[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF THE UPJOHN COMPANY]

Bisnor-5-cholenaldehyde Cyanohydrins

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The crystalline aldehydes prepared by the ozonization of acetoxy, methoxy and benzyloxy derivatives of stigmasterol were obtained by precipitation of the corresponding bisulfite addition products.[1] Since it was found that these bisulfite complexes were almost quantitatively converted to the corresponding cyanohydrins, these readily became available for dehydration studies looking to the removal of the elements of water at C-20 and C-22.

The cyanohydrin (V) prepared from 3β-acetoxybisnor-5-cholenaldehyde (I) was dehydrated indirectly, *via* the 22-bromo derivative (VIII), which was dehydrohalogenated upon refluxing with dry piperidine, thus giving a mixture of the *cis* and *trans* isomers of 22-cyanobisnor-5,20:22-choladiene-3β-ol acetate (XII and XIV). This mixture proved difficult to separate into its component isomers, but, upon saponification, the resulting mixture of hydroxydiene-nitriles was fractionally crystallized to yield the pure *cis* and *trans* forms (XIII and XV). Acetylation of these isomers gave pure *cis*- and *trans*-acetates (XII and XIV), both of which, upon treatment with one equivalent of bromine and ozonizing, gave excellent yields of 5-pregnene-3β-ol-20-one acetate (XX). This almost quantitative conversion to XX indicates the specificity with which the bromine addition takes place in the nucleus double bond, leaving the conjugated nitrile side chain free for degradation studies.

The key compound, 3β-acetoxybisnor-5-cholenaldehyde cyanohydrin (V), is probably a mixture of epimeric alcohols which were not separated. In the course of several dehydration experiments the cyanohydrin was further characterized by the preparation of several esters, *i. e.*, 22-cyanobisnor-5-cholene-3β,22-diol diacetate (VI), 22-cyanobisnor-5-cholene-3β-22-diol 3-acetate 22-tosylate (VII), 22-cyano-22-chlorobisnor-5-cholene-3β-ol acetate (IX) and the corresponding 22-bromo compound (VIII). The above halogenated compounds resulted from attempts to dehydrate the cyanohydrin directly by heating with phosphorus oxychloride and phosphorus oxybromide in tertiary bases such as pyridine.[2]

When dehydrohalogenation of the 22-bromo derivative (VIII) was attempted by refluxing with dimethylaniline, reduction occurred and the resulting product proved to be 22-cyanobisnor-5-cholene-3β-ol acetate (X). This saturated nitrile showed no ultraviolet absorption, while the *cis*- and *trans*-22-cyanobisnor-5,20:22-choladiene-3β-ols (XIII and XV) showed ultraviolet absorption peaks at 225.5 mμ for the isomer melting at 234° and 222.5 mμ for the diene melting at 195°.

For further characterization of 22-cyanobisnor-5-cholene-3β-ol acetate (X) it was converted by mild saponification to 22-cyanobisnor-5-cholene-3β-ol (XI), and, upon refluxing with strong alcoholic potassium hydroxide, the 3β-hydroxynor-5-cholenic acid amide (XVIII) resulted. When this acid amide was refluxed with acetic anhydride the corresponding 3β-acetoxy acid amide (XVII) was obtained, accompanied by some 22-cyanobisnor-5-cholene-3β-ol acetate (X). When the 3-hydroxy acid amide (XVIII) was subjected to the Oppenauer oxidation the expected 3-ketonor-4-cholenic acid amide (XIX) was obtained.

Upon heating 22-cyano-22-bromobisnor-5-cholene-3β-ol acetate with zinc and acetic acid the same nitrile (X) was obtained as in the dimethylaniline reaction.

In an attempt to prepare the cyanohydrin of nor-5-cholene-3β-ol-22-one acetate[3] it was found that the latter did not react with hydrogen cyanide.

Experimental[4]

Failure of Hydrogen Cyanide to React with Nor-5-cholene-3β-ol-22-one.—This ketone[3] quantitatively formed a semicarbazone (m. p. 235–237°) in the presence of pyridine.[5] However, when heated in a sealed tube with anhydrous hydrogen cyanide or when refluxed with a large excess of potassium cyanide in glacial acetic acid, the ketone was quantitatively recovered.

3β-Methoxybisnor-5-cholenaldehyde Cyanohydrin (III).—3β-Methoxybisnor-5-cholenaldehyde (II) bisulfite addition complex[1] (1.08 g.) was mixed to a paste with 2.0 ml. of water. To this was added 2.0 ml. of an aqueous solution containing 1.0 g. of potassium cyanide and the mixture was stirred for ten minutes; 20 ml. of water was added and the precipitate filtered off and washed with water until neutral. It was then washed with a little glacial acetic acid and finally with methanol. When dried it weighed 0.7 g., m. p. 195–205° (dec.). Recrystallized from acetic acid, it melted at 200–205° (dec.).

Anal. Calcd. for $C_{24}H_{37}O_2N$: C, 77.57; H, 10.04; N, 3.77. Found: C, 77.31; H, 9.74; N, 3.76.

22-Cyano-22-chlorobisnor-5-cholene-3β-ol methyl ether (IV) was prepared by refluxing 0.30 g. of the cyanohydrin (III) with 0.6 ml. of phosphorus oxychloride and 4.0 ml. of lutidine for ten minutes. Upon pouring the mixture onto ice and concentrated hydrochloric acid, extraction with ether, washing the ether solution with water, sodium bicarbonate solution, water, and drying over sodium sulfate, recrystallizing the residue from dilute acetone and 95% ethanol, the chloro compound was obtained in needles, m. p. 169–171°.

Anal. Calcd. for $C_{24}H_{36}ONCl$: Cl, 9.09; N, 3.59. Found: Cl, 9.75; N, 3.82.

3β-Acetoxybisnor-5-cholenaldehyde Cyanohydrin (V).—The bisulfite addition compound of this aldehyde (I)[1]

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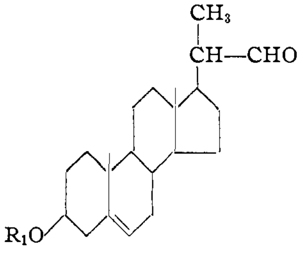
[1] Centolella, Heyl and Herr, THIS JOURNAL, **70**, 2953 (1948).

[2] Butenandt and Schmidt-Thome, *Ber.*, **71**, 1490 (1938); U. S. Patent 2,270,409 (1942).

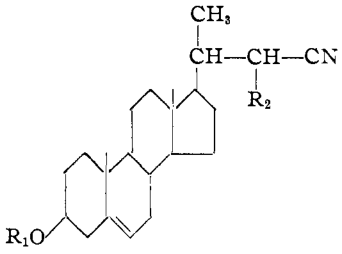
[3] Julian and Cole, THIS JOURNAL, **67**, 1369 (1945).

[4] Melting points are corrected. Analyses, rotations and ultraviolet absorption spectra by the Upjohn microanalytical and physics personnel.

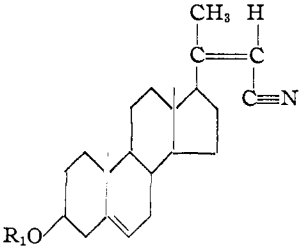
[5] Hopper and Wilson, *J. Chem. Soc.*, 2483 (1928).



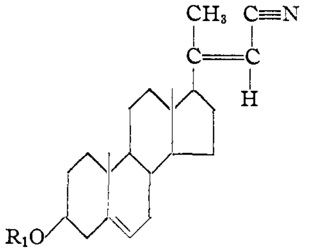
I, R_1 = Ac
II, R_1 = CH_3



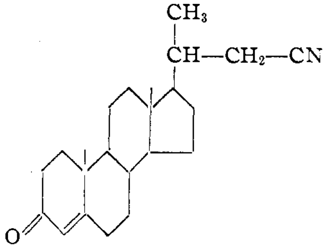
III, R_1 = CH_3, R_2 = OH
IV, R_1 = CH_3, R_2 = Cl
V, R_1 = Ac, R_2 = OH
VI, R_1 = Ac, R_2 = OAc
VII, R_1 = Ac, R_2 = OTs
VIII, R_1 = Ac, R_2 = Br
IX, R_1 = Ac, R_2 = Cl
X, R_1 = Ac, R_2 = H
XI, R_1 = R_2 = H



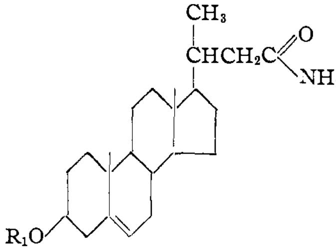
XII, R_1 = Ac
XIII, R_1 = H



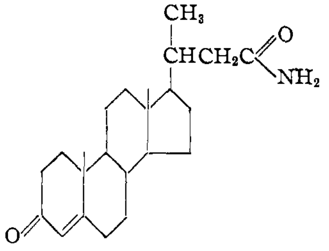
XIV, R_1 = Ac
XV, R_1 = H



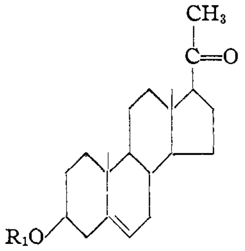
XVI



XVII, R_1 = Ac
XVIII, R_1 = H



XIX



XX, R_1 = Ac
XXI, R_1 = H

(4.19 g.) was finely ground and mixed with 160 ml. of water. The suspension was warmed on a steam-bath for five minutes and, while stirring, a solution of 2.0 g. of potassium cyanide in 40 ml. of water was added dropwise and the reaction allowed to proceed two hours at room temperature. The product was extracted many times with ether, the combined ether solution washed with water and dried over sodium sulfate. Upon evaporation of the solvent there was obtained 2.96 g. (84% yield) of fine needles, m. p. 174–178°. Recrystallized from methanol it melted at 165–170°.

Anal. Calcd. for $C_{25}H_{37}O_3N$: C, 75.15; H, 9.33; N, 3.51. Found: C, 74.90; H, 9.35; N, 3.52.

22-Cyanobisnor-5-cholene-3β,22-diol Diacetate (VI).—Five-tenths gram of 3β-acetoxycyanohydrin (V) was heated with 5 ml. of acetic anhydride to 100° for sixty minutes and the temperature raised to 130–140° for sixty minutes. The acetic anhydride was removed under reduced pressure. Recrystallization first from dilute acetone and finally from hexane gave the nicely crystalline diacetate, m. p. 185–187°.

Anal. Calcd. for $C_{27}H_{39}O_4N$: C, 73.44; H, 8.90; N, 3.17. Found: C, 73.42; H, 8.76; N, 3.18.

22-Cyanobisnor-5-cholene-3β,22-diol 3-Acetate 22-Tosylate (VII).—Twenty-four hundredths gram of 3β-acetoxycyanohydrin (V) was dissolved in 1 ml. of dry pyridine and 0.25 g. of *p*-toluenesulfonyl chloride was added. The mixture was heated for two minutes and allowed to stand at room temperature for twenty hours. The partially solidified mass was mixed with ether and the insoluble tosylate was filtered off. The yield was 0.15 g. and the melting point 237° with decomposition. It recrystallized from acetone in stout rods that melted at 240°.

Anal. Calcd. for $C_{32}H_{43}O_5NS$: C, 69.41; H, 7.83; N, 2.53; S, 5.79. Found: C, 69.67; H, 7.57; N, 2.79; S, 5.61.

When the tosylate was vigorously refluxed with pyridine, dimethylaniline, collidine and a solution of toluene and phenol,[6] the starting material was recovered unchanged.

22-Cyano-22-chlorobisnor-5-cholene-3β-ol Acetate (IX).—Two hundred and fifty milligrams of the above 3β-acetoxycyanohydrin (V) was dissolved in 3 ml. of lutidine and 0.5 ml. of phosphorus oxychloride was added. This reaction mixture was refluxed gently for ten minutes, cooled and poured upon a mixture of ice and concentrated hydrochloric acid. The reaction product was extracted with ether. The ether solution was washed with water, sodium bicarbonate solution, water and dried over sodium sulfate. Upon evaporation, a white crystalline residue weighing 250 mg. was obtained which melted at 178–180°. Upon recrystallization from methanol the long needles melted at 187–188°.

Anal. Calcd. for $C_{25}H_{36}O_2NCl$: C, 72.03; H, 8.68; N, 3.35; Cl, 8.48. Found: C, 72.00; H, 8.59; N, 3.72; Cl, 8.12.

22-Cyano-22-bromobisnor-5-cholene-3β-ol Acetate (VIII).—One gram of 3β-acetoxycyanohydrin (V) in 10 ml. of dry pyridine was added dropwise, with stirring, to a mixture of 1.0 g. of phosphorus oxybromide in 10 ml. of dry pyridine. The mixture was heated twenty minutes in an oil-bath, slowly raising the temperature to 105°. Upon cooling it was poured, with stirring, into a mixture of 30 ml. of concentrated hydrochloric acid and ice and extracted several times with ether. The ether solution was washed with water, saturated sodium bicarbonate solution and water and dried over sodium sulfate. Upon evaporation, there remained 1.04 g. of needles, m. p. 199–203°, which upon recrystallization from chloroform–methanol melted at 206–208°.

Anal. Calcd. for $C_{25}H_{36}O_2NBr$: Br, 17.28. Found: Br, 17.26.

Experiments on Dehydrohalogenation of the Bromo- and Chloronitriles.—Since it was found that direct dehydration of 3β-acetoxybisnor-5-cholenaldehyde cyanohydrin was not effected even upon prolonged refluxing with phosphorus oxychloride or phosphorus oxybromide in pyridine the following dehydrohalogenation experiments were tried.

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[6] Heyl, Herr and Centolella, THIS JOURNAL, 71, 247 (1949).

A. With Lutidine.—Fifty milligrams of the 22-cyano-22-bromo acetate (VIII) was refluxed in 4 ml. of lutidine (b. p. 142–146°) for two and one-half hours when the starting material was recovered unchanged.

B. With Dimethylaniline. Preparation of 22-Cyanobisnor-5-cholene-3β-ol Acetate (X).—Forty-three hundredths gram of the 22-bromonitrile (VIII) was refluxed one hour in 20 ml. of redistilled dimethylaniline. The mixture was cooled and poured, with stirring, into 25 ml. of concentrated hydrochloric acid and ice. This was extracted with ether, and the ether solution, after the usual washes with sodium bicarbonate solution and water and drying, gave 0.375 g. of slightly yellow, halogen free crystalline residue. This was taken up in 15 ml. of hexane and passed through a column of 15 g. of activated alumina. The column was eluted with 350 ml. of benzene. The combined eluate, upon removal of solvent, gave 0.31 g. (86%) of colorless crystals, m. p. 180–182°, which upon recrystallization from hexane and drying *in vacuo* at 100° melted at 186–187°. This substance has resulted from the reduction[7,8] of the bromo compound and agreed upon analysis with the requirements of 22-cyanobisnor-5-cholene-3β-ol acetate (X).

The same compound resulted in quantitative yield when the 22-bromo-derivative (VIII) was refluxed with zinc dust and acetic acid.

Anal. Calcd. for $C_{25}H_{37}O_2N$: C, 78.29; H, 9.72; N, 3.65. Found: C, 78.37; H, 9.80; N, 3.64.

When 0.4 g. of X in chloroform was treated with one equivalent of bromine and ozonized for thirty-nine minutes (10.8 mg. ozone per minute) and the product debrominated in the usual manner, unchanged starting material was recovered.

22-Cyanobisnor-5-cholene-3β-ol (XI).—The acetate (X) (260 mg.) was saponified by refluxing one-half hour with two molecular equivalents of potassium carbonate, 15 ml. methanol and a few drops of water. Upon working up the product it was crystallized from benzene–hexane forming plates, m. p. 190°.

Anal. Calcd. for $C_{23}H_{35}ON$: C, 80.88; H, 10.33; N, 4.10. Found: C, 81.03; H, 10.22; N, 4.21.

22-Cyanobisnor-4-cholene-3-one (XVI).—The above hydroxynitrile (XI) (0.59 g.) was dissolved in 60 ml. of toluene and 30 ml. of cyclohexanone. While distilling, a solution of 0.6 g. of aluminum isopropoxide in 15 ml. of toluene was added dropwise over fifteen minutes. To the cooled mixture was added 10 ml. of sodium potassium tartrate solution and the volatile material was removed by steam distillation. The ketone residue was taken up in ether, washed with water and dried over sodium sulfate. The nicely crystalline residue from the ether weighed 0.57 g. This was recrystallized from benzene–hexane and isopropyl ether to a constant melting point, 171–172° (rectangular plates).

Anal. Calcd. for $C_{23}H_{33}ON$: C, 81.35; H, 9.80; N, 4.13. Found: C, 81.30; H, 9.58; N, 4.09; $[\alpha]^{24}\text{D}$ + 104.8 (0.0739 g. made up to 10 ml. with chloroform, $\alpha^{24}\text{D}$ + 0.775, l, 1 dm.).

3β-Hydroxynor-5-cholenic Acid Amide (XVIII).—22-Cyanobisnor-5-cholene-3β-ol acetate (X) (0.86 g.) was taken up in 35 ml. of hot ethanol and a solution of 5 g. of potassium hydroxide in 15 ml. of water was added. After refluxing for fifteen hours the solution was poured into water. The mixture was acidified with 20% sulfuric acid and the precipitate collected by centrifuging. It was washed with water, dried and recrystallized from benzene–chloroform from which it separated in long needles weighing 0.61 g. and melting at 250–255° (dec.). For analysis it was recrystallized from acetone until a constant m. p. 268–270° (dec.) resulted.

Anal. Calcd. for $C_{23}H_{37}O_2N$: C, 76.83; H, 10.38; N, 3.91. Found: C, 76.84; H, 10.05; N, 4.09.

3β-Acetoxynor-5-cholenic Acid Amide (XVII).—Five-tenths gram of the above acid amide (XVIII) was refluxed seventy-five minutes in 10 ml. of acetic anhydride. The anhydride was removed *in vacuo* on the steam-cone and the residue was dissolved in 25 ml. of benzene and passed over a column of 15 g. of activated alumina. Upon elution with 300 ml. of benzene the first three fractions of 40 ml. each gave 0.25 g. of 22-cyanobisnor-5-cholene-3β-ol acetate (X), m. p. and mixed m. p. 184–186°.

The alumina was then eluted with 500 ml. of chloroform and upon evaporation of the solvent there remained 0.18 g. of crystals, m. p. 283–285°. Recrystallized from benzene–chloroform, the rods melted at 283–285° (dec.).

Anal. Calcd. for $C_{25}H_{39}O_3$: C, 74.73; H, 9.79; N, 3.49. Found: C, 74.70; H, 9.65; N, 3.65.

C. Dehydrohalogenation of 22-Bromonitrile Acetate (VIII) with Piperidine. Formation of 22-Cyanobisnor-5,20:22-choladiene-3β-ol Acetate and Ozonolysis to 5-Pregnene-3β-ol-20-one (XXI).—The 22-bromonitrile acetate (VIII) (2.19 g.) in 90 ml. of dry piperidine was refluxed three hours and the excess piperidine was removed *in vacuo* on the steam-bath. The residue was taken up in ether and the insoluble piperidine hydrobromide was filtered off and washed with ether. It weighed 0.75 g. (theory, 0.79 g.) and melted at 230° (dec.).

Anal. Calcd. for $C_5H_{12}NBr$: Br, 48.1. Found: Br, 47.22.

The ether filtrate was washed with 5% hydrochloric acid (an insoluble precipitate was separated and set aside), 5% sodium carbonate and water and dried over sodium sulfate. Upon evaporation of the ether there remained 1.61 g. of low melting (80–90°) material. This material was taken up in 100 ml. of chloroform and, while cooling and stirring in an ice-bath, 21.5 ml. of a bromine–chloroform solution containing 674 mg. of bromine was added dropwise. The ice-cooled solution was ozonized for fifty minutes (*ca.* 14.6 mg. of ozone per minute) and the solvent removed *in vacuo*. After taking the residue up in 40 ml. of glacial acetic acid 2 g. of zinc dust was added portionwise with shaking, and finally the whole was heated on the hot water-bath for ten minutes. The product was extracted with ether, washed with water, with saturated sodium bicarbonate solution, water and dried over sodium sulfate. The solvent was removed and upon refluxing the residue with semicarbazide hydrochloride and sodium acetate in methanol in the usual manner there was obtained 0.54 g. (30%) of 5-pregnene-3β-ol-20-one acetate semicarbazone which upon recrystallizing from ethanol–chloroform melted at 240–243°.

Anal. Calcd. for $C_{24}H_{37}O_3N_3$: N, 10.11. Found: N, 10.07.

Five-tenths gram of the semicarbazone in 100 ml. of ethanol was refluxed with 50 ml. of 5 *N* sulfuric acid for thirty minutes. The mixture was diluted with water and extracted with ether. The washed and dried solution gave 395 mg. of 5-pregnene-3β-ol-20-one (XXI), m. p. 175–180°. Recrystallization from isopropyl ether raised the m. p. to 185–190° and a mixture with an authentic sample showed no depression.

cis- **and** *trans*-**22-Cyanobisnor-5,20:22-choladiene-3β-ols (XIII, XV).**—The 3-acetoxy-22-bromonitrile (VIII) (4.8 g.) was refluxed in 200 ml. of dry piperidine for two hours and the excess piperidine removed *in vacuo* on the steam-bath. The residue was taken up in ether, the piperidine hydrobromide filtered off and the ether evaporated. The residue was refluxed one-half hour with 1.6 g. of potassium carbonate in 20 ml. of water and 150 ml. of methanol and the solvent removed *in vacuo*. The residue was taken up in ether and water and the ether layer was washed with water, dilute hydrochloric acid (an insoluble precipitate separated, fraction "A"), 5% sodium carbonate and water and dried over sodium sulfate, fraction "B."

Fraction "A" was washed well with ether, stirred with 10% sodium carbonate solution, extracted with ether and washed neutral. Upon evaporation of the solvent and recrystallizing from benzene–hexane the material melted at 97–105°. The compound analyzed for 22-cyano-22-piperidinobisnor-5-cholene-3β-ol.

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(7) Schwenk and Whitman, THIS JOURNAL, **59**, 949 (1937).

(8) Wieland and Miescher, *Helv. Chim. Acta*, **30**, 1877 (1947).

Anal. Calcd. for $C_{28}H_{44}ON_2$: N, 6.60. Found: N, 6.49, 6.73.

The ether solution, fraction "B," was evaporated to 25 ml., cooled and the crystalline material filtered off. This weighed 0.51 g., m. p. 229–232°. Recrystallized from 95% ethanol the well formed pyramids melted at 234°. This is one of the pure *cis–trans* isomers (XIII or XV).

Anal. Calcd. for $C_{23}H_{33}ON$: C, 81.35; H, 9.80; N, 4.10. Found: C, 81.42; H, 9.64; N, 4.20; $[\alpha]^{24}\text{D}$ -233 (0.0289 g. made up to 10 ml. in acetone, $\alpha^{24}\text{D}$ -0.674, l, 1 dm.); absorption spectrum, maximum at 225.5 mμ (log E, 4.09 in absolute alcohol).

The ether filtrate from fraction "B" above was evaporated to dryness to give 2.38 g. of gummy residue. This residue was recrystallized from methanol–chloroform, dilute acetone, benzene–hexane, and finally dilute acetone to give the other pure *cis–trans* isomer (XIII or XV), 0.75 g., m. p. 195° (long needles).

Anal. Calcd. for $C_{23}H_{33}ON$: C, 81.35; H, 9.80; N, 4.10. Found: C, 81.66; H, 9.61; N, 4.11; $[\alpha]^{24}\text{D}$ -51.4 (0.0887 g. made up to 10 ml. in acetone, $\alpha^{24}\text{D}$ -0.456, l, 1 dm.); absorption spectrum, maximum at 222.5 mμ (log E, 4.22 in absolute alcohol).

***cis*- and *trans*-22-Cyanobisnor-5,20:22-choladiene-3β-ol Acetate.**—The isomer above, m. p. 234° (0.90 g.), was taken up in 8 ml. of dry pyridine and heated to 100° with 1.5 ml. of acetic anhydride. After standing at room temperature for sixty-eight hours the mixture was poured onto concentrated hydrochloric acid and ice. The crystalline precipitate was extracted with ether and washed with water, sodium bicarbonate, water and dried. Removal of the solvent gave a quantitative yield of nicely crystalline acetate which recrystallized from dilute acetone yielded 0.92 g. of needles (XII or XIV), m. p. 182°.

Anal. Calcd. for $C_{25}H_{35}O_2N$: C, 78.69; H, 9.25. Found: C, 78.69; H, 9.27; $[\alpha]^{24}\text{D}$ -194 (0.0644 g. made up to 10 ml. in acetone, $\alpha^{24}\text{D}$ -1.250, l, 1 dm.).

When 1.51 g. of the isomer, m. p. 195°, was acetylated exactly as above there was obtained 1.55 g. of the pure acetate (XII or XIV), needles melting at 148°.

Anal. Calcd. for $C_{25}H_{35}O_2N$: C, 78.69; H, 9.25. Found: C, 78.42; H, 9.22; $[\alpha]^{24}\text{D}$ -50.5 (0.0721 g. made up to 10 ml. in acetone, $\alpha^{24}\text{D}$ -0.364, l, 1 dm.).

5-Pregnene-3β-ol-20-one Acetate (XX) from *cis-trans*-22-Cyanobisnor-5,20:22-choladiene-3β-ol Acetates (XII, XIV).—The isomer melting at 182° (0.5 g.) in 30 ml. of chloroform was cooled in an ice-bath. While stirring, 6.42 ml. of a bromine–chloroform solution containing 0.210 g. of bromine was slowly added dropwise and the ice-cooled solution was ozonized by passing a stream of ozone–oxygen through it for twenty-six minutes (*ca.* 10 mg. of ozone per minute). The solvent was removed *in vacuo* and the residue taken up in 10 ml. of glacial acetic acid and 10 ml. of ether. This was shaken and refluxed with 1 g. of zinc dust for ten minutes, made up to 150 ml. with ether and filtered from the excess zinc dust. The ether solution was washed with water, 5% sodium hydroxide, water and dried over sodium sulfate. The solvent was removed to obtain 0.46 g. of nicely crystalline crude 5-pregnene-3β-ol-20-one acetate (XX). Crystallized from dilute acetone and dilute alcohol the melting point was 145–146°. Mixed with an authentic sample of pregnenolone acetate there was no m. p. depression.

The isomer melting at 148° (0.5 g.) was brominated, ozonized and debrominated exactly as in the above experiment to obtain 0.45 g. of crude crystalline 5-pregnene-3β-ol-20-one acetate or 0.36 g. of pure compound, m. p. 145–146°. There was no m. p. depression when mixed with authentic pregnenolone acetate.

Summary

1. 3β-Acetoxybisnor-5-cholenaldehyde cyanohydrin and 3β-methoxybisnor-5-cholenaldehyde cyanohydrin were prepared from the corresponding bisulfite addition products.

2. The following derivatives of the former are reported: 22-cyanobisnor-5-cholene-3β,22-diol diacetate, 22-cyanobisnor-5-cholene-3β,22-diol 3-acetate 22-tosylate, 22-cyano-22-chlorobisnor-5-cholene-3β-ol acetate, 22-cyano-22-bromobisnor-5-cholene-3β-ol acetate.

3. Upon dehydrohalogenation of the 22-bromonitrile acetate (VIII) with piperidine a low melting mixture of isomeric 22-cyanobisnor-5,20:22-choladiene-3β-ol acetates along with 22-cyano-22-piperidinobisnor-5-cholene-3β-ol acetate resulted, which upon ozonization gave 5-pregnene-3β-ol-20-one acetate in 30% yield. *cis*- and *trans*-22-cyanobisnor-5,20:22-choladiene-3β-ols were separated after saponification of the acetates. Reacetylation of these afforded pure *cis*- and *trans*-acetates which were ozonized to give excellent yields of 5-pregnene-3β-ol-20-one acetate.

4. When dehydrohalogenation was attempted using dimethylaniline reduction ensued giving 22-cyanobisnor-5-cholene-3β-ol acetate. This was converted into the following derivatives: 22-cyanobisnor-5-cholene-3β-ol, 22-cyanobisnor-4-cholene-3-one, 3β-hydroxynor-5-cholenic acid amide, 3β-acetoxynor-5-cholenic acid amide, and 3-ketonor-4-cholenic acid amide.

KALAMAZOO, MICHIGAN RECEIVED SEPTEMBER 23, 1949