evaporated and crystallized from methanol: yield 0.32 g., m.p. 203–204°, $[\alpha]^{20}D$ −6°, $\lambda_{max}^{CS_2}$ 1736 cm.$^{-1}$.

Anal. Calcd. for $C_{29}H_{42}O_9$: C, 65.16; H, 7.92. Found: C, 65.39; H, 7.63.

Allopregnane-3β,11α,17α-triol-7,20-dione (XIa).—A solution of 1.0 g. of the bisketal X and 1.0 g. of lithium aluminum hydride in 80 cc. of tetrahydrofuran was refluxed for 15 minutes and the product was isolated by chloroform extraction. The semi-solid residue obtained after evaporation of the chloroform was dissolved in 50 cc. of acetone containing 0.1 g. of *p*-toluenesulfonic acid and the mixture was allowed to stand overnight in order to cleave the ketal groupings. Dilution with water, extraction with chloroform, evaporation to dryness and recrystallization from ethyl acetate–hexane furnished 0.35 g. of the triol XIa with m.p. 185–187°, $[\alpha]D$ −47°, $\lambda_{max}^{CHCl_3}$ 1704 and free hydroxyl band.

Anal. Calcd. for $C_{21}H_{32}O_5$: C, 69.20; H, 8.85. Found: C, 68.90; H, 8.63.

The **diacetate** XIb was recrystallized from ether whereupon it exhibited m.p. 170–172°, $[\alpha]^{20}D$ −32°.

Anal. Calcd. for $C_{25}H_{36}O_7$: C, 66.94; H, 8.09. Found: C, 66.91; H, 7.84.

9α,11α-Oxido-22a-5α-spirostan-3β-ol-7-one Acetate.[32]—A solution of 20 g. of $\Delta^{7,9(11)}$-22a-5α-spirostadien-3β-ol acetate[17] in 100 cc. of chloroform and 500 cc. of 90% formic acid was heated with stirring to 60°, an additional 500 cc. of formic acid was added followed by 40 cc. of 30% hydrogen peroxide, the temperature being maintained between 40–60°. After standing at room temperature for 2 hours, ice-water was added, the product was extracted with ether, washed until neutral, dried and evaporated. Crystallization from ether afforded 6.72 g. with m.p. 270–284°, which upon one recrystallization from chloroform–ether yielded 6.05 g. of the epoxyketone with m.p. 290–295°, $[\alpha]D$ −127°, satisfactory for subsequent transformations.[18] The analytical sample exhibited m.p. 297–299° (Kofler), $[\alpha]^{20}D$ −128°, λ_{max}^{Nujol} 1736 and 1718 cm.$^{-1}$.

Anal. Calcd. for $C_{29}H_{42}O_6$: C, 71.57; H, 8.70. Found: C, 71.74; H, 8.94.

(32) We are indebted to Sr. Enrique Batres for carrying out this experiment.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE RICE INSTITUTE]

Ouabagenin. I. The Relationship between Ouabagenin Monoacetonide and "Anhydroöuabagenin"[1]

BY R. P. A. SNEEDEN AND RICHARD B. TURNER

RECEIVED MARCH 16, 1953

Cleavage of the glycoside, ouabain, by the action of hydrochloric acid in acetone furnishes the aglycone, ouabagenin, as a sparingly soluble monoacetonide, variously reported as melting between 200 and 255°. Pure material is obtained as prisms, m.p. 300–303° (dec.), by recrystallization of the crude product from a large volume of acetone. On solution in hot nitrobenzene, ouabagenin monoacetonide yields a substance, hitherto designated as "anhydroöuabagenin," which separates from the warm solution as plates, melting point when pure, 303–305° (dec.). Carbon and hydrogen analyses do not serve to distinguish this substance from its precursor. Both compounds yield the same diacetyl derivative on acetylation and show identical absorption in the infrared. X-Ray powder diagrams of "anhydroöuabagenin" and of ouabagenin monacetonide are likewise indistinguishable. These and other considerations indicate that the two substances in spite of differences in crystal habit, are nevertheless identical.

Ouabain, also known as *g*-strophanthin, constitutes the active principle of a preparation long employed by East African aborigines as an arrow poison. The substance was first isolated in pure form from the roots and bark of *Acokanthera ouabaio* by Arnaud in 1888.[2] Arnaud recognized the glycosidic nature of the material and identified the sugar residue as rhamnose, but was unsuccessful in his attempts to prepare the free genin, owing to extensive decomposition resulting from the vigorous conditions required for hydrolysis of the glycoside.[3] Jacobs and Bigelow[4] in subsequent work established the empirical formula $C_{29}H_{44}O_{12}$ for ouabain and on the basis of this result proposed the formula $C_{23}H_{34}O_8$ for the then unknown aglycone.

Early investigation of the properties of ouabain[5] revealed the existence of a close relationship between this substance and the steroid glycosides of the heart poison group. The presence of the characteristic butenolide system was deduced from a positive Legal test and was later confirmed by degradative work and by ultraviolet absorption studies of various derivatives.[6,7] Conversion of the glycoside into an iso compound by the action of alcoholic potassium hydroxide provided evidence, based upon analogy, for the presence of a tertiary hydroxyl group at C_{14}.[4] Other transformations, notably acetolysis of the tetrahydro derivative of heptaacetylanhydroöuabain with loss of a carbon atom as formaldehyde,[4] led Fieser and Newman[8] to the tentative conclusion that one of the hydroxyl functions of the genin is incorporated in a hydroxymethyl group located at an angular position, probably C_{10}.

A major advance in the structural problem was the discovery of Mannich and Siewert[9] in 1942 that cleavage of ouabain may be accomplished without destruction of the resulting aglycone by treatment of the glycoside with small amounts of concentrated hydrochloric acid in acetone solution. The principal cleavage product, which crystallizes directly from the reaction mixture, is an extremely insoluble monoacetonide of the free genin. The crude ma-

(1) This investigation was supported by a research grant, H-1084, from the National Heart Institute, of the National Institutes of Health, Public Health Service.

(2) A. Arnaud, *Compt. rend.*, **106**, 1011 (1888).

(3) A. Arnaud, *ibid.*, **126**, 346, 1208 (1898).

(4) W. A. Jacobs and N. M. Bigelow, *J. Biol. Chem.*, **96**, 647 (1932); *ibid.*, **101**, 15 (1933).

(5) A review of the early literature has been given by T. Reichstein and H. Reich, *Ann. Revs. Biochem.*, **15**, 155 (1946); see also L. F. Fieser and M. Fieser, "Natural Products Related to Phenanthrene," 3rd ed., Reinhold Publ. Corp., New York, N. Y., 1949, p. 548.

(6) A. Meyrat and T. Reichstein, *Helv. Chim. Acta*, **31**, 2104 (1948).

(7) R. F. Raffauf and T. Reichstein, *ibid.*, **31**, 2111 (1948).

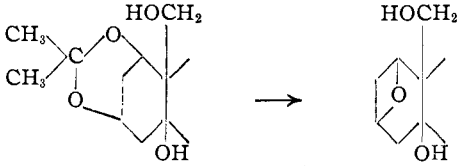
(8) L. F. Fieser and M. S. Newman, *J. Biol. Chem.*, **114**, 705 (1936).

(9) C. Mannich and G. Siewert, *Ber.*, **75**, 737 (1942).

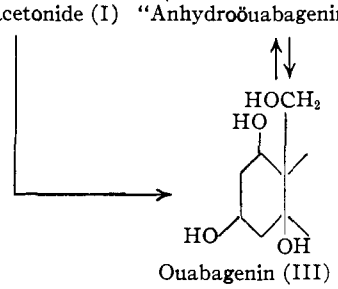
terial melts variously between 200 and 255°,[10] and on hydrolysis under mildly acidic conditions yields ouabagenin ($C_{23}H_{34}O_8$), m.p. 255–256°, together with a molecule of acetone, identified as the *p*-nitrophenylhydrazone. In addition to ouabagenin monoacetonide, the Mannich procedure furnishes also small amounts of a higher melting (303–305°) product, designated as "anhydro-ouabagenin," and of free ouabagenin.

Of the eight oxygen atoms of the aglycone, two are accounted for by the α,β-unsaturated lactone grouping and one, by the tertiary hydroxyl group (C_{14}) assumed from the conversion of ouabain into isoöuabain. The remaining five oxygen atoms are all hydroxylic in nature. Formation of a tetra-acetate from ouabagenin by treatment of this substance with acetic anhydride and pyridine suggests the presence of a second tertiary hydroxyl group, which has been tentatively assigned to C_5. The fact that no two hydroxyl groups can occupy adjacent positions is demonstrated by the failure of ouabagenin to react to any appreciable extent with lead tetraacetate[9] or with periodic acid. Ouabagenin monoacetonide has hence been formulated as a derivative of a 1,3-glycol. Attempts on the part of Mannich and Siewert to effect reconversion of ouabagenin into ouabagenin monoacetonide are stated to yield, not the desired product, but "anhydroöuabagenin."

Several unusual transformations in this series have been reported by the German investigators. Thus crude ouabagenin monoacetonide (prisms, m.p. 200°) on solution in hot nitrobenzene is converted into "anhydroöuabagenin," which crystallizes from this solvent, or from large volumes of neutral aqueous alcohol, as plates, m.p. 303–305° (dec.). The same change is brought about by prolonged boiling of a suspension of the monoacetonide in acetone. The fact that double bond formation is not involved in these reactions has been demonstrated by hydrogenation studies and by monoperphthalic acid titration. Moreover, the "anhydro" derivative, like the monoacetonide, yields ouabagenin when treated with dilute mineral acids. Mannich and Siewert have formulated these transformations as follows.



Ouabagenin monoacetonide (I) "Anhydroöuabagenin" (II)



Ouabagenin (III)

This scheme, however, suffers from several disadvantages,[11] and we have therefore re-examined the experimental evidence in the hope of arriving at a more plausible interpretation.

Important evidence that has hitherto been overlooked is the striking similarity of the diacetates obtained from ouabagenin monoacetonide and from "anhydroöuabagenin" by treatment of these substances with acetic anhydride and pyridine. A comparison of the properties of the two diacetates is given in Table I. This comparison constitutes a compelling argument for the view that the two products are identical. Conclusive evidence for this contention is provided by the fact that the infrared absorption spectra of these substances are superposable.

TABLE I

PROPERTIES OF OUABAGENIN MONOACETONIDE DIACETATE AND OF "ANHYDROÖUABAGENIN" DIACETATE

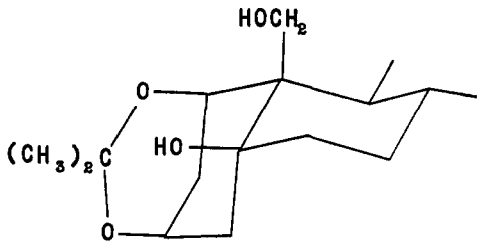
		Ouabagenin monoacetonide diacetate	"Anhydroöuabagenin" diacetate
M.p., °C.		268–269[9] 272–273[7] 271–272[a]	264–265[9] 270–272[7] 270–271[a]
M.m.p., °C.		268–272[7] 270–271[a]	
$[\alpha]^{29}D$		+40.5° (CH_3OH)[a]	+39.8° (CH_3OH)[a]
$\lambda_{max}^{CH_3OH}$		218 mμ, log ε 4.14[a]	218 mμ, log ε 4.14[a]
Empirical formula (Mannich[9])		$C_{30}H_{42}O_{10}$	$C_{27}H_{36}O_9$
Analyses[9]	Calcd.:	C, 64.03; H, 7.52 Acetyl, 15.3 Acetone, 10.3	C, 64.24; H, 7.20 Acetyl, 17.1
	Found:	C, 64.12; H, 7.21 Acetyl, 16.1 Acetone, 8.0	C, 64.03; H, 7.48 Acetyl, 16.1, 16.8

[a] This investigation.

Since the presence of an acetonide grouping in ouabagenin monoacetonide and in ouabagenin monoacetonide diacetate has been convincingly demonstrated by Mannich and Siewert, it follows from the relationship established above that "anhydroöuabagenin" must also be a monoacetonide derivative. Experimental justification for this conclusion is afforded by the isolation of acetone *p*-nitrophenylhydrazone in 55% yield (based upon a monoacetonide structure) from the reaction of "anhydroöuabagenin" with aqueous acetic acid. Further investigation of the properties of ouabagenin monoacetonide and of "anhydroöuabagenin" has

(10) Raffauf and Reichstein (ref. 7) report a melting point of 242–255° for this derivative.

(11) A 1,3-acetonide bridge of the type indicated can be formed only in the event that the hydroxyl groups involved are *cis* and polar (IV).



The formation of an oxide under these conditions would appear to be prohibited. It is furthermore unlikely that cleavage of an oxide of structure II would furnish a product stereochemically identical with that obtained by hydrolysis of the acetonide.

failed to reveal any significant differences between these substances, apart from the previously mentioned divergence of melting points and crystal habit. As in the case of the diacetyl derivatives, carbon and hydrogen analyses do not serve to differentiate the two products (Table II).

TABLE II

ANALYTICAL DATA FOR OUABAGENIN MONOACETONIDE AND FOR "ANHYDROÖUABAGENIN" (MANNICH AND SIEWERT[9])

		Ouabagenin monoacetonide	"Anhydro-öuabagenin"
Empirical formula		$C_{26}H_{38}O_8$	$C_{23}H_{37}O_7$
Analyses	Calcd.:	C, 65.23; H, 8.01	C, 65.67; H, 7.68
	Found:	C, 65.14; H, 8.26	C, 65.46; H, 7.92

In the earlier work no attempt was made to purify the inordinately insoluble ouabagenin monoacetonide. It appeared to us possible, therefore, that material isolated directly from the glycoside cleavage reaction may contain appreciable amounts of occluded impurities, and that these impurities are responsible for the wide variation in the melting point recorded for this substance.[7,9] A small sample of crude monoacetonide was accordingly recrystallized from a large volume of acetone by slow evaporation of the solvent at room temperature. These conditions are, if anything, milder than those employed for the original preparation, and the intrusion of untoward side reactions is regarded as a remote possibility. The product obtained by this procedure consists of prisms melting at 300–303° (dec.). Similarly, recrystallization of "anhydroöuabagenin" (plates, m.p. 303–305° dec.) from a large volume of acetone furnishes prisms, m.p. 300–303° (dec.), identical with the above sample. The infrared absorption spectra (Nujol) and X-ray powder diagrams[12] of the four specimens—ouabagenin monoacetonide (m.p. 200°, crude), ouabagenin monoacetonide (m.p. 300°, from acetone), "anhydroöuabagenin" (m.p. 300°, plates), and "anhydroöuabagenin" (m.p. 300°, prisms)—*are all identical.* On the basis of this evidence it is concluded that the compounds referred to as ouabagenin monoacetonide and as "anhydroöuabagenin" represent a single chemical substance. Identity of the X-ray patterns of samples crystallizing as plates and as prisms would appear to exclude the possibility of polymorphism. The difference in external appearance is thus probably attributable to a difference in crystal habit.

In addition to the work described in preceding paragraphs we have had occasion to investigate the hydrolysis of ouabagenin monoacetonide diacetate. Raffauf and Reichstein[7] have reported that treatment of this substance with dilute aqueous alcoholic sulfuric acid furnishes two products, melting at 262–265° and at 193–196°, which are designated as α-ouabagenin diacetate and as β-ouabagenin diacetate, respectively. The formation of isomeric substances under these conditions is perhaps attributable to acyl migration promoted by the strongly acidic medium. This difficulty is avoided by the use of aqueous acetic acid, which yields only the β-isomer. The latter substance crystallizes from water as a monohydrate, from which the solvent of crystallization can be removed by prolonged drying in vacuum at 130°. On treatment with acetone and anhydrous copper sulfate, ouabagenin diacetate is smoothly converted into ouabagenin monoacetonide diacetate. This behavior is consistent with the conversion of ouabagenin into ouabagenin monoacetonide ("anhydroöuabagenin") reported by Mannich and Siewert.

(12) We are indebted to Dr. W. O. Milligan and to Dr. H. Studer of this department for the X-ray data.

Experimental[13]

Preparation of Ouabagenin Monoacetonide.—The procedure employed was essentially that described by Mannich and Siewert.[9] Ouabain (10.0 g., S. B. Penick and Co., U.S.P. grade) was dissolved in 500 ml. of acetone containing 5 ml. of concentrated hydrochloric acid. After standing at room temperature (28°) for 5 days, the crystalline ouabagenin monoacetonide that had separated was removed by filtration and washed with acetone. The crude product weighed 4.0 g. and melted sharply with decomposition in the range 200–215°, depending upon the rate of heating. Purification of this material was accomplished in the following way.

A 60-mg. sample of the crude product was dissolved in 1 liter of pure acetone. The resulting solution was then concentrated under reduced pressure to 200 ml. and allowed to evaporate slowly at room temperature. Pure ouabagenin monoacetonide, 54 mg., was deposited as colorless prisms, m.p. 300–303° (dec.).

The mother liquors from the cleavage reaction (above), on standing for an additional 4 days, yielded 1.0 g. of a microcrystalline powder, m.p. 272–280° (dec.). Recrystallization of this material from nitrobenzene furnished "anhydroouabagenin" as plates melting at 300–303° (dec.).

Preparation of "Anhydroöuabagenin."—Finely powdered ouabagenin monoacetonide (500 mg., m.p. 200°) was dissolved in 6 ml. of boiling nitrobenzene. The solution was then cooled, and the product removed by filtration and washed with ether; yield 480 mg., m.p. about 280° (dec.). This material on washing with hot methanol and recrystallization from nitrobenzene, yielded 270 mg. of "anhydroouabagenin" as colorless plates melting at 300–303° (dec.).

Recrystallization of a 60-mg. sample from acetone by slow evaporation of the solvent as described in the preceding experiment furnished prisms (52 mg.), m.p. 300–303° (dec.). A mixed melting point with a purified sample of ouabagenin monoacetonide showed no depression.

Preparation of Ouabagenin Monoacetonide Diacetate.—Ouabagenin monoacetonide (1.5 g.) was stirred with 40 ml. of dry pyridine and 6 ml. of acetic anhydride for 48 hours, at the end of which time solution was complete. After standing for an additional 10 days at room temperature, the solvents were removed under high vacuum. The residual material was then taken up in methylene chloride and washed successively with water, dilute sulfuric acid, dilute sodium carbonate solution and water. The solution was finally dried and evaporated. Crystallization from acetone–petroleum ether gave 1.4 g. of ouabagenin monoacetonide diacetate[9] as prisms, m.p. 269–270°.[14] A pure sample, m.p. 271–272°, $[\alpha]^{29}D$ +40.5° (*c* 0.96, methanol), was obtained by chromatography on alumina.

Preparation of "Anhydroöuabagenin" Diacetate.—"Anhydroöuabagenin" (230 mg., m.p. 300°) was acetylated as described above in 5 ml. of dry pyridine containing 0.85 ml. of acetic anhydride. The total reaction time was 4 days. Crystallization of the crude product from acetone–petroleum ether afforded 215 mg. of material melting at 264–265°. Chromatography on alumina gave a pure sample, m.p. 270–271°, $[\alpha]^{29}D$ +39.8° (*c* 0.93, methanol). A mixed melting point with ouabagenin monoacetonide diacetate showed no depression.

Preparation of β-Ouabagenin Diacetate.[7]—Ouabagenin monoacetonide diacetate (1.0 g.) was dissolved in 5 ml. of hot acetic acid, and 5 ml. of water was added to the cooled solution. After standing for 3 hours at room temperature,

(13) All melting points are corrected. Microanalyses were carried out by S. M. Nagy, M.I.T., and by G. Weiler and F. Strauss, Oxford University.

(14) The same compound was obtained when the reaction product was crystallized directly without washing with acid.

the solution was evaporated to dryness under reduced pressure. The last traces of solvent were removed by repeated addition and evaporation of methanol. Crystallization of the residual material from water gave β-ouabagenin diacetate (815 mg.) as colorless prisms melting at 192–196°. The analytical sample, prepared by recrystallization from the same solvent, melted at 193–196°, $[\alpha]^{29}D$ +1.7° (*c* 1.76, methanol).

Anal. Calcd. for $C_{27}H_{38}O_{10}\cdot H_2O$ (540.59): C, 59.98; H, 7.46; CH_3CO, 16.3. Found: C, 59.85; H, 7.75; CH_3CO, 18.6.

An anhydrous sample, m.p. 193–196°, was obtained from the monohydrate by drying under vacuum at 130° for 3 hours.

Anal. Calcd. for $C_{27}H_{38}O_{10}$ (522.57): C, 62.05; H, 7.33. Found: C, 62.23; H, 7.39.

Conversion of Ouabagenin Diacetate into Ouabagenin Monoacetonide Diacetate.—Ouabagenin diacetate (70 mg., m.p. 192–193°) was added to a suspension of 1.3 g. of anhydrous copper sulfate in 10 ml. of acetone, and the mixture was heated under reflux for 5 hours. The copper sulfate was then removed by filtration, and the filtrate was concentrated to small volume and diluted with petroleum ether. The product obtained in this manner weighed 40 mg. and melted at 269–271°, $[\alpha]^{29}D$ +42.6° (*c* 2.24, methanol). A mixed melting point with an authentic sample of ouabagenin monoacetonide diacetate showed no depression. The infrared absorption spectra of the two samples were identical.

Acetone Determinations.—The per cent. of acetone in ouabagenin monoacetonide and in "anhydroöuabagenin" was estimated under identical conditions by the following procedure. A weighed sample of the compound to be analyzed, 2.5 ml. of acetic acid and 10 ml. of water were placed in a distilling flask connected to a condenser and receiver containing a filtered solution of 100 mg. of *p*-nitrophenylhydrazine in 2.5 ml. of acetic acid and 5 ml. of water. The contents of the distilling flask were heated gently until solution took place and then slowly distilled until the volume was about 4 ml. Water (5 ml.) was added to the receiver, and after 15 min. the precipitated acetone *p*-nitrophenylhydrazone was removed by filtration and dried under vacuum at 100° for one hour. From 120 mg. of ouabagenin monoacetonide, 26.2 mg. of acetone *p*-nitrophenylhydrazone, m.p. and mixed m.p. 147.5–149.5°, was obtained, representing 53% of the theoretical amount. "Anhydroöuabagenin" (100 mg.) furnished 22.7 mg. (55%) of an identical product.

Treatment of Ouabagenin with Periodic Acid.—A solution of 17.7 mg. of ouabagenin monohydrate[9] (prepared by hydrolysis of the monoacetonide with aqueous acetic acid) in 2 ml. of water was treated with 0.50 ml. of an aqueous solution containing 12.0 mg. of periodic acid dihydrate. After standing at room temperature for 30 min., 1 ml. of 1 *N* sulfuric acid and 0.2 g. of potassium iodide were added, and the liberated iodine was titrated with 0.0193 *N* sodium thiosulfate solution to the starch end-point. In all 20.55 ml. of thiosulfate was required as compared with 20.60 ml. in a blank run.[15] The difference, 0.05 ml., corresponds to 1.2% of the theoretical value (4.2 ml.) computed on the basis of one 1,2-glycol grouping per molecule of ouabagenin. A similar result was obtained with β-ouabagenin diacetate.

(15) A stable end-point in the titration of the ouabagenin reaction was obtained only after a considerable period of time. This behavior suggests the formation of a cycle, possibly involving 1,3-hydroxyl groups, that is only slowly hydrolyzed by sulfuric acid.

HOUSTON, TEXAS

[FROM THE CHEMO-MEDICAL RESEARCH INSTITUTE OF GEORGETOWN UNIVERSITY]

The Reaction of Saturated Steroid 3-Enol Acetates with N-Bromosuccinimide[1-3]

BY MARTIN RUBIN AND BERNARD H. ARMBRECHT

RECEIVED SEPTEMBER 8, 1952

The reaction of N-bromosuccinimide (NBS) with Δ^2-3-acetoxycholestene and Δ^3-3-acetoxycoprostene was investigated. From the Δ^2-3-acetoxycholestene reaction Δ^1- and Δ^4-cholesten-3-one, 2-bromocholestan-3-one and starting material were isolated. The amount of 2-bromocholestan-3-one, formed as a function of increasing reaction time, was found to increase at the expense of the Δ^1-cholestene-3-one. From the reaction of Δ^2-3-acetoxycoprostene with NBS, Δ^4-cholesten-3-one and crude Δ^1-coprosten-3-one were isolated.

In recent years the application of the reaction of N-bromoimides,[4] and especially N-bromosuccinimide[5] with olefins for the preparation of allyl bromides or the conjugated diene system formed from such compounds by dehydrohalogenation, has assumed increasing importance.[6] The special case in which one of the olefinic carbon atoms is also substituted by an esterified hydroxyl group (*i.e.*, the enol ester of a ketone) has received little attention. In the single previously described reaction of this type it had been observed that the reaction of NBS with the enol acetate of a 20-keto steroid, Δ^{17}-3,12,20-triacetoxypregnene, resulted in the formation of the corresponding α,β-unsaturated ketone, Δ^{16}-3,12-diacetoxypregnen-20-one.[7] We have now studied the reaction of NBS with the typical enol acetates of the 3-keto steroid ring, A/B *trans* or allo form, Δ^2-3-acetoxycholestene, and of the A/B *cis* or normal form Δ^2-3-acetoxycoprostene, XIV, in an attempt to utilize this reaction for the introduction of the Δ^4-double bond into the saturated A ring of the steroid nucleus. This step is of importance in the preparation of some steroid hormones.

In the absence of any directing influence of the 3-acetoxy group of II or of the steric arrangement of the allo molecule, we might expect that NBS substitution would result in the formation of V and VI in an equal amount. While VI might be expected to be a comparatively stable compound due to the absence of an available hydrogen atom for spontaneous dehydrohalogenation, V could lose hydrogen bromide by elimination of the bromine on C_4 and the available hydrogen on C_5. The course of the reaction appeared to follow such a hypothetical sequence. Within a minute of the typical NBS "bromination" color change, hydrogen bromide spontaneously evolved from the reaction mixture. Arrest of the reaction after one minute by cooling, followed by neutralization of the

(1) Presented at the April, 1951, Meeting of the American Chemical Society, Division of Organic Chemistry, Cleveland, Ohio.

(2) Abstracted from a thesis submitted by Bernard H. Armbrecht in partial fulfillment of the requirements for the degree of Doctor of Philosophy, June, 1951.

(3) Supported by research grant from the Chemical Specialties Company, Inc., New York, New York.

(4) A. Wohl, *Ber.*, **52**, 51 (1919).

(5) K. Ziegler, A. Spaeth, E. Schaaf, W. Schumann and F. Winkelman, *Ann.*, **551**, 80 (1942).

(6) C. Djerassi, *Chem. Revs.*, **43**, 271 (1948).

(7) C. Djerassi and C. Scholz, *J. Org. Chem.*, **14**, 660 (1949).