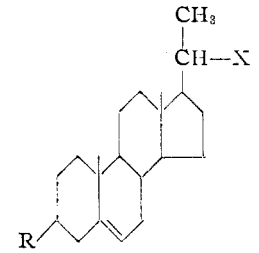
[CONTRIBUTION FROM THE RESEARCH DIVISION, THE UPJOHN COMPANY]

Steroid Acids and their Transformation Products. III. Desulfurization of Thiol Esters of 3(β)-Hydroxy-5-cholenic and -bisnor-5-cholenic Acids[1]

BY A. VERN. MCINTOSH, JR., ELIZABETH M. MEINZER AND ROBERT H. LEVIN

The second paper of this series[2] describes the Raney nickel desulfurization of thiol esters of desoxycholic acid to give the corresponding aldehyde and alcohol. We have now extended these desulfurization experiments to the thiol esters of 3(β)-hydroxy-5-cholenic acid and 3(β)-hydroxy-bisnor-5-cholenic acid.[3]

The 3-acyl-5-cholenediols (II, V) were prepared in essentially quantitative yield by stirring the 3-acyl-5-thiocholenates (I, IV) with standard (W-1) or superactive (W-4) Raney nickel catalyst[4] in 95% alcohol at room or reflux temperature for periods of fifteen to sixty minutes. The ratio of catalyst to thiol ester was varied from 5:1 to 20:1, depending on the activity of the catalyst. Within the limits of our experiments the nature of R′ and X in the thiol esters (I, IV) had no influence on the yield of primary alcohol (II, V). The nuclear double bond was not reduced, and the 3-acyl group (except formyl) was not hydrolyzed during the course of this reductive desulfurization. The presence of the C 5:6 double bond in the diols (II, V) was established by preparation of the dibromides of IIc and Vf, and oxidation of 3(β)-acetoxy-22-hydroxy-bisnor-5-cholene (IIa) and 3(β)-acetoxy-24-hydroxy-5-cholene (Va) to the corresponding cholenic acids. The preparation of the cholenediols (II, V) by the sodium and alcohol reduction of the esters of cholenic acid is recorded in a patent.[5] By this method acyl groups in the molecule are also removed. These groups are not lost under the conditions of the thiol ester–nickel catalyst process, thus permitting the preparation of selectively acylated and mixed acylated diols of possible interest in side chain degradation work. 3(β)-Hydroxy-24-benzoxy-5-cholene (Ve) was prepared by the partial saponification of the 3(β)-acetoxy-24-benzoxy compound (Vd). The other diols (II, V) require no further explanation and their preparation is summarized in the experimental section. 3(β)-Acetoxy-22-hydroxy-bisnor-5-cholene (IIa) and 3(β)-acetoxy-24-hydroxy-5-cholene (Va) were also prepared by reduction of the crystalline aldehydes (III, VI) with Raney nickel catalyst under the conditions used in the one-step process of going from the thiol ester to the corresponding alcohol.



I, X = —C(=O)—SR′ II, X = —CH₂R′

IV, X = —CH₂CH₂C(=O)—SR′

R	R′
Ia, OAc	C_2H_5
b, OAc	$CH_2C_6H_5$
IVa, OAc	C_2H_5
b, OAc	i-C_3H_7
c, OAc	$CH_2C_6H_5$
d, OAc	C_6H_5
e, OH	C_2H_5
f, O formyl	C_2H_5
g, OBz	C_2H_5

V, X = —CH₂CH₂CH₂R′

R	R′
IIa, OAc	OH
b, OH	OH
c, OAc	OAc
d, OBz	OBz
Va, OAc	OH
b, OH	OH
c, OBz	OH
d, OAc	OBz
e, OH	OBz
f, OAc	OAc

III, X = —CHO R = OAc

VI, X = —CH₂CH₂CHO R = OAc

VII, X = —CH=NNHC₆H₅(NO₂)₂ R = OAc

VIII, X = —CH₂CH₂CH=NNHC₆H₃(NO₂)₂

R
VIII, a, OAc
b, OH
c, O formyl

The cholenaldehydes (III, VI) were prepared crystalline in yields of 50–55% by use of a modified or deactivated Raney catalyst. The desulfurization was found to be reproducible with different lots of catalyst and with variations in X and R′ of the thiol ester (I, IV). As described previously,[2] pretreatment of W-1 Raney nickel catalyst[4] with acetone lowers the activity of the catalyst so that reduction beyond the aldehyde stage can be controlled. We have also used other hydrogen acceptors, such as formaldehyde, for this purpose. The modified catalyst retains a fair amount of adsorbed hydrogen because, when used at a higher ratio, it is still capable of transforming a thiol ester to a primary alcohol.

3(β)-Acetoxy-bisnor-5-cholenaldehyde (III) was prepared by refluxing the catalyst in acetone for one hour, adding the thiol ester (Ia) in aqueous acetone, and continuing the refluxing for two hours. The aldehyde (III) was isolated as the bisulfite complex according to the procedure developed in this laboratory.[6,7] In the desulfurization of ethyl 3(β)-acetoxy-5-thiolcholenate (IVa) to form the cholenal (VI) a deactivation period of

(1) Presented before the Division of Organic Chemistry, 113th American Chemical Society meeting, Chicago, Ill., April 22, 1948.

(2) Spero, McIntosh and Levin, THIS JOURNAL, **70**, 1907 (1948).

(3) Levin, McIntosh, Spero, Rayman and Meinzer, *ibid.*, **70**, 511 (1948).

(4) Adkins and Pavlic, *ibid.*, **69**, 3039 (1947). A commercial, Raney, active nickel catalyst obtained from the Gilman Paint and Varnish Co., Chattanooga, Tenn., gave similar results after it had been washed alkali free.

(5) Johannessohn and Hatzig, U. S. Patent 2,259,698, October 21, 1941.

(6) Centolella, Heyl and Herr, THIS JOURNAL, **70**, 2953 (1948).

(7) Heyl, Centolella and Herr, *ibid.*, **69**, 1957 (1947).

two hours and a reaction time of one hour gave the best results. 3(β) - Acetoxy - 5 - cholenaldehyde (VI) is a new compound which was recrystallized from glacial acetic acid, after decomposition of its bisulfite complex. Its 2,4-dinitrophenylhydrazone and semicarbazone were also prepared. The yield of aldehyde could also be determined by preparing the 2,4-dinitrophenylhydrazone from the reaction mixture. In each case the correspondence between the yields of the bisulfite complex and the 2,4-dinitrophenylhydrazone derivatives (VII, VIIIa) was good.

In the desulfurization of the ethyl (IVa), isopropyl (IVb), benzyl (IVc) and phenyl (IVd) 3(β)-acetoxy-5-thiolcholenates with the deactivated catalyst, the ethyl and benzyl thiol esters gave the aldehyde (VI) as the 2,4-dinitrophenylhydrazone in yields of 53–68%, while the isopropyl and phenyl esters gave yields of 49–62%. In the bisnor series only the ethyl and benzyl thiol esters were studied, with the benzyl giving slightly higher yields of the aldehyde (III). Ethyl 3(β)-hydroxy-5-thiolcholenate (IVe), and ethyl 3(β)-formoxy-5-thiolcholenate (IVf) were also desulfurized with deactivated Raney nickel to give the corresponding 3(β)-hydroxy, and 3(β)-formoxy-aldehydes, which were isolated as the 2,4-dinitrophenylhydrazones (VIIIb, VIIIc).

A number of new thiol esters have been prepared by the published methods[3] and their properties summarized in the experimental section.

Experimental[8]

Several new steroid thiol esters were prepared. These are described in Table I.

The alcohols and their derivatives are described in Table II. The parent alcohols were prepared by reduction of the corresponding thiol esters with W-4 Raney nickel, usually in yields of around 90%. The general method is illustrated in the following preparation.

3(β)-Acetoxy-22-hydroxy-bisnor-5-cholene (IIa).—A mixture of 0.200 g. of ethyl 3(β)-acetoxy-bisnor-5-thiolcholenate, 5 ml. of 95% ethyl alcohol, and 3 g. of W-4 Raney nickel was allowed to stand for one hour at room temperature with occasional shaking. The nickel was then separated by filtration and washed with 15 ml. of hot ethyl alcohol. The filtrate and washings were combined and diluted with water, giving 0.16 g. (93%) of 3(β)-acetoxy-22-hydroxy-bisnor-5-cholene, m. p. 143–148°. After several crystallizations from a 3:1 alcohol–water mixture the compound melted at 152–154.5°.

Reduction of ethyl 3(β)-benzoxy-5-thiolcholenate by this method failed apparently because this ester was extremely insoluble in alcohol. When the ester was suspended in ether and stirred for thirty minutes at room temperature with W-4 Raney nickel, a 73% yield of 3(β)-benzoxy-24-hydroxy-5-cholene (Vc), m. p. 184–185°, was obtained.

3(β)-Acetoxy-24-hydroxy-5-cholene (Va) and the bisnor analog (IIa) were also prepared in 80–85% yields by reduction of the corresponding aldehydes under conditions similar to those described for reduction of the thiol esters.

In preparing the aldehydes described in this paper an 8:1 ratio by weight of catalyst to thiol ester was appropriate, although a variation of 25% in the ratio caused no appreciable change in the yield of aldehyde. However, when twenty parts of deactivated catalyst was used with one part of the thiol ester (Ia), the primary alcohol (IIa) was the main product.

3(β)-Acetoxy-5-cholen-24-al. (VI).—A suspension of 40 g. of W-1 Raney nickel in 120 ml. of acetone was heated under reflux with stirring for one hour, then a solution of 3.97 g. of ethyl 3(β)-acetoxy-5-thiolcholenate in 80 ml. of acetone was added, followed by addition of 80 ml. of water. The mixture was heated under reflux for one hour, then the Raney nickel was separated by filtration and washed with hot acetone. The filtrate and washings were combined and evaporated *in vacuo* until a heavy white precipitate formed. The mixture was diluted with an equal amount of water and the precipitate was separated by filtration and air-dried, giving 3.3 g. of a powder melting at 115–133°. A 100-mg. sample gave 97 mg. of the dinitrophenylhydrazone derivative, corresponding to a 67% yield of aldehyde.

Following the procedure used by Heyl, Centolella and Herr[7] in the purification of 3(β)-acetoxy-bisnor-5-cholen-22-al the remaining 3.2 g. of crude aldehyde was dissolved in 110 ml. of ether and shaken with 90 ml. of 40% aqueous sodium bisulfite for fifteen minutes. Water was then added and the bisulfite complex was collected by centrifuging. The wet complex was suspended in 75 ml. of 10% sodium carbonate in a separatory funnel, then ether was added and the mixture was agitated for two hours by a current of nitrogen. The ether layer was separated and evaporated, giving 2.16 g. (63%) of 3(β)-acetoxy-5-cholen-24-al, m. p. 139–147°. After crystallization from aqueous acetic acid, then from hexane, the compound melted at 148–152°; $[\alpha]^{25}D$ −52.0° (100.0 mg. in 10.0 ml. $CHCl_3$, α = −0.52°, *l*, 1 dm.).

Anal. Calcd. for $C_{26}H_{40}O_2$: C, 77.95; H, 10.07. Found: C, 77.87; H, 10.15.

3(β)-Acetoxy-5-cholen-24-al 2,4-Dinitrophenylhydrazone (VIIIa).—A solution of 315 mg. of crude 3(β)-acetoxy-5-cholen-24- al (VI) and 125 mg. of 2,4-dinitrophenylhydrazine in 20 ml. of 3A alcohol was prepared by boiling, then several drops of concentrated hydrochloric acid were added. The mixture was allowed to cool, then was diluted with 6 ml. of water and allowed to stand for three hours. The yield of yellow crystals was 323 mg., m. p. 156–173°. The compound was chromatographed over acid-washed Fisher adsorption alumina. The main fraction, eluted with 2% methanol in benzene, was recrystallized several times from acetic acid and water. A constant melting point of 189–193° after softening at 173° was obtained, using the Fisher–Johns block. Using a capillary tube in a bath, the m. p. was 172.5–173.5°; $[\alpha]^{25}D$ −37° (100 mg. in 10 ml. chloroform, 1-dm. tube, $\alpha^{25}D$ −0.37°).

Anal. Calcd. for $C_{32}H_{44}O_6N_4$: C, 66.18; H, 7.64; N, 9.65. Found: C, 66.08; H, 7.35; N, 9.46.

3(β)-Acetoxy-5-cholen-24-al 2,4-dinitrophenylhydrazone was obtained in 68% yield from benzyl 3(β)-acetoxy-5-thiolcholenate (IVc), in 62% yield from phenyl 3(β)-acetoxy-5-thiolcholenate (IVd), and in 49% yield from isopropyl 3(β)-acetoxy-5-thiolcholenate (IVb) by desulfurization as described above.

3(β)-Hydroxy-5-cholen-24-al 2,4-Dinitrophenylhydrazone (VIIIb).—The desulfurization of ethyl 3(β)-hydroxy-5-thiolcholenate (IVe) was carried out as described above for the acetoxy ester. The crude aldehyde in alcohol was treated with excess 2,4-dinitrophenylhydrazine and concentrated hydrochloric acid to give a 55% yield (based on the ester) of the dinitrophenylhydrazone, melting at 176–188°. The compound was crystallized several times from a mixture of chloroform and ethyl alcohol, reaching a melting point of 189–192°; $[\alpha]^{25}D$ −39° (100.0 mg. in 10 ml. chloroform, *l*, 1 dm., $\alpha^{25}D$ −0.39).

Anal. Calcd. for $C_{30}H_{42}O_5N_4$: C, 66.88; H, 7.86; N, 10.41. Found: C, 66.64; H, 7.67; N, 10.45.

3(β)-Formoxy-5-cholen-24-al 2,4-Dinitrophenylhydrazone (VIIIc).—Ethyl 3(β)-formoxy-5-thiolcholenate

(8) Analyses by the Upjohn microanalytical group. Rotations by Mr. Norman Drake of the Upjohn physics department.

TABLE I

THIOL ESTERS OF STEROID ACIDS

Compound	M. p., °C.[c]	Rotation[d] $[\alpha]_D$	Yield, %	Molecular formula	Analyses, % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	Sulfur Calcd.	Sulfur Found
Benzyl 3(β)-acetoxy-bisnor-5-thiolcholenate[a] (Ib)	142.5–144	−35.0[e]	79	$C_{31}H_{24}O_3S$	75.26	75.64	8.56	8.60	6.48	6.17
Benzyl 3(β)-acetoxy-5-thiolcholenate[a] (IVc)	85–86.5	−30.7[f]	82	$C_{33}H_{46}O_3S$	75.82	75.80	8.87	8.88	6.13	6.24
Phenyl 3(β)-acetoxy-5-thiolcholenate[a] (IVd)	130.5–132.5	−38.1[g]	84	$C_{32}H_{44}O_3S$	75.54	75.48	8.72	8.56	6.30	6.48
Ethyl 3(β)-benzoxy-5-thiolcholenate[b] (IVg)	172.5–173.5	−13.0[h]	84[b]	$C_{33}H_{46}O_3S$	75.82	75.55	8.87	8.96	6.13	6.11

[a] Prepared by treating the steroid acid chloride with a mercaptan in the presence of pyridine. For a detailed example see reference (2). [b] Prepared by benzoylation of ethyl 3(β)-hydroxy-5-thiolcholenate. [c] All m. p.'s taken on the Fisher-Johns block and corrected. [d] Rotations taken in chloroform with a 1-dm. tube. [e] 108.6 mg. in 10 ml., $\alpha^{27}D$ −0.38°. [f] 101.0 mg. in 10 ml., $\alpha^{24}D$ −0.31°. [g] 115.4 mg. in 10 ml., $\alpha^{24}D$ −0.44°. [h] 100.0 mg. in 10 ml., $\alpha^{25}D$ −0.13°.

TABLE II

CHOLENEDIOLS AND DERIVATIVES

Compound	M. p., °C.[l]	Rotation[m] $[\alpha]_D$	Molecular formula	Analyses, % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found
3(β),22-Dihydroxy-bisnor-5-cholene[a] (IIb)	196–205	−55.4[n]	$C_{22}H_{36}O_2 \cdot {}^1/_2H_2O$	77.37	77.63	10.92	10.76
3(β)-Acetoxy-22-hydroxy-bisnor-5-cholene[b] (IIa)	152–154.5	−61.6[o]	$C_{24}H_{38}O_3$[v]	76.96	77.01	10.46	10.09
3(β),22-Diacetoxy-bisnor-5-cholene (IIc)[c]	127–129	−51.0[p]	$C_{26}H_{40}O_4$	74.96	74.90	9.68	9.39
3(β),22-Diacetoxy-5,6-dibromo-bisnorcholane[d]	139–141.5	.....	$C_{28}H_{44}O_4Br_2$[w]				
3(β),22-Dibenzoxy-bisnor-5-cholene[e] (IId)	168.5–170	.....	$C_{36}H_{42}O_4$	79.81	79.85	8.04	8.14
3(β),24-Dihydroxy-5-cholene[f] (Vb)	193–195	−41.8[q]	$C_{24}H_{40}O_2$	79.94	80.40	11.18	10.94
3(β)-Acetoxy-24-hydroxy-5-cholene[g] (Va)	143.5–146	−47.5[r]	$C_{26}H_{42}O_3$[x]	77.56	77.52	10.52	10.45
3(β),24-Diacetoxy-5-cholene[h] (Vf)	126–127	−35.5[s]	$C_{28}H_{44}O_4$[y]	75.63	75.61	9.97	9.91
3(β)-Benzoxy-24-hydroxy-5-cholene[i] (Vc)	184.5–186	−193.3[t]	$C_{31}H_{44}O_3$	80.12	80.27	9.55	9.22
3(β)-Acetoxy-24-benzoxy-5-cholene[j] (Vd)	93.5–95.5	−38.0[u]	$C_{33}H_{46}O_4$	78.22	78.29	9.15	9.18
3(β)-Hydroxy-24-benzoxy-5-cholene[k] (Ve)	41.5–44.5	.....	$C_{31}H_{44}O_3$	80.13	79.67	9.59	9.77

[a] Prepared from 3(β)-acetoxy-22-hydroxy-bisnor-5-cholene by hydrolysis with alcoholic sodium hydroxide. [b] Yield 93% from ethyl 3(β)-acetoxy-bisnor-5-thiolcholenate; 84% from 3(β)-acetoxy-bisnor-5-cholen-22-al. [c] Nearly quantitative yield on acetylation of 3(β)-acetoxy-22-hydroxy-bisnor-5-cholene or 3(β),22-dihydroxy-bisnor-5-cholene. [d] Bromination of 3(β)-22-diacetoxy-bisnor-5-cholene in glacial acetic acid gave a 92% yield of compound, m. p. 90–95°; 62% after crystallization to a m. p. of 138–139°. [e] Prepared from 3(β),22-dihydroxy-bisnor-5-cholene. [f] Prepared by hydrolysis of 3(β)-acetoxy-24-hydroxy-5-cholene, also by treatment of ethyl 3(β)-hydroxy-5-thiolcholenate with W-4 Raney nickel. [g] Yield 93% from ethyl 3(β)-acetoxy-5-thiolcholenate; 81% from 3(β)-acetoxy-5-cholen-24-al. [h] Prepared by acetylation of 3(β)-acetoxy-24-hydroxy-5-cholene or 3(β),24-dihydroxy-5-cholene. [i] Yield 73% from ethyl 3(β)-benzoxy-5-thiolcholenate in ether suspension on treatment with W-4 Raney nickel. [j] Yield 95% by benzoylation of 3(β)-acetoxy-24-hydroxy-5-cholene. [k] Yield 70% by treatment of 0.5 g. (0.001 mole) of 3(β)-acetoxy-24-benzoxy-5-cholene in 100 ml. of acetone with 15 ml. of 0.1 *N* aqueous potassium hydroxide at 36° for 3 hours. [l] All m. p.'s taken on a Fisher-Johns block and corrected. [m] Rotations taken in chloroform with a 1-dm. tube. [n] 45.54 mg. in 10 ml., $\alpha^{25}D$ −0.252°. [o] 100.0 mg. in 10 ml., $\alpha^{25}D$ −0.616°. [p] 100.0 mg. in 10 ml., $\alpha^{25}D$ −0.51°. [q] 41.8 mg. in 25 ml., $\alpha^{25}D$ −0.14°. [r] 61.0 mg. in 10 ml., $\alpha^{25}D$ −0.29°. [s] 104.1 mg. in 10 ml., $\alpha^{25}D$ −0.37°. [t] 3.973 mg. in 2 ml., $\alpha^{27}D$ −0.384°. [u] 100.0 mg. in 10 ml., $\alpha^{25}D$ −0.38°. [v] Calculated acetyl, 11.5%; found, 12.5%. [w] Calculated Br, 26.4%; found, 25.77%. [x] Calculated acetyl 10.5%; found, 10.5%. [y] Calculated acetyl, 19.3%; found, 19.6%.

(IVf), treated with deactivated W-1 Raney nickel as described above, gave 3(β)-formoxy-5-cholen-24-al 2,4-dinitrophenylhydrazone, m. p. 232–233.5° from chloroform and alcohol: $[\alpha]^{24}D$ −43° (100.0 mg. in 10 ml. chloroform, *l*, 1 dm.; αD −0.43).

Anal. Calcd. for $C_{31}H_{42}O_6N_4$: C, 65.70; H, 7.47; N, 9.89. Found: C, 65.45; H, 7.29; N, 9.61.

Chromic Acid Oxidation of 3(β)-Acetoxy-22-hydroxy-bisnor-5-cholene (IIa).—Ten ml. of 0.2 *M* bromine in glacial acetic acid was added in portions to a solution of 718.6 mg. (1.92 millimoles) of 3(β)-acetoxy-22-hydroxy-bisnor-5-cholene in 20 ml. of acetic acid. The solution was allowed to stand for fifteen minutes at room temperature, then a solution of 0.4 g. of chromic oxide in 0.4 ml. of water and 20 ml. of acetic acid was added over a period of an hour at room temperature. The reaction mixture was allowed to stand for one hour, then the excess chromic acid was destroyed by addition of 5 ml. of methanol. The solution was diluted with water and extracted with ether. The ether solution was evaporated *in vacuo* and the residue was dissolved in 10 ml. of acetic acid and treated with an excess of zinc dust. After addition of ether and filtration, the ether solution was washed with 5% sodium carbonate until alkaline, when an insoluble sodium salt formed. This was collected by centrifuging and treated with hydrochloric acid to give 515.5 mg. (69%) of 3(β)-acetoxy-bisnor-5-cholenic acid, m. p. 200–233°. After crystallization from ether the compound melted at 227–235°. The methyl ester melted at 138.5–139.5°.

3(β)-Acetoxy-24-hydroxy-5-cholene (253 mg.) was similarly oxidized to give 208 mg. of 3(β)-acetoxy-5-cholenic acid, m. p. 178–183°, after recrystallization from acetic acid.

Summary

3(β)-Acetoxy-22-hydroxy-bisnor-5-cholene and the 3(β)-hydroxy-3(β)-acetoxy- and 3(β)-benzoxy-24-hydroxy-5-cholenes have been produced by the reductive desulfurization of the corresponding ethyl thiol esters with Raney nickel catalyst.

Derivatives of these alcohols have been prepared by acylation and hydrolysis.

3(β)-Acetoxy-5-cholen-24-al and 3(β)-acetoxy-bisnor-5-cholen-22-al have been obtained from the ethyl and benzyl thiol esters of the corresponding acids by treatment with a deactivated Raney nickel catalyst.

The 2,4-dinitrophenylhydrazones of 3(β)-hydroxy- and 3(β)-formoxy-5-cholen-24-al have been prepared from crude aldehydes obtained by desulfurization of the corresponding thiol esters with a deactivated Raney nickel catalyst.

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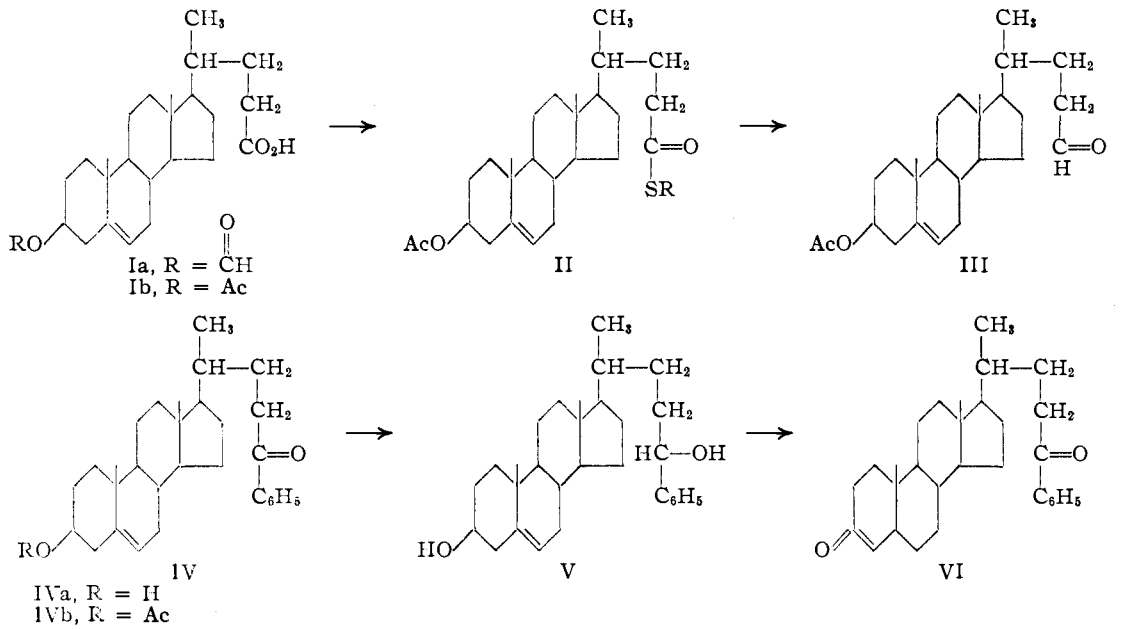
[CONTRIBUTION FROM THE RESEARCH DIVISION, THE UPJOHN COMPANY]

Steroid Acids and their Transformation Products. IV. Epimeric 24-Phenyl-5-cholen-3(β),24-diols and Related Compounds

BY ROBERT H. LEVIN, GEORGE B. SPERO, A. VERN MCINTOSH, JR., AND DOUGLAS E. RAYMAN

The preparation of 3(β)-acetoxy-5-cholenic aldehyde (III) from 3(β)-acetoxy-5-thiolcholenates (II)[1] by the use of deactivated W-1 Raney nickel has recently been reported.[2] The aldehyde (III) has now been treated with phenylmagnesium bromide to form the 24-phenyl-5-cholene-3(β),24-diols, epimeric at C-24, in yields of 70–80%. The same diols (V) also have been obtained by the reduction of the corresponding phenyl ketone (IVb), previously prepared from 3(β)-formoxy-5-cholenic acid (I).[3] The reduction of the phenyl ketone (IVb) with aluminum isopropoxide in isopropanol gave a reaction mixture difficult to work up, and the diols (V) were obtained in total yields averaging 40%, although in one experiment the yield was 80%. With lithium aluminum hydride[4] the reaction proceeded rapidly and smoothly in ether at room temperature giving the same mixture of diols (V) in 80–90% yields.



It was found possible to separate the epimeric diols (V) by solubility differences in benzene or ether and the acetates and benzoates of both isomers were prepared. The diols and their derivatives are listed in Table I.

TABLE I

EPIMERIC 24-PHENYL-5-CHOLEN-3(β),24-DIOLS

Compound	A M. p., °C.	A $[\alpha]^{25}D$	B M. p., °C.	B $[\alpha]^{25}D$
Diol	214–217	− 7.0	184–186	−38.2
Diacetate	92–94	−22.3	164–165	−60.4
Dibenzoate	160–161	−27.2	175–177	−10

(1) Levin, McIntosh, Spero, Rayman and Meinzer, THIS JOURNAL, **70**, 511 (1948).

(2) McIntosh, Meinzer and Levin, *ibid.*, **70**, 2955 (1948).

(3) Hoehn and Moffett, *ibid.*, **67**, 740 (1945).

(4) Finholt, Bond and Schlesinger, *ibid.*, **69**, 1199 (1947). Ott and Murray, Abstracts 113th American Chemical Society Meeting, Medicinal Section, Chicago, Ill., April, 1948.