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C-10 SUBSTITUTED 19-NORSTEROIDS—VIII[1]

10-CYANOSTEROIDS WITH AN OXYGEN AT C-3

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Abstract—A synthetic sequence leading to 3-keto-10α-cyano steroids is described. A number of 10α-cyano and 10β-cyano ring A ketols have been prepared, and their rearrangements observed. The effect of the 10-cyano group on the rearrangement and conformation of ring A ketols is discussed.

INTRODUCTION of a cyano group into the angular C-10 position in steroids via hydrogen cyanide addition to $\Delta^{1(10)}$-2-ketones, has been described in the preceding papers.[3] The predominance of α substitution and the chemical versatility of the cyano group, make this synthetic sequence of particular interest for the preparation of heretofore inaccessible 5α,9α,10α-steroids with different C-10 substituents. The starting material employed in the hydrocyanation reaction yields products with oxygen at C-2 but none at C-3. In order to realize the full potential of this synthesis it was important to oxygenate C-3 while retaining the 10-cyano group. This had been achieved and in the course of the work information has been provided on some features of the chemistry of this novel steroid system.

Reaction of 17β-acetoxy-10α-cyano-5α-estran-2-one (I) with lead tetra-acetate under the mild conditions of Henbest,[4] yielded two isomeric compounds which could be separated by fractional crystallization. From previous experience with the 10α-methyl-2-ketone system[5] it was anticipated that lead tetraacetate attack would occur at C-3. The multiplet nature of the methine proton absorption of both isomers in the NMR spectrum eliminated the possibliity of C-1 acetoxylation for either compound since the C-1 proton absorption would then be a singlet. On the basis of stability considerations and NMR spectra, the major product m.p. 238–240° obtained in 40% yield was assigned the 2-oxo-10α-cyano-5α-estrane-3α,17β-diol diacetate (II) structure. The less abundant isomer m.p. 180–182°, obtained in 30% yield, was the epimeric 2-oxo-10α-cyano-5α-estrane-3β,17β-diol diacetate (III). Each of these isomers (II and III) rearranged to different extent when refluxed with potassium acetate in acetic acid,[6]

[1] Part VII: M. Torigoe and J. Fishman, *Tetrahedron* **21**, 3669 (1965). Part of this work was presented at the VI*th Pan-American Congress of Biochemistry and Pharmacology*. Mexico City, Dec. (1963).

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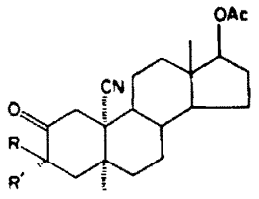
[3] M. Torigoe and J. Fishman, *Tetrahedron Letters* 1251 (1963); M. Torigoe and J. Fishman, *Tetrahedron* **21**, 3669 (1965).

[4] H. B. Henbest, D. N. Jones and G. P. Slater, *J. Chem. Soc.* 4472 (1961); J. D. Cocker, H. B. Henbest, O. H. Phillips, G. P. Slater and D. A. Thomas, *Ibid.* 6 (1965).

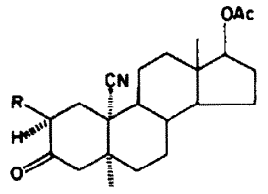
[5] J. A. Settepani, M. Torigoe and J. Fishman, *Tetrahedron* **21**, 3661 (1965).

[6] R. L. Clarke, K. Dobriner, A. Mooradian and C. M. Martin, *J. Amer. Chem. Soc.* **77**, 662 (1955).

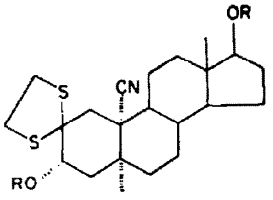
II was in part unchanged and in part converted to a different isomeric compound, (IV) m.p. 240–244°. Similar treatment of III gave a mixture of II and IV and none of the initial III was recovered. Thus both II and III rearranged to a similar mixture of II and IV. It is clear therefore that the more stable C-3-acetoxylated product is II which must



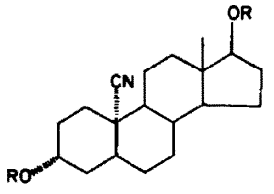
I R=R'=H
II R=H, R'=OAc
III R=OAc, R'=H



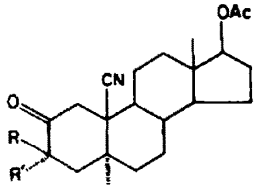
IV R=H
V R=OAc



VI a R=H
b R=CH_3CO



VII a R=H
b R=CH_3CO

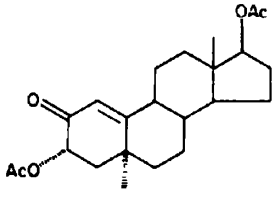


VIII R=R'=H
IX R=OAc, R'=H
X R=H, R'=OAc

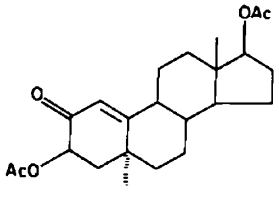
have the equatorial 3α-acetoxy structure based on a chair form of ring A; the compound III would then have the axial and epimeric 3β-acetoxy group. The isomer IV obtained from both II and III is the rearrangement product 3-oxo-10α-cyano-5α-estrane-2β,17β-diol diacetate (IV) and its structure is obtained from the following observations. Deacetoxylation of either II or III with zinc in acetic acid[7] gave 17β-acetoxy-10α-cyano-5α-estran-2-one (I) in excellent yield which confirms the location of C-2 ketone in both. Similar deacetoxylation of isomer IV gave a new cyano ketone, 17β-acetoxy-10α-cyano-5α-estran-3-one (V), the structure of which was established by the following synthesis. The more stable acetoxylation product II was converted to the thioketal (VIb) in adequate yield. In order to diminish hydrogenolysis during subsequent desulphurization,[8] the acetate was hydrolyzed to the free diol VIa. With Raney nickel in acetone VIa gave a 30% yield of 10α-cyano-5α-estrane-3α,17β-diol

[7] R. S. Rosenfeld and T. F. Gallagher, *J. Amer. Chem. Soc.* **77**, 4367 (1955).
[8] J. Fishman, *Chem. & Ind.* 1467 (1962).

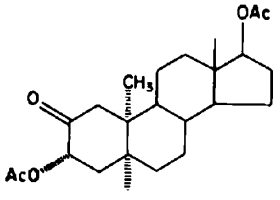
(VIIa) isolated as the diacetate (VIIb). Compound VIIb was identical with the diacetate of the borohydride reduction product of the ketone (V). This sequence not only served to confirm the structure of V but also demonstrated the equatorial nature of the C-3 hydroxy group in II, since this orientation was regenerated from the ketone by hydride reduction. A byproduct of the desulphurization of VIa was identified as an olefin with no other substituents in ring A. This compound was different from the olefin (XVI) obtained[3] from the desulphurization in acetone[9] of the thioketal of I and must therefore be the Δ^2 or Δ^3 olefin (XV). Hydrogenation of either XV or XVI leads to the same saturated compound (XVII) and establishes the isomeric nature of the two olefins. The nature of the precursor suggests that XV has the Δ^2 structure and hence XVI is the Δ^1 olefin, but these assignments must be regarded as tentative.



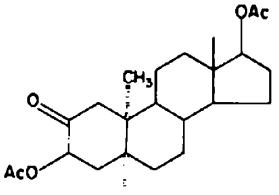
XI



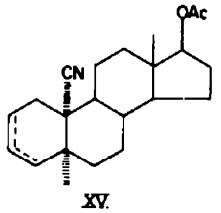
XII



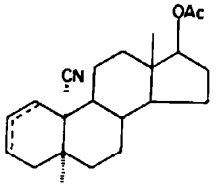
XIII



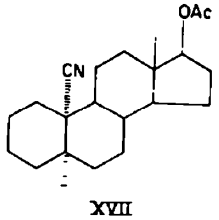
XIV



XV



XVI



XVII

Lead tetraacetate oxidation of 17β-acetoxy-10β-cyano-5α-estran-2-one (VIII), under the same mild conditions employed for I gave a mixture, from which one crystalline product was isolated in 50% yield. The new compound, m.p. 170° was unaltered by reflux with potassium acetate in acetic acid and on deacetoxylation

[9] J. Fishman, M. Torigoe and H. Guzik, *J. Org. Chem.* **28**, 1443 (1963).

afforded the starting material (VIII). It is therefore 2-oxo-10β-cyano-5α-estran-3β,17β-diol diacetate (IX), with an equatorial acetoxy group at C-3. Although the other product of the lead tetraacetate reaction was not obtained crystalline, its nature as a 3α-acetoxy epimer of IX was indicated from the NMR spectrum and by conversion to IX with potassium acetate in acetic acid. There was no indication of rearrangement of either IX or X to a 3-keto isomer under these conditions.

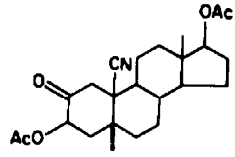
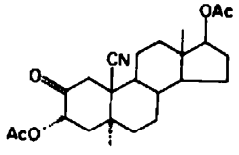
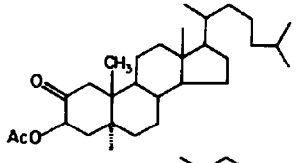
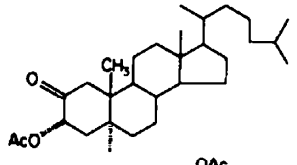
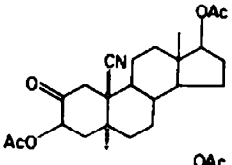
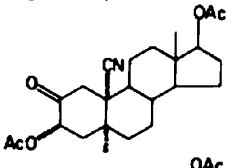
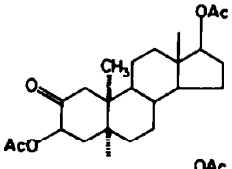
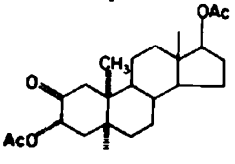
The above described reactions permit a relatively simple synthesis of 3-oxo-5α,9α,10α-steroids with various substituents at C-10. The sequence involves preparation of a mixture of the epimeric 10α-cyano-2-ketosteroids (II and III) which need not be separated since they both rearrange to the same 3-ketone (IV) from which compound V is obtained by deacetoxylation. An alternative and particularly attractive procedure for obtaining C-3 oxygenated 10-cyanosteroids would be the introduction of the cyano group into a molecule already bearing the desired C-3 oxygen substituent. Fortunately suitable substrates for this reaction 2-oxo-5α-estra-1 (10)-en-3α,17β-diol diacetate (XI) and the 3β isomer (XII) were available.[10] Reaction of XI with potassium cyanide in the presence of ammonium chloride[11] proceeded rapidly as indicated by a 90% decrease in the UV absorption at 239 mμ after 45 min. After acetylation only one product, identical with IV, was obtained in about 60% yield. Interestingly, no 10β-cyano products could be identified, suggesting that the hydrocyanation of XI is unusually stereoselective. The initial product of the hydrocyanation is presumably II which under the alkaline conditions rearranged to IV. This was confirmed by exposure of II and III to the hydrocyanating conditions, with rearrangement to IV in both instances.

Similar hydrocyanation of the 3β-acetoxy compound (XII) gave different results. Addition of the cyanide ion proceeded much more slowly than with XI. A 50% decrease in UV absorption at 237 mμ was observed after 45 min and after 3 hr, when the reaction was interrupted, the extinction coefficient showed that 25% of XII had failed to react. Chromatography of the acetylated crude product, in addition to a 25% recovery of XII, gave approximately equal (25%) amounts of the 10α-cyano compound (IV) and the 10β-cyanosteroid (IX). The contrast in stereoselectivity and reaction rate between the 3α and 3β-acetoxy compounds (XI and XII) is noteworthy. The axial 3α-acetoxy group in XI is in a position to assist α-cyanation at C-10 by either complexing with the cyanide ion or polarization of the double bond. This possibility does not exist in the β-acetoxy structure (XII) and may account for the slower rate and lessened stereoselectivity.

The NMR spectra of the ring A ketols described in this and previous papers provide valuable information of the effects of the 10-cyano group on the ring A conformation. The resonance of the methine proton on the carbon bearing the acetoxyl group in ring A is of primary interest. In Table 1 are listed the pertinent NMR values found for the various compounds. Comparison of the 10β-cyano compounds (IX and X) with the values of the corresponding cholestane ketols obtained by Williamson and Johnson[12] shows that the only significant effect of the cyano group is a deshielding of the C-3 proton to shift its resonance downfield. The coupling constants and even the shape of the multiplets are almost identical. This agreement between the

[10] J. Fishman, *J. Org. Chem.* **28**, 1529 (1963).
[11] W. Nagata, S. Hirai, H. Itazaki and K. Takeda, *J. Org. Chem.* **26**, 2413 (1961).
[12] K. L. Williamson and W. S. Johnson, *J. Amer. Chem. Soc.* **83**, 4623 (1961).

TABLE 1

Compound	J*		Chemical shift		
	H_2,H_{4a}	H_2,H_{4e}	H_3	18-Methyl	19-Methyl
	13·5	6·0	318	52	
	3·0	3·0	305	52	
	13·0	6·2	300		41
	2·5	2·5	280		41
	7·7	5·4	326	48·5	
	12·5	8·5	321	47·5	
	6·0	3·0	307	46·0	59·0
	12·0	8·0	321	47·5	64·5

* Coupling constants J are expressed in c/s and are accurate to ±0·5 c/s.

** Chemical shifts are expressed in c/s downfield from tetramethylsilane at 0·0 c/s and are accurate to ±1 c/s.

10β-cyano and 10β-methyl compounds is important since it indicates that the conformation of ring A in IX and X is closely comparable with the cholestane ketols[13] and that the 10-cyano group per se does not induce changes in the C-3 proton resonance pattern. Some correspondence exists also between the 10α-cyano-3α-acetoxy derivative (II) and the 10α-methyl compound (XIII[5]) although the shape of the multiplets is not superimposable. However, the 3α proton resonance in the 10α-cyano-3β-acetoxy compound (III) differs from the 10α-methyl compound (XIV) more markedly. It is suggested that in III the steric interaction of the axial 3β-acetoxy group with the 6β-hydrogen is relieved by a change to a partial boat or half-chair conformation of ring A. This change in conformation of III is aided by two factors which distinguish it from the 10α-methyl compounds. The dipole repulsion of the carbonyl and cyano groups[14] is relieved by this conformational change, and the 3α hydrogen, now in a partial axial position, interacts less with the sterically smaller cyano group than it does with the 10α-methyl group in XIV. The larger coupling constants observed in III compared to XIV are in agreement with the greater axial character of the 3α proton in this partial boat conformation. The greater stability of III as contrasted with XIV also suggests some relief of strain. It is pertinent to note that the orientation of the acetoxy group at C-3 in the 10α compounds affects the chemical shifts of the C-19 and, to a lesser extent, the C-18 methyl groups, a finding not observed in the 10β-methyl series.[12]

The rearrangement of the 2-keto compounds (II and III) to the 3-ketone (IV) under mild conditions requires comment since it was not observed in the corresponding 10α-methyl compound (XIII). The rearrangement presumable proceeds, through a cyclic intermediate of the type postulated in similar instances.[15] The products resultant, then, are dependent on the relative ease of formation of the intermediate and on the relative stability of the isomers that can form when the intermediate collapses. In compounds II and III there are two main factors of destabilization, which are lacking in the rearranged product IV. One is the interaction between the dipoles of the C-2 ketone and 10-cyano groups; the other is the severe non-bonded interaction of the 3β substituent and the 6β hydrogen. Thus both factors operate to favour formation of IV. Although in the case of the 10α-methyl derivative (XIII) the 3β,6β non-bonded interaction is present, the first factor is lacking and therefore XIII does not rearrange under these conditions. The 10β-cyano compounds (IX and X) on the other hand, have the dipole repulsion but the 3β,6β interaction is absent and therefore there was also no rearrangement under the mild reaction conditions.[16]

EXPERIMENTAL[17]

Lead tetracetate acetoxylation of I

To a solution of 900 mg I in 36 ml glacial acetic acid was added 3·6 ml freshly distilled BF_3-etherate and 1·29 g purified lead tetracetate. After standing at room temp for 1 hr an additional 3·6 ml BF_3-etherate was added, and the mixture allowed to stand for another hr, after which it was poured into 200 ml cold ether. The ether solution was cautiously washed with $NaHCO_3$aq to neutrality and then

[13] The conformations suggested[18] for ring A in the cholestane ketols are open to some question [D. H. Williams and N. S. Bhacca, *J. Amer. Chem. Soc.* **86**, 2472 (1964)]. Therefore no actual conformations are implied for the 10β-cyano derivatives IX and X, only that their ring A conformation is coincident with that of the corresponding cholestane ketols whatever these may be.

[14] A. D. Cross and I. T. Harrison, *J. Amer. Chem. Soc.* **85**, 3223 (1963).

[15] R. Wenger, H. Dutler, H. Wehrli, K. Schaffner and O. Jeger, *Helv. Chim. Acta* **45**, 2420 (1962).

[16] In case of strongly enolizing conditions rearrangement may very well occur. L. F. Fieser and R. Stevenson, *J. Amer. Chem. Soc.* **76**, 1728 (1954).

with water. After drying and evaporation the oily residue was crystallized from MeOH to give 386 mg *2-oxo-10α-cyano-5α-estrane-3α,17β-diol diacetate* (II) m.p. 234–240°. The mother liquors were taken to dryness and the residue recrystallized once from acetone–pet. ether to yield 283 mg *2-oxo-10α-cyano-5α-estrane-3β,17β-diol diacetate* (III) m.p. 178–180°. The remaining mother liquor by IR analysis represented a mixture of II and III in approximately equal amounts.

The analytical sample of II was obtained from MeOH and melted 236–240° $[\alpha]_D^{25}$ −24°. The NMR spectrum showed 3 proton resonances at 47·5 c/s (18 CH_3), 122 c/s (17 acetate), 129 c/s (3 acetate). A one proton quartet (3βH) was at 321 c/s (J = 12·5, 8·5). IR spectrum showed bands at 1737, 1749 cm^{-1} for carbonyl and 2220 cm^{-1} (CN). (Found: C, 69·08; H, 7·92; N, 3·21. Calc. for $C_{28}H_{31}O_6N$: C, 68·80; H, 7·78; N, 3·49%.)

The analytical sample of III melted 178–180° $[\alpha]_D^{24}$ −68°. NMR 3 proton singlets at 49 c/s (18 CH_3), 122 c/s (17 acetate), 126 c/s (3β acetate). One proton quartet at 326 c/s J = 7·7, 5·4 (3αH). IR bands at 1733, 1747 cm^{-1} (carbonyl) and 2229 cm^{-1} (CN). (Found: C, 68·87; H, 7·66; N, 3·29. Calc. for $C_{28}H_{31}O_6N$: C, 68·80; H, 7·78; N, 3·49%.)

Lead tetracetate acetoxylation of VIII

A 240 mg sample of VIII was reacted with lead tetracetate exactly as above except that the reaction was allowed to continue for 4 hr. The product isolated was an oil which resisted crystallization. The NMR spectrum of the crude product exhibited resonances at 52 c/s (18 CH_3), 122 c/s (17β acetate), 127 c/s (3β acetate) and a quartet at 318 c/s, J = 6·0, 13·5 (3αH) which could be assigned to IX and resonances at 129 c/s (3α-acetate) and a poorly resolved triplet at 306 c/s (3βH) which could be assigned to X.

Chromatography on acid washed alumina and elution with benzene gave 156 mg *2-oxo-10β-cyano-5α-estrane-3β,17β-diol diacetate* (IX) m.p. 165–172°. Recrystallization from acetone–pet. ether raised the m.p. to 168–172°. NMR exhibited resonances at 51 c/s, 122 c/s, 127 c/s and a quartet at 318 c/s. IR carbonyl absorption at 1720, 1735, 1754 cm^{-1}, Cyanide at 2230 cm^{-1}. (Found: C, 69·18; H, 7·87; N, 3·55. Calc. for $C_{28}H_{31}O_6N$: C, 68·80; H, 7·78; N, 3·49%.) Further elution with benzene gave mixtures of IX and X which on repeated chromatography provided essentially pure IX due to the rearrangement of X on the alumina. The purest sample of *2-oxo-10β-cyano-5α-estrane-3α,17β-diol diacetate* (X) still resisted crystallization, and its NMR spectrum exhibited resonances at 51 c/s (18 CH_3), 122 c/s (17 acetate), 129 c/s (3α acetate) and multiplet at 306 c/s (3βH).

Potassium acetate-acetic acid rearrangements

(a) *Rearrangement of* II. A mixture of 100 mg of II and 500 mg potassium acetate in 30 ml acetic acid was refluxed for 17 hr. The acetic acid was removed *in vacuo*, water was added and the mixture was extracted with $CHCl_3$, which was washed with $NaHCO_3$aq and then water, dried and evaporated. The crystalline residue was separated into two compounds by preparative TLC on silica in the system ethyl acetate–cyclohexane 1:1. The major product weighing 72 mg was recrystallized from acetone–pet. ether to give *3-oxo-10α-cyano-5α-estrane-2β,17β-diol diacetate* (IV) m.p. 240–243°, depressed on admixture with II to 211–240°.

The analytical sample melted 242–245° $[\alpha]_D^{24}$ −40°. Pertinent IR absorptions were present for ketone at 1738 cm^{-1} and cyanide 2235 cm^{-1}.

The NMR spectrum exhibited bands at 48·5 c/s (18 CH_3), 123 c/s (17 acetate) 130 c/s (2β acetate) and 1 proton quartet at 330 c/s J = 12·5, 7·5 (2αH). (Found: C, 68·87; H, 7·82; N, 3·24. Calc. for $C_{28}H_{31}O_6N$: C, 68·80; H, 7·78; N, 3·49%.)

The second component of the mixture consisted of 20 mg of recovered starting material II.

(b) *Rearrangement of* III. A 50 mg sample of III was treated exactly as above with potassium acetate in acetic acid, to give 28 mg IV m.p. 240–245° and 10 mg II m.p., 234–240°. No starting material could be isolated or was observed.

(c) *Rearrangement of* X. A 50 mg sample of the noncrystalline X containing some of the isomeric

[17] The mps. were determined on a Kofler block and are corrected. Rotations were obtained in $CHCl_3$. The NMR spectra were obtained on a Varian A60 instrument at 60 Mc in $CDCl_3$ solution. Values are quoted in c/s downfield from tetramethylsilane as an internal standard at 0 c/s. IR spectra were obtained in KBr and are not corrected. The analyses are by Spang Microanalytical Laboratory, Ann Arbor, Mich.

compound IX was reacted with potassium acetate and acetic acid as above. Upon workup 45 mg *2-oxo-10β-cyano-5α-estrane-3β,17β-diol diacetate* (IX) m.p. 165–170° was obtained. TLC of the mother liquors did not show the presence of any of the starting material X.

Zinc–acetic acid deacetoxylation

(a) *Of compound* II. A mixture of 25 mg II and 2 g Zn dust in 3 ml acetic acid containing 0·2 ml acetic anhydride was refluxed for 17 hr. The Zn was filtered off, washed with EtOH and the combined filtrates were taken to dryness *in vacuo*. The residue was purified by preparative TLC on silica in the system 70% cyclohexane–30% ethyl acetate to give 11 mg I m.p. 198–201°, identical in all respects with the authentic material.[8]

(b) *Of compound* IV. A 35 mg sample of IV was deacetoxylated exactly as above. TLC separation gave in addition to 8 mg starting material, 16 mg of *17β-acetoxy-10α-cyano-5α-estrane-3-one* (V) m.p. 145–148° from MeOH. The IR spectrum of V exhibited bands at 1720, 1730 cm^{-1} (carbonyl) and 2238 cm^{-1} (cyanide). The NMR spectrum showed resonances at 48 c/s (18 CH_3) and 123 c/s (17β Acetate). (Found: C, 73·81; H, 8·46. Calc. for $C_{21}H_{29}O_2N$: C, 73·43; H, 8·51%.)

Hydrocyanation of 2-oxo-5α-estra-1 (10)-ene-3α,17β-diol diacetate (XI)

A mixture of 500 mg XI, 195 mg KCN and 140 mg NH_4Cl in 7 ml MeOH and 2 ml water was refluxed for 45 min at which time the UV absorption at 239 mμ decreased 90%. Water was then added and the mixture was extracted with ethyl acetate which was washed with water, dried and evaporated. The residue was acetylated overnight with acetic anhydride in pyridine. After workup, the material was crystallized from MeOH and gave 237 mg of *3-oxo-10α-cyano-5α-estrane-2β,17β-diol diacetate* (IV) m.p. 237–243°. The mother liquor on concentration yielded an additional 41 mg IV. The remaining mother liquor residue was chromatographed on alumina and gave an additional 46 mg IV but no other crystalline products.

Hydrocyanation of 2-oxo-5α-estra-1-(10)-en-3β,17β-diol diacetate (XII)

A 350 mg sample of XII was reacted with KCN as described above. At the end of 45 min the UV absorption at 237 mμ had decreased by 50% and when the reaction was stopped after 3 hr, it had decreased by 75%. The reaction product was obtained and acetylated as described above. The product after acetylation could not be crystallized and was chromatographed on 20 g acid washed alumina. Elution with 2:1 pet. ether–benzene gave 100 mg starting material (XII). Elution with benzene gave 80 mg of IV m.p. 235–240°. Further elution with benzene–$CHCl_3$ 2:1 gave 74 mg of IX m.p. 165°–172°.

2,2-Ethylenedithio-10α-cyano-5α-estrane-3α,17β-diol diacetate (VIb)

A solution of 303 mg II in 9·5 ml acetic acid containing 1·2 ml ethanedithiol and 1·2 ml BF_3-etherate was allowed to stand for 30 min at room temp. It was then poured into ice cold water and extracted with $CHCl_3$, which was washed with $NaHCO_3$aq and water, dried and evaporated to leave 360 mg crystals. Two recrystallizations from acetone–pet. ether gave 283 mg VIb as the analytical sample m.p. 268–270°, $[\alpha]_D^{28}$ +16°. (Found: C, 62·73; H, 7·08; N, 2·92. Calc. for $C_{25}H_{35}O_4NS_2$: C, 62·87; H, 7·39; N, 2·93%.)

2,2-Ethylenedithio-10α-cyano-5α-estrane-3α,17β-diol (VIa)

A solution of 250 mg VIb in 20 ml 0·1 N methanolic KOH was stirred at room temp for 7 hr, and then added to an excess of ice cold 5% H_2SO_4aq. The product was extracted into $CHCl_3$ which was washed with water, dried and evaporated. The crystalline residue weighed 216 mg m.p. 227–233°. The analytical sample of VIa was obtained from ethyl acetate and melted 234–237°, $[\alpha]_D^{28}$ +40°. (Found: C, 64·28; H, 8·10. Calc. for $C_{21}H_{31}O_2NS_2$: C, 64·10; H, 7·94%.)

Raney nickel desulphurization of VIa

A mixture of 110 mg VIa and about 3·0 g Raney Ni (W2) in 200 ml acetone was refluxed for 24 hr. The catalyst was filtered off and washed with acetone. The solvent was removed by evaporation and the oily residue was acetylated overnight. After the usual workup the product was chromatographed on acid washed alumina. Elution with pet. ether–benzene 1:4 gave 15 mg crystals

which were recrystallized from MeOH to give 10 mg XV, m.p. 130–134°, showing unsaturation bands in the IR at 1660 cm^{-1}. Compound XV was different from the acetate of the olefin XVI m.p. 150–152° obtained from the desulphurization of 2,2-ethylenedithio-10α-cyano-5α-estrane-17β-ol.[3] The analytical sample of XV melted 132–134°. (Found: C, 77·14; H, 8·84. Calc. for $C_{31}H_{39}O_3N$: C, 77·02; H, 8·93%.)

Further elution with the same solvent gave 18 mg crystals, which were recrystallized from MeOH to give 12 mg *10α-cyano-5α-estrane-3α,17β-diol diacetate* (VII) m.p. 149–151°, $[\alpha]_D^{23}$ +10°. (Found: C, 71·84; H, 8·78; N, 3·21. Calc. for $C_{23}H_{33}O_4N$: C, 71·29; H, 8·58; N, 3·61%.)

$NaBH_4$ *reduction of* V

A 10 mg solution of V in 5 ml EtOH was stirred with 10 mg $NaBH_4$ for 1 hr at room temp. The product isolated by the usual workup, was acetylated overnight to give after crystallization from MeOH 6 mg of VII m.p. 146–150° undepressed on admixture with that prepared by the other route. The IR spectra were also identical.

Hydrogenation of XV

A 8 mg sample of XV was hydrogenated for 15 min in 3 ml EtOH over 8 mg 10% PdC. Filtration of the catalyst and evaporation gave a crystalline residue which was recrystallized from MeOH for analysis to give 5 mg of *17β-acetoxy-10α-cyano-5α-estrane* (XVII) m.p. 156–157°, showing the presence of the cyano band in the IR at 2210 cm^{-1} and no unsaturation band. The saturated compound (XVII) was identical in all respects with that obtained by the reduction of XVI.[3]

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