The base was soluble in 10% acetic acid and was therefrom precipitated by Meyer reagent. For the preparation of the hydrochloride a solution of 5.6 mg. of mother liquor material in chloroform was distributed with 2 *N* hydrochloric acid. A fine precipitate of crystals appeared in the aqueous phase. The suspension was brought to dryness. The residue on recrystallization from water yielded fine needles, m.p. 305–315° dec., which gave positive Beilstein and silver nitrate tests.

Acetylation of the base (10.8 mg.) with acetic anhydride–pyridine yielded an amorphous product (15 mg.) which behaved like the tetraacetate XI in that it formed a gelatinous precipitate from warm ethanol. Its infrared spectrum was identical with that of XI.

By-products in the Acetolysis of Diacetyltetrahydrojervine.—The mother liquor from the first recrystallization of the crude acetolysis product II in two instances deposited large square blocks (yield from I about 3 and 5%) which after repeated recrystallization from methanol melted at 210.5–212.5°, $[\alpha]^{25}D$ +51° (*c* 0.921). The ultraviolet spectrum showed only end absorption and no indication of a peak at 305 mμ ($E^{1\%}_{1cm}$ 280–320 mμ, 0.1). The analytical data were best compatible with a tetraacetate $C_{35}H_{51}O_7N$ (II + C_2H_2O).

Anal. Calcd. for $C_{35}H_{51}O_7N$ (597.8): C, 70.32; H, 8.60; 4 $COCH_3$ 28.8, 3 $COCH_3$ 21.6. Found: C, 70.19, 70.76; H, 8.68, 8.45; $COCH_3$, 23.1.

In one run fluffy, felt-like crystals, m.p. 190–202°, $[\alpha]^{25}D$ −35°, also were obtained from such a mother liquor. This product showed strong specific absorption at 250 mμ ($E^{1\%}_{1cm}$ 78) and therefore probably corresponds to the unsaturated ketone obtained as a by-product in the 3-chloro series (*cf.* paper VI). The amount isolated was too small for further investigation.

In one of the early experiments the mother liquors from 5 successive recrystallizations of II were combined and brought to dryness, and the residue was chromatographed in the usual manner on alumina. Except for some additional II eluted with benzene–ether 9:1, no crystalline products were obtained. All the subsequent eluates (benzene–ether 5:1, 1:1, ether, ether–methanol 9:1, 1:1) showed more or less strong specific absorption in the 245–250 mμ region. Pure methanol eluted a sizable amount of amorphous, water-soluble material which the analysis showed to be the (impure) sodium salt of a sulfonic acid; λ^{alc}_{max} 247, 330 mμ ($E^{1\%}_{1cm}$ 149, 7.5).

Anal. Calcd. for $C_{31}H_{46}O_5N{\cdot}SO_3Na$ (615.7): N, 2.28; S, 5.21; Na, 3.73. Found: N, 3.13; S, 5.06; Na, 3.04.

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NEW BRUNSWICK, N. J.

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Jervine. VI. The Sulfuric Acid-catalyzed Acetolysis of N-Acetyl-3-desoxy-3(α)-chlorotetrahydrojervine

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The sulfuric acid-catalyzed acetolysis of N-acetyl-3-desoxy-3(α)-chlorotetrahydrojervine (I) gives rise to a complex mixture of products, three of which have been structurally identified. The normal course of the acetolysis is exemplified by the unsaturated diacetate II, analogous to the main product formed in the same reaction from diacetyltetrahydrojervine.[4] The other two compounds, the α,β-unsaturated 11-ketone VIII and the isomeric tertiary base XI (derived from VIII by rearrangement) are abnormal products, since they represent a higher state of oxidation than I. The probable mode of formation of VIII is discussed.

The work described in this paper was initiated before the nature of the structural abnormality in the steroid-like tetracyclic nucleus of jervine had been elucidated through the acetolysis studies on jervine itself reported in previous papers of this series.[2-3] At that time, the most promising approach open to us seemed to be the oxidative degradation of the acetolysis product of diacetyltetrahydrojervine,[4] in which advantage could be taken of the new hydroxyl function and double bond formed in the acetolytic opening of the oxidic bridge linking rings D and F. In following this line of attack we thought it expedient to replace the hydroxyl function at C_3 by an inert substituent such as chlorine in order to minimize the difficulties likely to arise in the characterization of the expected oxygen-rich degradation products. Accordingly N-acetyl-3-desoxy-3(α)-chlorotetrahydrojervine (I) was prepared from N-acetyltetrahydrojervine[4,5] and subjected to the acetolysis reaction. The results, as far as they pertain to the main acetolysis product II, merely supplement and confirm those obtained with diacetyltetrahydrojervine.[4] However, it was possible in the 3-chloro series to isolate in addition to II a number of by-products of the reaction and to identify structurally the two most important of these, and it is this latter aspect of the study with which we are primarily concerned in this paper.

The starting product I (m.p. 245–247°, $[\alpha]^{23}D$ +18°) was obtained by treatment of N-acetyltetrahydrojervine with phosphorus pentachloride in chloroform solution at 0°, or with phosphorus oxychloride and pyridine at reflux temperature (prolonged exposure to the latter reagents at room temperature gave anomalous results, *cf.* Experimental). The α-configuration is assigned to the halogen substituent in analogy with the behavior of normal 3(β)-stanols toward these reagents. As in the case of diacetyltetrahydrojervine, the crude material obtained from I on treatment with the acetolysis mixture exhibited strong specific ultraviolet absorption in the 245–250 mμ region, while the main

(1) Research Laboratories Ciba A.G., Basel, Switzerland.

(2) J. Fried, O. Wintersteiner, A. Klingsberg, M. Moore and B. M. Iselin, THIS JOURNAL, **73**, 2970 (1951); J. Fried and A. Klingsberg, *ibid.*, **75**, 4929 (1953).

(3) O. Wintersteiner and M. Moore, *ibid.*, **75**, 4938 (1953).

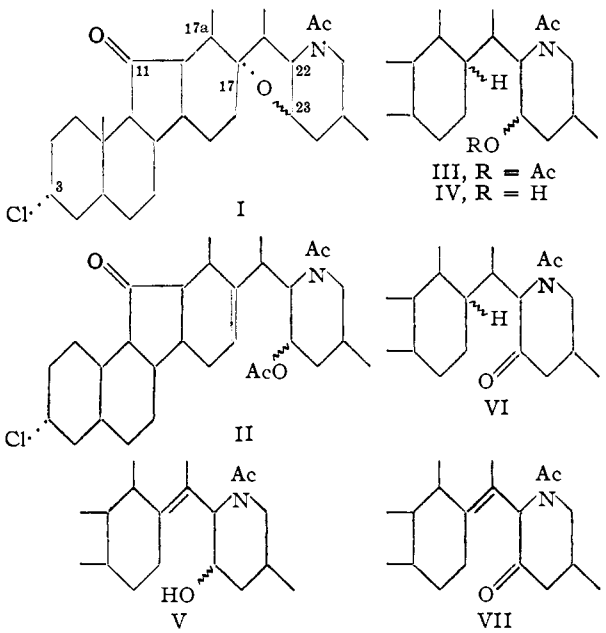
(4) O. Wintersteiner, M. Moore and B. M. Iselin, *ibid.*, **76**, 5609 (1954).

(5) W. A. Jacobs and C. F. Huebner, *J. Biol. Chem.*, **170**, 635 (1947).

crystalline product secured from it by chromatography (II, m.p. 135–138°, $[\alpha]^{21}D$ −52°) showed only the weak band at 305 mμ characteristic for the unconjugated 11-keto group in I. Catalytic hydrogenation of II afforded the dihydro derivative III (m.p. 203–205°, $[\alpha]^{23}D$ −26°), which was hydrolyzed with alkali to the saturated N-acetate IV (m.p. 224–226°, $[\alpha]^{23}D$ −38°). When II itself was subjected to the latter reaction, a dextrorotatory N-acetate (m.p. 134–135°, $[\alpha]^{21}D$ +28°) resulted, which in analogy with the corresponding product in the 3-hydroxylated series[4] is tentatively formulated as the 17,20-olefin V. Further characterization of this iso compound by acetylation to the 23,N-diacetate (corresponding to the isotriacetate VI of the preceding paper) was dispensed with.

The molecular rotation shifts accompanying the formation of the acetolysis products and their subsequent transformations show reasonably good agreement in the two series. Thus $\Delta[M]D$ for the acetolysis reaction I → II is −345°, and in the 3-hydroxylated series, −376°; the saturation of the double bond in II raises $[M]D$ by +137°, and in the 3-hydroxylated series by +183°; the shift of the double bond from the 16,17- to the 17,20-position is accompanied by a high positive rotation change in both series. On account of the simultaneous O-desacetylation these values must be computed as follows: $\Delta[M]D$ for II → V (over-all change caused by alkali) is +418°; for III → IV (O-desacetylation at C_{23}) −48°; hence $\Delta[M]D$ for the double bond shift is +466°. The same computation for the compounds of the 3-hydroxylated series gives +480° for the over-all reaction as well as for the double bond shift alone, since $\Delta[M]D$ for the O-desacetylation at both C_3 and C_{23} happens to be zero.[4]

Mild chromic acid oxidation of the N-acetates IV and V gave, respectively, the saturated diketone VI (m.p. 226–228°, $[\alpha]^{23}D$ −99°) and the unsaturated diketone VII (m.p. 224–226°). The new keto group formed in the oxidation was reactive, as both compounds readily yielded monoximes. However, some degree of hindrance was indicated by the fact that the formation of the monosemicarbazone of VI required heating for several hours. The infrared spectra of VI and VII showed broad bands at 5.83 μ, obviously representing the combined absorption of the 11-keto group (5.80 μ) and of the new ketonic carbonyl at C_{23}. In the ultraviolet region this carbonyl gives rise to a band at 305 mμ of much higher intensity than is usually encountered with isolated keto groups. Thus the ε values for VI and VII were 190 and 205, respectively, which, corrected for the contribution of the 11-keto group (λ_{max} 305 mμ, ε 30) gives an ε of about 170 for the 23-carbonyl. We already have called attention to the fact that the 23-keto group in N-acetyldihydroveratramine-3,23-dione gives rise to a band at 305 mμ of similar intensity (ε 230).[6] It seems probable that it is the substitution of the adjacent carbon atom 22 with an amidic nitrogen atom which is responsible for this hyperchromic effect as well as for the bathochromic shift of the ketone band to 305 mμ from the usual position (280–295 mμ) observed with isolated keto groups in alicyclic 6-membered rings.[7]

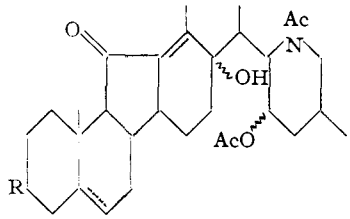


By-products of the Acetolysis.—Extensive chromatographic fractionation of the acetolyzed material yielded in addition to the main acetolysis product II three neutral crystalline compounds as well as substantial amounts of the amorphous sodium salt of a sulfonic acid. Preponderant among the crystalline products (yield from I 5%) was a compound, m.p. 237–239°, $[\alpha]^{23}D$ −43°, the ultraviolet absorption spectrum of which was indistinguishable from that of jervine. The obvious inference that this substance was an isomer of II in which the double bond had shifted into conjugation with the 11-keto group was, however, not borne out by the analytical data, which showed it to be a diacetate of the composition $C_{31}H_{46}O_5NCl$, *i.e.*, II + O. The infrared spectrum revealed the additional oxygen atom as a hydroxyl group (3.08 μ), while otherwise exhibiting the expected bands (5.78 μ, O-acetyl; 5.85 μ, unsaturated ketone; 6.17 μ, broad, N-acetyl + conjugated —C=C—). That this compound must have structure VIII became evident from the fact that on treatment with alkali at room temperature it did not yield the expected N-monoacetate, but underwent a rearrangement previously observed with a compound IX of very similar properties formed in the sulfuric acid-catalyzed acetolysis of diacetyljervine.[3] With IX, this reaction led, with loss of jervine absorption and shift of N-acetyl to the free hydroxyl group at C_{17}, to the monoacetylated tertiary base XII, and thence by acetylation to the triacetate XIII, an isomer of the starting compound. In the present case the intermediate O-monoacetate X was amorphous, but gave on acetylation the crystalline diacetate XI (m.p. 233–234°, $[\alpha]^{22}D$ −65°) corresponding in all its properties to XIII (basic group titratable with perchloric acid; λ^{alc}_{max} 308 mμ, ε 60; μ λ^{nujol}_{max} 5.77 (O-acetyl), 5.81 μ (11-ketone)).

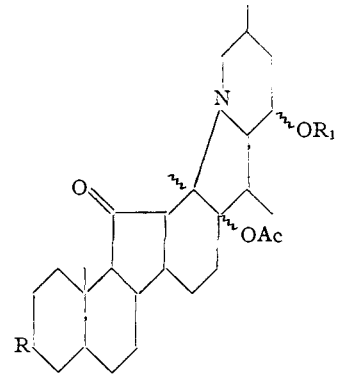
The above finding was instrumental in elucidating the nature of one of the other companion sub-

(6) Ch. Tamm and O. Wintersteiner, THIS JOURNAL, **74**, 3842 (1952).

(7) R. C. Cookson, *J. Chem. Soc.*, 282 (1954).



VIII, R = Cl, no Δ^5
IX, R = OAc, Δ^5



X, R = Cl, R_1 = H, no Δ^5
XI, R = Cl, R_1 = Ac, no Δ^5
XII, R = OH, R_1 = H, Δ^5
XIII, R = OAc, R_1 = Ac, Δ^5

stances of II (yield 1%), a diacetate m.p. 239–242°, $[\alpha]^{25}D$ −61° isomeric with VIII, but differing from it by showing only the usual tetrahydrojervine spectrum. However, it was noted early that its infrared spectrum lacked the N-acetyl band, and after the conversion of VIII to the rearranged diacetate XI had been carried out, it became clear that this product was identical with XI (identity of infrared spectra). The divergency in the melting points must be ascribed to the existence of several polymorphous forms, for at the time when the mixed melting point was determined, both specimens as well as the mixture melted at 220–222°. The rearrangement of VIII to the isomeric base probably occurred during the decomposition of the acetolysis mixture with excess sodium bicarbonate, and the immediate precursor of XI may not be VIII itself, but a sulfuric acid salt analogous to the alkali-labile perchlorate which is formed when either diacetyljervine or its acetolysis product IX is treated with an acetic anhydride–acetic acid mixture containing perchloric acid.[3] This salt, the cationic component of which is probably IX, but with the N-acetyl group already transposed to the tertiary 17-hydroxy group, on decomposition with bicarbonate undergoes instantaneous rearrangement to the weakly basic triacetate XIII analogous to XI.

There remains to be explained how the unsaturated ketone VIII, which represents a higher state of oxidation than the starting product I, could have arisen from the latter. That I might have been contaminated with some of the corresponding 13,-17a-unsaturated derivative is out of the question because each of the four intermediates in the preparation of I from jervine was isolated and purified, and, moreover, the first of these, 13,17a-dihydrojervine, was routinely checked for the absence of jervine absorption. The double bond in VIII must therefore have arisen during the acetolysis itself through a side reaction equivalent to oxidation. The only explanation we can advance at present is that sulfonation in position 13 followed by elimination of sulfurous acid with loss of the 17a-hydrogen atom has occurred. It is well known that saturated steroidal ketones on treatment with sulfuric acid containing acetic anhydride–acetic acid mixtures are readily sulfonated, probably *via* enolic intermediates, at one of the α-carbon atoms.[8,9] On the other hand, there is admittedly no precedent for the subsequent elimination under these or similar conditions of the sulfonic acid group, from compounds of this type. However, in none of the known examples does the sulfonate group occupy a tertiary carbon atom, and it is conceivable that in the present case the sulfonate ion, after having entered at C_{13} in β-orientation by addition to the enolic double bond, might undergo *trans* elimination with the α-hydrogen at 17a. The situation is further complicated by the fact that the sulfonic acid present among the acetolysis products (*cf.* Experimental) likewise exhibits strong jervine-like absorption, and hence cannot be the postulated intermediate in the formation of VIII, but would rather seem to be derived from the latter.

The third crystalline by-product (m.p. 202–204°, $[\alpha]^{25}D$ +70°) was obtained in very small amounts only. The elementary analysis best fitted the triacetate $C_{33}H_{48}O_5NCl$ (II + C_2H_2O) and, although the acetyl determination indicated only two such groups, this could be rationalized on the assumption that the N-acetyl group, like that in II and many other N-acetylated jervine derivatives, is resistant to liberation under the conditions of the Kuhn–Roth procedure.[3] Surprisingly, the ultraviolet spectrum was devoid of the low intensity band at 305 mμ originating in the 11-keto group. The *a priori* unlikely possibility that this product is an 11-enol acetate of II is excluded by the fact that the infrared spectrum did not show a band near 5.7 μ. Whatever structure this compound might have its formation must be more than an accidental event in the course of the over-all reaction, since the acetolysis of diacetyltetrahydrojervine gives rise to an analogous product, a dextrorotatory tetraacetate, m.p. 212°, which likewise lacks the 11-ketone band in its ultraviolet spectrum.[4]

Experimental

The melting points were taken in open Pyrex glass capillaries and are corrected for stem exposure. The rotation measurements were carried out in a 1-dm. semi-micro tube with chloroform as the solvent. The ultraviolet spectra were determined in a quartz Beckman spectrophotometer, model DU, and the infrared measurements were taken on nujol suspension in a Perkins–Elmer model 12-B single beam instrument. The analytical samples were dried over phosphorus pentoxide at 110° (1 mm.). The alumina used for chromatography (Harshaw) was washed with dilute sulfuric acid and water to *p*H 4.5 and reactivated by heating at 150° for 48 hours.

N-Acetyltetrahydrojervine was conveniently secured directly from the free base by selective N-acetylation with acetic anhydride in methanol solution (a method which works well in the jervine series but fails with veratramine and its dihydro derivative). For example, a solution of

(8) A. Windaus and E. Kuhr, *Ann. Chem.*, **532**, 52 (1937).
(9) E. Kuhr, *Ber.*, **72**, 929 (1939).

tetrahydrojervine (7.5 g.) in dry methanol (150 cc.) and acetic anhydride (2.5 cc.) was allowed to stand at room temperature for 4 hours. The solvents were removed *in vacuo*, and the residue taken into chloroform, which was washed with 1 *N* sulfuric acid, 1 *N* sodium hydroxide and water, dried and evaporated. The product was recrystallized from methanol (prisms, 6.62 g., m.p. 262–266°), $[\alpha]^{25}D$ +3 ± 1° (*c* 0.91); lit. m.p.[5] 266–269°.

Anal. Calcd. for $C_{29}H_{45}O_4N$ (471.7): C, 73.84; H, 9.62; $COCH_3$, 9.12. Found: C, 74.02; H, 9.32; $COCH_3$, 7.45.

N-Acetyl-3-desoxy-3(α)-chlorotetrahydrojervine (I).—N-Acetyltetrahydrojervine (2 g.) was dissolved in dry chloroform (100 cc.). After the addition of freshly dried calcium carbonate (4 g.) and cooling to 0°, freshly sublimed phosphorus pentachloride (5 g.) was added in portions over the course of 2 hours while the solution was shaken in an ice-bath. The excess reagent was decomposed by the gradual addition (0°, shaking) of saturated potassium bicarbonate solution (180 ml.). The layers were separated, and the chloroform phase was washed with bicarbonate and water, dried and brought to dryness *in vacuo*. The sirupy residue was crystallized from absolute ethanol (1.26 g., m.p. 237–238°). Repeated recrystallizations afforded needles melting at 245–247°, $[\alpha]^{23}D$ +18° (*c* 0.89).

Anal. Calcd. for $C_{29}H_{44}O_3NCl$ (490.1): C, 71.06; H, 9.05; N, 2.86; Cl, 7.23. Found: C, 71.33; H, 8.89; N, 2.99; Cl, 7.01.

Treatment of N-acetyltetrahydrojervine with phosphorus oxychloride in boiling pyridine (2 hours) likewise afforded I, but in lower yield. However, when this reaction was carried out at room temperature (2–4 days), two other products (A and B) of unknown structure were obtained instead in 36 and 16% yield, respectively. For example, a solution of the starting product (2.5 g.) in pyridine (25 cc.) to which freshly distilled phosphorus oxychloride (10 cc.) had been added slowly at 0°, was allowed to stand at 25° for 90 hours. The solvents were removed and the residue was extracted with chloroform. The residue from the acid and carbonate washed solution (3.13 g. after prolonged drying in a high vacuum) was recrystallized twice from benzene, from which it formed needles (832 mg., substance A) melting at 115–120° and resolidifying at 135–140°. Further heating resulted in softening at 240°, but no distinct melting up to 280°, $[\alpha]^{25}D$ −52° (*c* 0.86); λ_{max}^{alc} 320 mμ, shoulder 240 mμ ($E_{1cm}^{1\%}$ 14, 94, respectively). Found: Cl, 9.26. The product was readily soluble in water and alcoholic solvents, chloroform and dioxane, but insoluble in ether. That substance A is not, as was at first suspected, the 3-pyridinium salt corresponding to I, but a complex containing the latter, followed from the fact that on chromatography on alumina it afforded pure I in 54% yield.

The material recovered from the combined benzene mother liquors of A (2.3 g.) was dissolved in hexane–benzene 1:1 and adsorbed on a column of alumina. Elution with the same solvent mixture yielded substance B (1.036 g.), which on recrystallization from chloroform–methanol formed large needles melting at 175–177° and exhibiting the remarkably high levorotation $[\alpha]^{25}D$ −639° (*c* 1.14). The compound was practically insoluble in methanol, ethanol and acetone, slightly soluble in ether and readily soluble in benzene and chloroform. It slowly decomposed in the desiccator with discoloration. Neither its spectral properties nor the analyses, which best fitted the formula $C_{27}H_{37}O_3N_2Cl_2$, gave any clue to its structure: $\lambda_{max}^{chlf-MeOH}$ 326, λ_{min} 290, shoulder 240 mμ, with ε 4200, 2400, 6000, respectively; λ_{max}^{nujol} 5.78, 6.07, 6.44 μ (N=C?).

Anal. Calcd. for $C_{27}H_{37}O_3N_2Cl_2$ (508.5): C, 63.77; H, 7.34; N, 5.51; Cl, 13.94; $COCH_3$, 8.46. Found: C, 63.41; H, 7.17; N, 5.47; Cl, 13.6; $COCH_3$, 10.5.

That A and B do not arise from N-acetyltetrahydrojervine directly but *via* the normal chlorination product I followed from the finding that the latter could as well be used as the starting material in the room temperature reaction with phosphorus oxychloride for securing the two products (yield of A 67%, of B 11%).

Acetolysis of N-Acetyl-3-desoxy-3(α)-chlorotetrahydrojervine; 22,26-Imino-3α-chloro-16-jervene-23-ol-11-one 23,N-Diacetate (II).—N-Acetyl-3-desoxy-3(α)-chlorotetrahydrojervine (1.0 g.) was dissolved in a mixture consisting of acetic anhydride (35 cc.), acetic acid (15 cc.) and concentrated sulfuric acid (0.5 cc.). The solution showed an initial specific rotation of $[\alpha]^{25}D$ +51° which gradually decreased to +22° within 7 hours and then increased again to a constant value of $[\alpha]^{25}D$ +35° overnight. After standing for 28 hours, the mixture was concentrated to a small volume (10 cc.) *in vacuo* of 0.3 mm. pressure, diluted with ice and extracted with chloroform. The chloroform extracts were washed with water, cold saturated potassium bicarbonate solution and water, dried and evaporated to dryness. The resulting sirup (1.12 g., λ_{max}^{alc} 247 mμ, $E_{1cm}^{1\%}$ 68; λ_{min} 230mμ, $E_{1cm}^{1\%}$ 53, shoulder 310 mμ, $E_{1cm}^{1\%}$ 4.7) was subjected to chromatographic fractionation on aluminum oxide. The fractions eluted with benzene–hexane 1:1 yielded 255 mg. of a product, m.p. 133–135°, which, after repeated recrystallization from acetone–ether, was obtained as colorless needles melting at 135–138°, $[\alpha]^{21}D$ −52° (*c* 0.99); λ_{max}^{alc} 305 mμ (44); λ_{max}^{nujol} 5.76, 6.13, 7.97 μ.

Anal. Calcd. for $C_{31}H_{46}O_4NCl$ (532.15): C, 69.95; H, 8.71; Cl, 6.66; 2 $COCH_3$, 16.17. Found: C, 69.88; H, 8.92; Cl, 6.35; $COCH_3$, 12.73.

Catalytic Reduction of II; 22,26-Imino-3α-chlorojervane-23-ol-11-one 23,N-Diacetate (III).—The acetolysis product II (800 mg.) was hydrogenated in acetic acid (25 cc.) in the presence of platinum oxide catalyst (200 mg.). One molar equivalent of hydrogen was consumed rapidly. The sirupy reduction product, isolated in the usual manner, crystallized on addition of ether. The crystalline fraction (621 mg.) was recrystallized from acetone–ether and then melted at 203–205°, $[\alpha]^{23}D$ −26° (*c* 1.80).

Anal. Calcd. for $C_{31}H_{48}O_4NCl$ (534.2): C, 69.69; H, 9.06. Found: C, 69.40; H, 8.87.

Hydrolysis of III; 22,26-Imino-3α-chlorojervane-23-ol-11-one N-Acetate (IV).—A solution of the diacetate III (600 mg.) in 5% methanolic potassium hydroxide (30 cc.) was boiled under reflux for one hour. The crystalline hydrolysis product, isolated in the usual manner, was recrystallized twice from acetone–ether, yielding 386 mg. of the hydroxyketone IV, m.p. 224–226°, $[\alpha]^{23}D$ −38° (*c* 0.97).

Anal. Calcd. for $C_{29}H_{46}O_3NCl$ (492.1): C, 70.77; H, 9.42. Found: C, 70.36; H, 9.58.

Hydrolysis of II; 22,26-Imino-3α-chloro-17(20)?-jervene-23-ol-11-one N-Acetate (V).—The acetolysis product II (100 mg.) was hydrolyzed in the same manner as III and isolated in the usual fashion. The sirupy chloroform residue (95 mg.) was purified by chromatography on alumina, yielding a crystalline fraction (50 mg.) which after recrystallization from methanol melted at 134–135° and showed $[\alpha]^{21}D$ +28° (*c* 1.11). The hydroxyketone was not analyzed, but used *in toto* for the oxidation to the diketone VI.

22,26-Imino-3α-chlorojervane-11,23-dione N-Acetate VI from IV.—The N-acetate IV (300 mg., 0.61 millimole) was dissolved in acetic acid (10 cc.), and 2.45 cc. of a 2% solution of chromium trioxide (49 mg. = 0.73 milliatom of oxygen) in acetic acid was added. After standing for 1 hour at room temperature the mixture was evaporated to dryness *in vacuo*. The residue was extracted with chloroform and the chloroform extracts were washed with water, 1 *N* sodium carbonate solution and water, dried and evaporated to dryness. The neutral product was dissolved in acetone, filtered through aluminum oxide and again brought to dryness. Recrystallization of the crude reaction product (291 mg.) from acetone–ether–pentane gave 167 mg. of the diketone which, after two additional recrystallizations from the same solvents, melted at 226–228°, $[\alpha]^{23}D$ −99° (*c* 1.11); λ_{max}^{alc} 305 mμ (190); λ_{max}^{nujol} 5.83, 6.13 μ; increase of intensity on standing in 6% KOH in ethanol: immediate reading λ 305 mμ, ε 235; after 6 hours 430, after 24 hours 730.

Anal. Calcd. for $C_{29}H_{44}O_3NCl$ (490.1): C, 71.06; H, 9.05. Found: C, 71.16; H, 9.19.

The monoöxime was formed readily on treatment of the diketone with excess hydroxylamine acetate in methanol at room temperature over a period of 24 hours. It melted, after recrystallization from acetone–ether, at 250–253°; λ_{max}^{alc} 305 mμ (210).

Anal. Calcd. for $C_{29}H_{45}O_3N_2Cl$ (505.1): N, 5.55. Found: N, 5.84.

The monosemicarbazone was prepared by refluxing a solution of the diketone with excess semicarbazide acetate

in methanol for 3 hours. After recrystallization from acetone–ether, it melted at 251–254° dec. The ultraviolet spectrum showed the normal semicarbazone maximum λ_{max}^{alc} 230 mμ (14,200), and shoulder at 305 mμ (40).

Anal. Calcd. for $C_{30}H_{47}O_3N_4Cl$ (547.2): N, 10.24. Found: N, 10.03.

22,26-Imino-3α-chloro-17(20)?-jervene-11,23-dione N-Acetate (VII) from V.—The unsaturated N-acetate V (48 mg., 0.1 millimole) was dissolved in 1.5 cc. of acetic acid and 1.6 cc. of a 0.5% solution of chromium trioxide (8 mg. = 0.12 milliatom of oxygen) in acetic acid was added. After standing for one hour, the mixture was evaporated to dryness *in vacuo*. The residue was extracted with chloroform, and the chloroform solution was successively washed with dilute sulfuric acid, saturated potassium bicarbonate solution and water, dried and evaporated to dryness. The resulting neutral product (47 mg.) crystallized partially on addition of ether. The solid material (26 mg.) was dissolved in acetone, filtered through aluminum oxide and concentrated to dryness. The residual material yielded, after recrystallization from acetone–ether, 15 mg. of the diketone melting at 224–226°, λ_{max}^{alc} 305 mμ (205), λ_{max}^{nujol} 5.82, 6.08 μ.

Anal. Calcd. for $C_{29}H_{42}O_3NCl$ (488.1): C, 71.36; H, 8.67. Found: C, 71.66; H, 8.43.

The **monoöxime** was prepared by treatment of the diketone with excess hydroxylamine acetate in methanol at room temperature for 24 hours. After recrystallization from acetone–ether it melted at 247–249°, λ_{max}^{alc} 285–290 mμ (500).

Anal. Calcd. for $C_{29}H_{43}O_3N_2Cl$ (503.1): N, 5.57. Found: N, 6.21.

By-products in the Acetolysis of N-Acetyl-3-desoxy-3(α)-chlorotetrahydrojervine.—The fractions eluted with benzene–ether 9:1 and 4:1 in the chromatogram of the neutral acetolysis products of I were all crystalline. Recrystallized twice from acetone–ether this material afforded **22,26-imino-3α-chloro-13(17a)-jervene-17,23-diol-11-one 23,N-diacetate** (VIII) as needles, m.p. 237–239°, $[\alpha]^{23}D$ −43° (*c* 1.02); λ_{max}^{alc} 250 mμ (13,600), 358 mμ (78); λ_{max}^{nujol} 3.08, 5.78, 5.85 (doublet), 6.17, 7.95 μ.

Anal. Calcd. for $C_{31}H_{46}O_5NCl$ (548.1): C, 67.91; H, 8.46; N, 2.56; Cl, 6.47; 2 $COCH_3$, 15.7. Found: C, 68.08; H, 8.20; N, 2.13; Cl, 6.44; $COCH_3$, 12.5.

In another acetolysis experiment starting from 5 g. of I, 1.05 g. of II and 108 mg. of VIII were obtained. The material in the mother liquor from the crude crystals of II (790 mg.) was dissolved in hexane–benzene 9:1 and chromatographed on alumina (14 g.). There was isolated from the hexane–benzene 9:1 and 4:1 eluates 42 mg. of **17a,22,26-nitrilo-3α-chlorojervane-17,23-diol-11-one-17,23-diacetate (XI)** as prisms from ether–pentane, m.p. 239–242°, $[\alpha]^{25}D$ −61° (*c* 0.944); λ_{max}^{alc} 308 mμ (33); λ_{max}^{nujol} 3.45, 5.77, 5.81, 7.98 μ; no bands in 6–7 μ region.

Anal. Calcd. for $C_{31}H_{46}O_5NCl$ (548.1): C, 67.92; H, 8.46; N, 2.56; 2 $COCH_3$, 15.7. Found: C, 68.11; H, 8.26; N, 2.74; $COCH_3$, 14.0.

The same compound was obtained from the acetolysis product VIII by treatment with alkali and reacetylation. A solution of VIII (66 mg.) in 5% methanolic potassium hydroxide was allowed to stand at room temperature for 19 hours, then diluted with water and extracted 3 times with chloroform. The combined extracts were washed with 1 *N* hydrochloric acid and water, dried over sodium sulfate and brought to dryness. The residue (61 mg.) could not be crystallized, and was therefore acetylated with pyridine–acetic anhydride (room temperature, 20 hours). The crystalline product thereby obtained was recrystallized three times from methanol from which it formed rosettes of platelets (29 mg.) melting at 233–234° dec. It strongly depressed the melting point of the starting product VIII; when the melting point was taken in mixture with the sample of XI m.p. 239–242° which had been isolated directly from the acetolysis mixture two years previously, both specimens as well as the mixture melted at 220–222°, $[\alpha]^{22}D$ −65° (*c* 0.695), λ_{max}^{alc} 308 mμ (60); the infrared spectrum was identical over the entire measurable range with that of the preparation originally melting at 239–242°.

Anal. Found: C, 67.74; H, 8.26; $COCH_3$, 15.6; neut. equiv. (perchloric acid titration), 526.

In the above chromatogram compound XI was followed by another crystalline product appearing in the hexane–benzene 7:3 eluates (81 mg.). On recrystallization from ether–pentane it formed prisms (48 mg.), m.p. 202–204°, $[\alpha]^{25}D$ +70°. This compound exhibited no specific absorption in the ultraviolet range. Infrared spectrum: 5.77, 5.94, 6.13, 7.93 μ; no bands in 3 μ region.

Anal. Calcd. for $C_{33}H_{48}O_5NCl$ (574.2): C, 69.04; H, 8.43; N, 2.44; 3 $COCH_3$ 22.49, 2 $COCH_3$, 14.99. Found: C, 69.33; H, 8.34; N, 2.68; $COCH_3$, 15.2.

The sulfonic acid fraction, recovered as an amorphous sodium salt from the original chromatogram by elution with methanol, was not investigated in detail. Like the corresponding product in the 3-hydroxylated series it showed strong specific absorption at 248 mμ ($E_{1cm}^{1\%}$ 204). That this substance is the salt of a sulfonic acid and not of a sulfuric acid ester was confirmed by the observation that after treatment with 1 *N* sulfuric acid–methanol 1:1 at reflux temperature for one hour and isolation by extraction with chloroform, it remained readily soluble in water, and was precipitated from the aqueous solution as the free sulfonic acid on addition of mineral acid, as was the original product.

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