $20\beta CH_3$, 22α-*O*, $25\alpha_F H$ has not been hitherto authenticated.[13] On treatment of VIa in methanol–acetic acid at room temperature a product identical to VIb, the more tenaciously adsorbed component of the chromatographed mixture, was obtained in almost quantitative yield. VIb was not affected by similar treatment. The infrared spectrum of VIb was charac-

(8) R. E. Marker and co-workers, *J. Am. Chem. Soc.*, **62**, 647, 1162 (1940).

(9) M. E. Wall, *Experientia*, **11**, 340 (1955); *cf.* also reference 3a, p. 826.

(10) L. J. Bellamy, *The Infrared Spectra of Complex Molecules*, John Wiley and Sons, Inc., 2nd ed., New York, 1959, p. 34.

(11) M. E. Wall, C. R. Eddy, and S. Serota, *J. Am. Chem. Soc.*, **77**, 1230 (1955).

(12) Because of limited quantity of VIIa available and because the sequence had been worked out in detail in the tigogenin series,[5b] the osmylation and tosylation steps were carried out without characterization of the reaction products other than the infrared spectrum.

(13) A formulation of this type was ascribed to cyclopseudosmilagenin by Ziegler, Rosen, and Shabica, *J. Am. Chem. Soc.*, **77**, 1223 (1955), but was later withdrawn on the basis of NMR evidence, *J. Am. Chem. Soc.*, **81**, 1687 (1959).

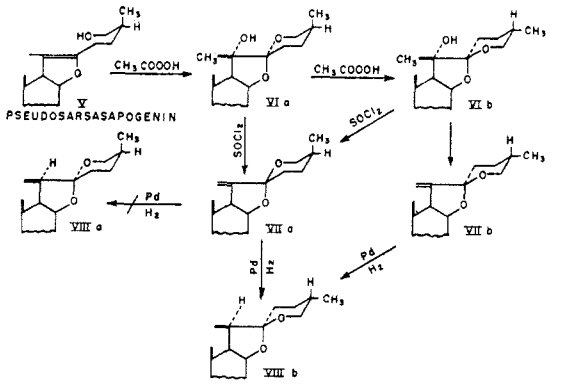

Figure 2B

terized by the presence of a nonhydrogen bonded hydroxyl band at 3605 cm.$^{-1}$ of much weaker intensity than was the case for the bonded hydroxyl band in VIa. The optical rotation of VIb was characterized by a positive value ($[\alpha]_D^{25}$ +32.4°) comparable to that noted for cyclopseudosarsasapogenin.[9] The lack of hydrogen bonding of the 20α-hydroxyl group and the positive optical rotation are consistent only with the formulation of VIb with the 22β-*O* configuration. The greater stability of VIb as compared with VIa is what would be expected from conformational analysis since in passing from VIa to VIb the axial methyl group in VIa becomes equatorial and the $C_{20}\beta CH_3$-$C_{23}\beta CH_2$ interaction in VIa should be of greater magnitude than the comparable $C_{20}\beta CH_3$-$C_{22}\beta$-O interaction in VIb.[14]

The conversion of VIa to VIb represents the first case of transformation of the 22α-*O* to the 22β-*O* configuration.[15] Dehydration of VIb in thionyl chloride–pyridine unexpectedly gave an unseparable mixture of VIIa and VIIb, $\Delta^{20,21}$-22β-*O*-sarsasapogenin acetate,[16] in approximately equal proportions.

In an attempt to prepare the hitherto unknown 22α-*O*-cyclopseudosarsasapogenin acetate, VIIIa, the unsaturated precursor VIIa was catalytically hydrogenated in ether in the absence of added acid using 5% palladium-charcoal catalyst. The product obtained in high yield was not VIIIa but its 22β-*O* isomer, the known cyclopseudosarsasapogenin acetate, VIIIb. The mixture of VIIa and VIIb also gave VIIIb as the sole hydrogenation product.

Attempts to conduct the hydrogenation of VIIa under conditions which would insure total absence of any acidic species[17] yielded only starting material. Consequently, we must assume that catalytic hydrogenation of the $\Delta^{20,(21)}$ double bond of VIIa requires the presence of at least traces of acid. Under these conditions we believe that the reaction sequence may be depicted as VIIa → [VIIIa] → VIIIb. The change in $C_{22}\alpha$-*O* configuration to $C_{22}\beta$-*O* is analogous to the previously discussed acid catalyzed conversion of VIa to VIb. In each case the $C_{22}\alpha$-*O* compound is represented by a spiroketal side chain formulation with the maximal possible unfavorable interactions.[18] In the 20α-hydroxy series, there is sufficient stabilization by the hydrogen bonding of the 20α-OH with the 22α-*O* to permit isolation of VIa. This is a striking effect of the stabilization of an inherently unstable structure by hydrogen bonding.[19] In the 20α-H series, compound VIIIa lacking hydrogen bonding stabilization cannot be isolated under our experimental conditions. Nevertheless, it should be regarded as an important intermediate in the conversion of VIIa to VIIIb or of pseudosarsasapogenin to VIIIb.

If one accepts the existence of VIIIa as a transitory form, a completely consistent mechanism can be formulated for the reactions of all pseudosapogenins, with acids or peracids as shown in Figures 3A and 3B. In every case the initial reaction product (shown on the left of Figures 3A and 3B) is formed by a rear-side electrophilic attack of the reagent on the C-20–C-22 double bond followed by a nonconcerted rear-side cyclization at C-22. The situation in the 20α-OH series is clear-cut. Initial attack of the electrophilic peracid reagent may lead directly to the 20α-hydroxy-22-carbonium ion as shown or a C_{20},C_{22}-α-oxide may be formed which

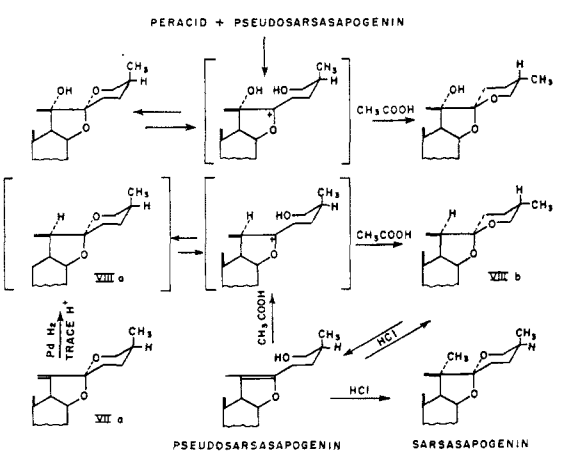

Figure 3A

(14) M. E. Wall and S. Serota, *J. Am. Chem. Soc.*, **79**, 6481 (1957); *cf.* also reference 3b, pp. 824–830. H. Hirschmann and F. B. Hirschmann, *Tetrahedron*, **3**, 243 (1958) give an excellent discussion of this subject.

(15) The only other case involving a change in C-22 configuration occurs in conversion of cyclopseudosarsasapogenin. In this case hydrochloric acid catalysis is required, and the process involves not only an inversion from the 22β-*O* to the 22α-*O* configuration but a change in the C-20 configuration.

(16) This result was obtained repeatedly and is anomalous as VIIb would be expected to be more stable than VIIa.

(17) For example, the hydrogenation was conducted in ether containing a little pyridine or potassium hydroxide or with palladium–calcium carbonate as a catalyst.

(18) The Fiesers, ref. 3a, pp. 824–830 give an excellent discussion of this topic.

(19) M. E. Wall and S. Serota, *Tetrahedron*, **10**, 238 (1960) give another example of structure stabilization by hydrogen bonding in the pregnene series.

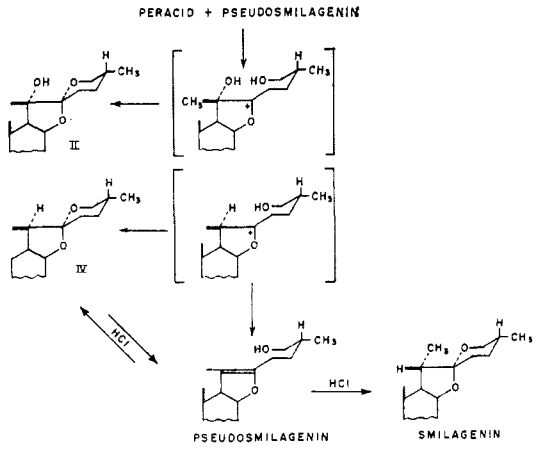

Figure 3B

then opens to the same C-22 carbonium ion.[20] Rear-side cyclization then takes place and in the $25\alpha_F$ series gives VIa, which then *via* the same carbonium ion, forms the more stable VIb. With the $25\beta_F$ series a similar process leads to II as the product of kinetic control and also, in this case, the product of thermodynamic control. The situation in regard to reaction of acids with pseudosapogenins is more complex because one of the key intermediates VIIIa cannot be isolated but must be inferred as discussed previously. With hydrogen ion concentrations of the order of acetic acid the route mirrors that discussed under the peracid reactions. However, the final products cyclopseudosmilagenin acetate, IV, and cyclopseudosarsasapogenin acetate, VIIIb, are still in a high energy state because of severe nonbonded interactions between the C-18 and C-21 methyl groups. With higher acid concentrations, of the order obtainable with hydrochloric acid, IV and VIIIb are smoothly converted at room temperature to smilagenin and sarsasapogenin, respectively,[11] by a route which must involve the corresponding pseudosapogenins[21] and requires frontal attack by the electrophilic reagent. The final stable products require a rear-side cyclization at C-22 as a front-side cyclization would again yield unstable compounds due to the strong interaction between the 21α methyl and the C-23 methylene group which occur in this conformation.[22]

(20) Direct cyclization at C-22 prior to the opening of the α-oxide is ruled out since the product by this mechanism should be the stable VIb and no VIa should be formed.

(21) Callow and co-workers, ref. 6, have found that in very dilute hydrochloric acid, solutions of IV and VIIIb exist in equilibrium with the corresponding pseudosapogenins.

(22) It should be noted that in the 20α-H or 20α-OH series the stable species always is associated with the presence of a C-25 equatorial methyl group and ring opening at C-22 occurs whenever the $C_{22}\alpha$-*O* is found in conjunction with a C-25 axial methyl group. In this series interactions between the $C_{21}\beta$ methyl group and the C-22 *O* or C-23 methylene are not decisive as far as ultimate stability is concerned. On the other hand in the $C_{20}\beta$H series (natural sapogenins) the last named interaction is decisive. Hirschmann and Hirschmann, *Tetrahedron*, **3**, 243 (1958) discuss in detail the reasons for the different behavior of the two series.

EXPERIMENTAL[23]

Preparation of 20α-hydroxytigogenin acetate. Pseudotigogenin, 1.0 g., was suspended in 50 ml. of benzene at room temperature. To the stirred suspension was added 2 ml. of 0.24*M* perbenzoic acid. The suspended material went into solution in 2 min., and the reaction was allowed to continue 15 min. longer. The solution was poured into water, and extracted with three 10-ml. portions of ether. The ether was washed with sodium bicarbonate solution, water, dried over sodium sulfate, and concentrated to dryness. The residue was acetylated with acetic anhydride in pyridine at room temperature, and after the usual work-up, the product was crystallized from methanol yielding 0.55 g., m.p. 232–234°, infrared spectrum identical to an authentic specimen of 20α-hydroxycyclopseudotigogenin acetate from the chromium trioxide oxidation of cyclopseudotigogenin acetate.[5b] Similar results were obtained by the action of peracetic acid.[24]

20α-Hydroxycyclopseudosmilagenin acetate (II). A suspension of 10.0 g. of pseudosmilagenin in 250 ml. of benzene was treated with 10 ml. of 30% peracetic acid in acetic acid at room temperature. The suspended material quickly passed into solution. After 10 min. the solution was diluted with water and treated as described above. The crude product was acetylated with acetic anhydride–pyridine (1:2) by heating for 50 min. on the steam bath. After standard work-up, 8.7 g. of II was obtained. The analytical sample was crystallized from methanol, m.p. 204–206°; $[\alpha]_D^{25}$ −72°; infrared spectrum shows strong band at 3520 cm.$^{-1}$ (bonded hydroxyl), 1735 cm.$^{-1}$ (acetate), and 982, 922, 870, 860 cm.$^{-1}$ (spiroketal bands).

Anal. Calcd. for $C_{29}H_{46}O_5$: C, 73.38; H, 9.77. Found: C, 73.04; H, 9.85.

$\Delta^{20(21)}$-Smilagenin acetate (III). To a solution of 1.0 g. of II in pyridine and cooled to 4° in an ice bath was added 0.1 ml. of thionyl chloride. After 10 min., the solution was poured into an ice-water mixture and extracted with ether in the manner described above. The residue was crystallized from methanol to give 0.5 g. of III. The analytical sample from methanol crystallization gave m.p. 208–210°, $[\alpha]_D^{25}$ −77°, the infrared spectrum showed absence of hydroxyl bands and presence of bands at 3077 and 1670 (= CH_2), 1734 (acetate), 985, 921, 903, and 863 cm.$^{-1}$ (spiroketal side chain).

Anal. Calcd. for $C_{29}H_{44}O_4$: C, 76.27; H, 9.71. Found: C, 76.31; H, 9.65.

Cyclopseudosmilagenin acetate (IV). To a solution of 0.1 g. of III in 20 ml. of ether was added 0.1 g. of 5% palladium on carbon. Hydrogenation was carried out at room temperature and atmospheric pressure for 16 hr. The catalyst was removed by filtration, and the solvent evaporated. The residue was pure IV identical to an authentic specimen.[11]

20α-Hydroxy-22α-O-cyclopseudosarsasapogenin acetate (VIa). To a suspension of 3.5 g. of pseudosarsasapogenin (V) in benzene was added 3.5 ml. of 30% peracetic acid in acetic acid. The suspended steroid dissolved in 2 min.; after 10 min. the solution was poured into 100 ml. of water and given the standard extraction and acetylation (steam bath). The infrared spectrum showed two hydroxyl bands at 3605 and 3520 cm.$^{-1}$, thus indicating the possible presence of a mix-

(23) Infrared spectra were carried out in carbon bisulfide solution, optical rotations in chloroform at 25° at concentrations of approximately 0.01 g./ml. We wish to thank S. Serota for the optical rotation data, C. S. Fenske for infrared spectra, and O. Panasiuk for carbon and hydrogen analyses.

(24) A commercial product containing 30% peracetic acid in acetic acid solution containing a small quantity of sulfuric acid.

ture. The product was taken up in petroleum ether (b.p. 60–68°) and chromatographed on Florisil.[25] Elution with petroleum ether (b.p. 60–68°) gave a product which after methanol crystallization weighed 1.2 g. and showed only a single band at 3520 cm.$^{-1}$ This product was designated as VIa. The analytical sample from methanol gave m.p. 177–182°; $[\alpha]_D^{25}$ −82.5°, infrared spectrum shows bands at 3520 (bonded hydroxyl), 1736 (acetate), 990, 925, and 855 cm.$^{-1}$ (spiroketal side chain).

Anal. Calcd. for $C_{29}H_{46}O_5$: C, 73.38; H, 9.77. Found: C, 73.39; H, 9.91.

20α-Hydroxy-22β-O-cyclopseudosarsasapogenin acetate (VIb). Elution of the Florisil chromatography column, described under VIa above, with benzene gave a small quantity of a mixture in the early fractions. Continued elution with benzene and then chloroform gave a product which on crystallization from petroleum ether (b.p. 60–68°) yielded 1.6 g. of VIb with only one hydroxyl band at 3605 cm.$^{-1}$ The analytical sample from petroleum ether (b.p. 60–68°) gave m.p. 192–197°; $[\alpha]_D^{25}$ + 32.4; infrared spectrum shows bands at 3605 (nonbonded hydroxyl), 1735 (acetate), 988, 925, 910, 872 cm.$^{-1}$ (spiroketal side chain).

Anal. Calcd. for $C_{29}H_{46}O_5$: C, 73.38; H, 9.77. Found: C, 73.08; H, 9.95.

Conversion of VIa *to* VIb. To a solution of 0.1 g. of VIa in 5 ml. of methanol was added 1 ml. of glacial acetic acid. The solution was allowed to stand overnight at room temperature. The product was isolated by ethereal extraction in the usual manner. Infrared examination showed an almost complete conversion to VIb; about 5–10% VIa was present. Similar treatment of VIb gave only unchanged starting material.

$\Delta^{20(21)}$-22α-O-Sarsasapogenin acetate (VIIa). To a solution of 1.2 g. of VIa in 30 ml. of pyridine cooled in an ice bath was added 0.07 ml. of thionyl chloride. The solution began to darken immediately. After 5 min., the reaction product was diluted with water and given the standard ether extraction, yielding 0.6 g. of crude VIIa. The analytical sample was crystallized from methanol, m.p. 181–183°; $[\alpha]_D^{25}$ −85°, infrared spectrum shows absence of hydroxyl bands at 3080, and presence of bands at 1670, 895 (C=CH_2), 1737 (acetate), 986, 922, 852 cm.$^{-1}$ (spiroketal side chain).

(25) Mention of trade names does not signify recommendation over similar equivalent products.

Anal. Calcd. for $C_{29}H_{44}O_4$: C, 76.27; H, 9.71. Found: C, 76.29; H, 9.80.

Conversion of VIIa *to* VIa. A solution of 0.2 g. of VIIa and 0.11 g. of osmium textroxide in 6 ml. of benzene and 0.14 ml. of pyridine was stored in the dark at room temperature for 12 days. Work-up proceeded as in reference 5b compound III. Infrared examination of the crude product showed two hydroxyl groups at 3620 and 3515 cm.$^{-1}$ consistent with formation of 20α, 21β-dihydroxy-22α-O-sarsasapogenin acetate. The total crude product was dissolved in 0.3 ml. of pyridine to which was added 0.15 g. of *p*-toluenesulfonyl chloride. The mixture was heated briefly on the steam bath and then allowed to stand overnight at room temperature. After standard work-up the residue was treated with lithium aluminum hydride and reacetylated as in reference 5b, conversion of III to I. Crystallization from methanol gave 0.04 g. of VIa.

Catalytic hydrogenation of VIIa. A sample of 0.1 g. of VIIa was catalytically hydrogenated in the presence of 5% palladium on charcoal as described under the preparation of IV. The product obtained was exclusively the known cyclopseudosarsasapogenin acetate,[11] VIIIb. Catalytic hydrogenation under similar conditions in the presence of a trace of pyridine (1 drop) gave only unchanged VIIa, as did substitution of palladium–calcium carbonate for palladium-charcoal catalyst (no pyridine added to ether).

Dehydration of VIb. A sample of 1.6 g. of VIb was dehydrated with 0.1 ml. of thionyl chloride as described under the preparation of VIIa. Crystallization of the crude product gave 0.7 g. of a crystalline mixture. The product could not be separated by chromatography on Florisil. Infrared analysis of the mixture showed absence of hydroxyl bands and presence of bands at 3080 and 1672 indicative of the presence of C=CH_2. Spiroketal bands were present but in a manner indicating that a mixture of two spiroketal types might be present. This was confirmed by $[\alpha]_D^{25}$ values ranging from −40° to −20° in various experiments indicating an approximately equal mixture of VIIa and the desired VIIb.

Hydrogenation of mixture of VIIa *and* VIIb. A sample of 0.1 g. of the above mixture was catalytically hydrogenated with 5% palladium charcoal in ether as described under the hydrogenation of VIIa. The exclusive product was cyclopseudosarsasapogenin acetate, VIIIb.

PHILADELPHIA 18, PA.

[CONTRIBUTION FROM THE NATIONAL INSTITUTE OF ARTHRITIS AND METABOLIC DISEASES, NATIONAL INSTITUTES OF HEALTH, PUBLIC HEALTH SERVICE, U. S. DEPARTMENT OF HEALTH, EDUCATION AND WELFARE]

Chemistry of the Spiroaminoketal Side Chain of Solasodine and Tomatidine. VI.[1] The Beckmann Rearrangement of the Oximino Derivatives

YOSHIO SATO AND NOBUO IKEKAWA[2]

Received July 12, 1961

The oximes of the pseudo derivative "B" of solasodine and tomatidine undergo an "abnormal" Beckmann rearrangement to yield amidonitriles which can be hydrolyzed to the respective 3β,16β-dihydroxy-5-bisnorcholenic and allobisnorcholanic 22 → 16-lactones. Alternatively, the lactones can be obtained from the rearrangement and hydrolysis of the 23-oximino alkamines.

In the course of our studies of the so-called pseudo derivatives "B" of solasodine,[3] IIa, and tomatidine,[4] IIb, obtained from the treatment of the respective steroidal alkaloids, Ia and Ib, with

(1) For previous papers of this series see *J. Org. Chem.*, 26, 1945 (1961).

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