no depression of m.p. on admixture with the product derived from the Wohl–Aue mixture.

Concentration of the benzene mother liquor from the Wohl–Aue reaction yielded a mixture of *o*-chloronitrobenzene and 0.5 g. of 2,2′-dichloroazobenzene, orange needles and plates, m.p. 136°. A m.p. of 134° has previously been reported for this compound.[20]

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(20) M. Meltsner, L. Greenstein, G. Gross and M. Cohen, THIS JOURNAL, **59**, 2660 (1937).

LOS ANGELES, CALIFORNIA RECEIVED APRIL 9, 1951

[JOINT CONTRIBUTION FROM THE RESEARCH LABORATORIES OF SYNTEX, S. A., AND THE INSTITUTO DE QUÍMICA DE LA UNIVERSIDAD NACIONAL AUTÓNOMA DE MÉXICO]

Steroids. XX.[1a] Cyclic Steroidal Hemithioketals[1b]

BY J. ROMO, G. ROSENKRANZ AND CARL DJERASSI

Unconjugated carbonyl groups of steroids at C-3, C-17 and C-20 react with β-mercaptoethanol to form cyclic ethylenehemithioketals. These substances are stable to base or lithium aluminum hydride, but on acid hydrolysis are reconverted to the parent ketones. In contrast to thioenol ethers or mercaptoles, the presently described ethylenehemithioketals on treatment with Raney nickel yield the original ketone rather than the corresponding hydrocarbon. Since α,β-unsaturated ketones do not react with β-mercaptoethanol under those conditions, it is possible in certain cases to protect a saturated carbonyl group in the presence of a Δ^4-3-keto moiety. Cyclic ethylenehemithioketals of Δ^4-3-ketosteroids can be prepared by the more drastic *p*-toluenesulfonic acid-catalyzed condensation, but the yields are poor. In the presence of piperidine, β-mercaptoethanol undergoes 1,4-addition with a sterically unhindered α,β-unsaturated keto grouping as illustrated with $\Delta^{5,16}$-pregnadien-3β-ol-20-one and 16-dehydroprogesterone (XI).

In an earlier article[2] there was described the reaction of a number of steroidal ketones with benzyl mercaptan. Under the reaction conditions employed, a saturated keto group did not react while an α,β-unsaturated carbonyl system underwent either 1,4-addition or thioenol ether formation. Using $\Delta^{4,16}$-pregnadiene-3,20-dione (XI) as an illustration, it was possible to either add benzyl mercaptan at the C-16 position (piperidine or hydrochloric acid catalysts), effect thioenol ether formation at C-3 (pyridine hydrochloride catalyst) or accomplish both reactions simultaneously at C-3 and C-16 (in the presence of *p*-toluenesulfonic acid); the 20-keto remained unaffected in every instance. It was thus found possible to protect a Δ^4-3-keto system in the presence of another saturated carbonyl group, since acid hydrolysis of the 3-benzylmercapto-$\Delta^{3,5}$-diene regenerated the original Δ^4-3-keto moiety. Raney nickel desulfurization, on the other hand, afforded the $\Delta^{3,5}$-diene.

Considerably different results were observed on extending this study to β-mercaptoethanol. In contrast to benzylmercaptan, β-mercaptoethanol reacted readily in the presence of zinc chloride[3] with *unconjugated* carbonyl groups to yield the corresponding cyclic ethylenehemithioketals. This was true of saturated 3-ketosteroids regardless of the configuration at C-5 [androstan-17β-ol-3-one 17-acetate (Ia), etiocholan-17β-ol-3-one 17-acetate (IIa)], of 17-ketosteroids [estrone acetate (IIIa), Δ^5-androsten-3β-ol-17-one 3-acetate (VIIa)] as well as of 20-ketosteroids [allopregnan-3β-ol-20-one 3-acetate (IVa), Δ^5-pregnen-3β-ol-20-one 3-acetate (Va)].

In the presence of a Δ^4-3-keto moiety a saturated carbonyl group could be attacked selectively under proper conditions. Again employing zinc chloride as the condensing agent, Δ^4-androstene-3,17-dione (VIIIa) afforded the corresponding 17-ethylenehemithioketal (VIIIb), whose structure was proved[4] by its ultraviolet absorption maximum at 240 mμ (log ϵ 4.29) and infrared carbonyl maximum at 1674 cm.$^{-1}$, typical of Δ^4-3-ketosteroids,[5] as well as by an independent synthesis involving Oppenauer oxidation of the 17-ethylenehemithioketal (VIIc) of Δ^5-androstene-3β-ol-17-one. The more drastic *p*-toluenesulfonic acid-catalyzed condensation of VIIIa led in poor yield to the 3,17-bisethylenehemithioketal (IXa) of Δ^4-androstene-3,17-dione, which did not show any selective absorption in the ultraviolet nor did it exhibit an infrared carbonyl band. Similarly, testosterone or its acetate were converted to the 3-ethylenehemithioketals IXb and IXc in less than 20% yield. In agreement with the results in the androstane series, Oppenauer oxidation of Δ^5-pregnen-3β-ol-20-one 20-ethylenehemithioketal (Vc) produced progesterone 20-ethylenehemithioketal (VIb).

The hemithioketal grouping remains unchanged in dilute base (*cf.* saponification of IIIb, Vb and VIIb) and is resistant toward reduction with lithium aluminum hydride as illustrated by the conversion of progesterone 20-ethylenehemithioketal (VIb) to Δ^4-pregnen-3-ol-20-one 20-ethylenehemithioketal (IXd). Although requiring somewhat more drastic conditions than the benzylthioenol ethers, acid hydrolysis of the various hemithioketals described in this paper readily regenerated the parent ketone, thus serving as further proof for the above structure assignments. It is possible, therefore, to achieve under certain conditions the selective protection of an unconjugated carbonyl group in the presence of a Δ^4-3-keto moiety using β-mercaptoethanol, in contrast to the reaction with benzyl mercaptan,[2] where the opposite aim was accomplished. It is interesting to note that while Raney nickel treatment of benzylthioenol

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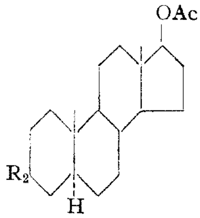
(1) (a) Paper XIX, *Experientia*, **7**, 2601 (1951). (b) Presented in part at the XIIth International Congress of Pure and Applied Chemistry, New York City, September, 1951.

(2) J. Romo, M. Romero, C. Djerassi and G. Rosenkranz, THIS JOURNAL, **73**, 1528 (1951).

(3) G. Rosenkranz, St. Kaufmann and J. Romo, *ibid.*, **71**, 3689 (1949), showed that Δ^4-androstene-3,17-dione (VIIa) reacted with benzyl mercaptan in the presence of zinc chloride with formation of the 3-benzylthioenol ether, the isolated 17-keto group remaining untouched.

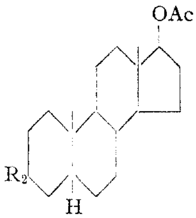
(4) It was believed earlier (ref. 3) that condensation had occurred at C-3 rather than at C-17.

(5) R. N. Jones, P. Humphries and K. Dobriner, THIS JOURNAL, **72**, 956 (1950).



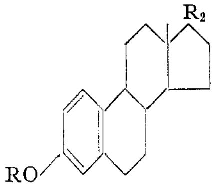
Ia, R_2 = O

b, $R_2 = \left\langle\begin{array}{l}S—CH_2\\ \quad\;|\\ O—CH_2\end{array}\right.$



IIa, R_2 = O

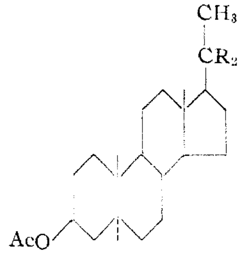
b, $R_2 = \left\langle\begin{array}{l}S—CH_2\\ \quad\;|\\ O—CH_2\end{array}\right.$



IIIa, R = Ac; R_2 = O

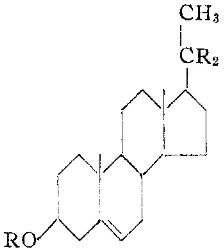
b, R = Ac; $R_2 = \left\langle\begin{array}{l}S—CH_2\\ \quad\;|\\ O—CH_2\end{array}\right.$

c, R = H; $R_2 = \left\langle\begin{array}{l}S—CH\\ \quad\;|\\ O—CH_2\end{array}\right.$



IVa, R_2 = O

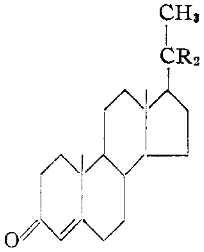
b, $R_2 = \left\langle\begin{array}{l}S—CH_2\\ \quad\;|\\ O—CH_2\end{array}\right.$



Va, R = Ac; R_2 = O

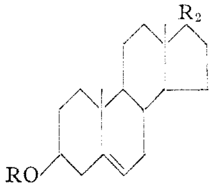
b, R = Ac; $R_2 = \left\langle\begin{array}{l}S—CH_2\\ \quad\;|\\ O—CH_2\end{array}\right.$

c, R = H; $R_2 = \left\langle\begin{array}{l}S—CH_2\\ \quad\;|\\ O—CH_2\end{array}\right.$



VIa, R_2 = O

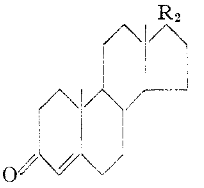
b, $R_2 = \left\langle\begin{array}{l}S—CH_2\\ \quad\;|\\ O—CH_2\end{array}\right.$



VIIa, R = Ac; R_2 = O

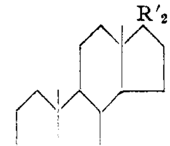
b, R = Ac; $R_2 = \left\langle\begin{array}{l}S—CH_2\\ \quad\;|\\ O—CH_2\end{array}\right.$

c, R = H; $R_2 = \left\langle\begin{array}{l}S—CH_2\\ \quad\;|\\ O—CH_2\end{array}\right.$



VIIIa, R_2 = O

b, $R_2 = \left\langle\begin{array}{l}S—CH_2\\ \quad\;|\\ O—CH_2\end{array}\right.$

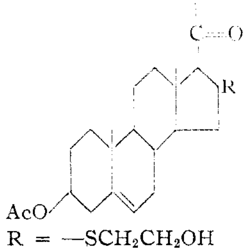


IXa, $R_2 = R'_2 = \left\langle\begin{array}{l}S—CH_2\\ \quad\;|\\ O—CH_2\end{array}\right.$

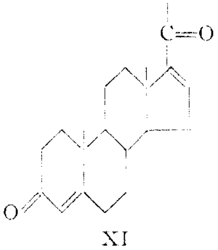
b, $R_2 = \left\langle\begin{array}{l}S—CH_2\\ \quad\;|\\ O—CH_2\end{array}\right.$; $R'_2 = \left\langle\begin{array}{l}H\\ OH\end{array}\right.$

c, $R_2 = \left\langle\begin{array}{l}S—CH_2\\ \quad\;|\\ O—CH_2\end{array}\right.$; $R'_2 = \left\langle\begin{array}{l}H\\ OAc\end{array}\right.$

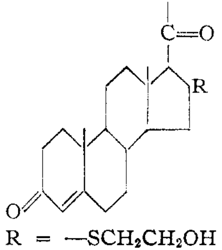
d, $R_2 = \left\langle\begin{array}{l}H\\ OH\end{array}\right.$; $R'_2 = \begin{array}{c}CH_3\\ |\\ C\\ |\\ H\end{array}\left\langle\begin{array}{l}S—CH_2\\ \quad\;|\\ O—CH_2\end{array}\right.$



Xa, R = $—SCH_2CH_2OH$
b, R = $—SCH_2CH_2OCOC_6H_5$



XI



XIIa, R = $—SCH_2CH_2OH$
b, R = $—SCH_2CH_2OCOC_6H_5$

ethers[2,3] or cyclic ethylenemercaptoles[6] results in desulfurization and hence conversion of the original carbonyl group into methylene, a similar reaction with the above hemithioketals regenerates the parent ketones in good yield. Although by no means the only possibility, the following mechanism appears plausible[6a]

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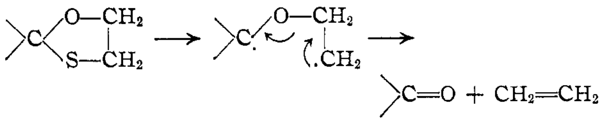
(6) *Cf.* A. Ruff and T. Reichstein, *Helv. Chim. Acta*, **34**, 70 (1951), and references cited therein.

(6a) According to this mechanism, non-cyclic hemithioketals should not regenerate the parent ketone, which is in agreement with the work of L. F. Fieser, H. Heymann and S. Rajagopalan [This Journal **72**, 3206 (1950)].



β-Mercaptoethanol resembled benzyl mercaptan in its ability to add to a sterically unhindered α,β-unsaturated ketone system in the presence of piperidine. $\Delta^{5,16}$-Pregnadien-3β-ol-20-one and $\Delta^{4,16}$-pregnadiene-3,20-dione (XI) afforded in excellent yield the corresponding 16-β-hydroxyethylmercapto derivatives (X and XII). Raney nickel desulfurization of the latter led to Δ^5-pregnen-3β-ol-20-one and progesterone, respectively.

Estrone 17-ethylenehemithioketal (IIIc) proved to possess about one-tenth the estrogenic activity of estrone in rats. Further biological work is in progress, since a substance with weak estrogenic activity but possessing other desirable physiological properties of the estrogens is of obvious clinical importance.

Experimental[7]

General Procedure for Preparation of Ethylenehemithioketals of Unconjugated Ketones.—A solution of 8 g. of the steroid ketone in *ca.* 20 cc. of pure dioxane was treated with 8 g. of β-mercaptoethanol followed by the addition of 10 g. of freshly fused zinc chloride and 10 g. of anhydrous sodium sulfate. The solution was cooled initially in ice to offset the exothermic reaction produced during the zinc chloride addition and the mixture was then allowed to stand at room temperature for approximately 20 hours. After dilution with water, the product was extracted with chloroform, the latter was washed with water until neutral, dried and evaporated. The solid residue was then recrystallized from a suitable solvent.

Androstan-17β-ol-3-one 17-Acetate 3-Ethylenehemithioketal (Ib).—Prepared in 72% yield from androstan-17β-ol-3-one 17-acetate (Ia) ($[\alpha]^{20}_{\mathrm{D}}$ + 33°). After recrystallization from acetone–methanol, the product exhibited m.p. 164–167°, $[\alpha]^{20}_{\mathrm{D}}$ +20°.

Anal. Calcd. for $C_{23}H_{36}O_3S$: C, 70.37; H, 9.24; S, 8.15. Found: C, 70.57; H, 9.05; S, 8.35.

Etiocholan-17β-ol-3-one 17-Acetate 3-Ethylenehemithioketal (IIb).—Obtained as brilliant plates in 60% yield after recrystallization from acetone–methanol, m.p. 163–165°, $[\alpha]^{20}_{\mathrm{D}}$ +24.5°. A marked depression in melting point was observed on admixture with a sample of the isomer Ib.

Anal. Calcd. for $C_{23}H_{36}O_3S$: C, 70.37; H, 9.24; S, 8.15. Found: C, 70.50; H, 8.96; S, 8.05.

When 1 g. of the hemithioketal IIb was refluxed for three hours with 4 cc. of concd. hydrochloric acid, 10 cc. of water and 200 cc. of ethanol, followed by acetylation of the crude product, there was obtained 52% of pure etiocholan-17β-ol-3-one 17-acetate (IIa) with m.p. 144–146°, $[\alpha]^{20}_{\mathrm{D}}$ +30°.

Estrone Acetate 17-Ethylenehemithioketal (IIIb).—Large needles (79% yield) after recrystallization from chloroform–methanol; m.p. 124–126°, $[\alpha]^{20}_{\mathrm{D}}$ −4°.

Anal. Calcd. for $C_{22}H_{28}O_3S$: C, 70.94; H, 7.57; S, 8.59. Found: C, 70.96; H, 7.86; S, 8.49.

A solution of 1.5 g. of the above acetate IIIb in 200 cc. of ethanol was refluxed for two hours with 3 g. of potassium bicarbonate and 30 cc. of water. Precipitation with water and recrystallization from hexane–acetone led in 83% yield to **estrone 17-ethylenehemithioketal (IIIc)** with m.p. 160–162°, $[\alpha]^{20}_{\mathrm{D}}$ 0°, ultraviolet absorption maximum at 282 mμ (log ϵ 3.29) and minimum at 248 mμ (log ϵ 2.32).

Anal. Calcd. for $C_{20}H_{26}O_2S$: C, 72.69; H, 7.92; S, 9.68. Found: C, 72.59; H, 8.19; S, 9.33.

Acid hydrolysis in the manner described above for IIb afforded estrone in 67% yield, m.p. 257–259°, $[\alpha]^{20}_{\mathrm{D}}$ +164.3°.

Δ^5-Androsten-3β-ol-17-one 3-Acetate 17-Ethylenehemithioketal (VIIb).[8]—Shiny plates (90% yield) from chloroform–methanol, m.p. 174–176°, $[\alpha]^{20}_{\mathrm{D}}$ −86.7°.

Anal. Calcd. for $C_{23}H_{34}O_3S$: C, 70.73; H, 8.77; S, 8.19. Found: C, 70.88; H, 8.93; S, 8.08.

Desulfurization of the hemithioketal was accomplished by refluxing 2.0 g. of VIIb in 400 cc. of acetone with 20 g. of W-2 Raney nickel catalyst[9] for three hours, filtering the catalyst and evaporating to dryness. Recrystallization from acetone–hexane gave 1.35 g. of Δ^5-androsten-3β-ol-17-one 3-acetate (VIIa) with m.p. 171–172°, $[\alpha]^{20}_{\mathrm{D}}$ +8.5° (chloroform); the m.p. remained unchanged on admixture with an authentic specimen of VIIa.

Anal. Calcd. for $C_{21}H_{30}O_3$: C, 76.32; H, 9.15. Found: C, 76.65; H, 9.41.

Bicarbonate saponification of the acetate VIIb produced **Δ^5-androsten-3β-ol-17-one 17-ethylenehemithioketal (VIIc)** in 78% yield, m.p. 151–153°, $[\alpha]^{20}_{\mathrm{D}}$ −90.3°.[10]

Anal. Calcd. for $C_{21}H_{32}O_2S$: C, 72.37; H, 9.25; S, 9.18. Found: C, 72.63; H, 9.48; S, 8.78.

Δ^4-Androstene-3,17-dione 17-Ethylenehemithioketal (VIIIb) (a) By Oppenauer Oxidation of Δ^5-Androsten-3β-ol-17-one 17-Ethylenehemithioketal (VIIc).—A mixture of 10 g. of the alcohol VIIc, 8 g. of aluminum *t*-butoxide, 100 cc. of cyclohexanone and 200 cc. of toluene was refluxed for 40 minutes and the solution was then washed with dilute Rochelle salt solution and water. Removal of the volatile components by steam distillation and extraction of the product with ether, followed by washing, drying, evaporating and crystallizing from methanol yielded 7.1 g. of Δ^4-androstene-3,17-dione 17-ethylenehemithioketal (VIIIb) with m.p. 192–193°, $[\alpha]^{20}_{\mathrm{D}}$ +46°, ultraviolet absorption maximum at 240 mμ (log ϵ 4.29) and infrared carbonyl band at 1674 cm.$^{-1}$. The product proved to be identical in all respects with a specimen prepared according to procedure (b).

(b) By Condensation of Δ^4-Androstene-3,17-dione with β-Mercaptoethanol.[4]—The preparation of the analytical sample of the 17-monoethylenehemithioketal VIIIb by this method has already been described.[3] Repetition of this experiment, but employing an equal weight of β-mercaptoethanol as outlined in the present paper, resulted in a product which did not necessitate purification by chromatography. The hydrochloric acid and cadmium carbonate hydrolyses of the hemithioketal VIIIb to Δ^4-androstene-3,17-dione (VIIIa) have already been recorded.[3]

Treatment of 3 g. of the 17-hemithioketal VIIIb with 30 g. of W-2 Raney nickel catalyst[9] in 400 cc. of acetone for three hours yielded 1.6 g. of Δ^4-androstene-3,17-dione (VIIIa) with m.p. 171–173°, $[\alpha]^{20}_{\mathrm{D}}$ +197° (chloroform).

Allopregnan-3β-ol-20-one 3-Acetate 20-Ethylenehemithioketal (IVb).—Shiny plates (86% yield) after recrystallization from ethyl acetate–methanol, m.p. 207–209°, $[\alpha]^{20}_{\mathrm{D}}$ +3°.

Anal. Calcd. for $C_{25}H_{40}O_3S$: C, 71.39; H, 9.58; S, 7.60. Found: C, 71.15; H, 9.83; S, 7.26.

Acid hydrolysis, followed by acetylation, or Raney nickel desulfurization of the hemithioketal IVb led to allopregnan-3β-ol-20-one 3-acetate (IVa), m.p. 145–146°, $[\alpha]^{20}_{\mathrm{D}}$ +72° (chloroform), + 76° (dioxane) in 92 and 67% yields, respectively.

Δ^5-Pregnen-3β-ol-20-one 3-Acetate 20-Ethylenehemithioketal (Vb).—Brilliant plates (72% yield) after recrystallization from chloroform–methanol; m.p. 186–188°, $[\alpha]^{20}_{\mathrm{D}}$ −34°.

Anal. Calcd. for $C_{25}H_{38}O_3S$: C, 71.73; H, 9.15; S, 7.64. Found: C, 71.76; H, 9.45; S, 7.55.

An ethanolic solution of 8 g. of the above acetate Vb was refluxed for 1.5 hours with 8 g. of sodium hydroxide and 30

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[7] Melting points are uncorrected. Rotations were measured in dioxane (unless noted otherwise), ultraviolet absorption spectra in 95% ethanol and infrared spectra (Perkin-Elmer model 12C spectrometer with sodium chloride prism) in carbon disulfide solution. We are grateful to Srta. Paquita Revaque and her staff for these measurements and to the Srtas. Amparo Barba and Rachel Cervera for the microanalyses.

[8] This experiment was carried out for the first time by Sr. J. Norymberski in this Laboratory.

[9] H. Adkins and A. Pavlic, THIS JOURNAL, **69**, 3039 (1947).

[10] This remarkably large levorotatory change on going from the ketone to the ethylenehemithioketal seems to be characteristic of 17-ketosteroids (III, VII, VIII). 3-Ketosteroids (I, II) exhibit only a very slight change in the rotation, while the 20-keto compounds (IV, V, VI) appear to be intermediate in this respect.

cc. of water, the product was precipitated with water and recrystallized from methanol–chloroform; yield 5.6 g., m.p. 148–150°. Further recrystallization afforded the analytical sample of **Δ^5-pregnen-3β-ol-20-one 20-ethylenehemithioketal (Vc)** with m.p. 153–155°, $[\alpha]^{20}\mathrm{D}$ −28.3°.

Anal. Calcd. for $C_{23}H_{36}O_2S$: S, 8.49. Found: S, 8.14.

Progesterone 20-Ethylenehemithioketal (VIb).—The Oppenauer oxidation of the alcohol Vc (5 g.) was carried out in the usual manner with 5 g. of aluminum *t*-butoxide, 50 cc. of cyclohexanone and 125 cc. of toluene for one-half hour. The usual work-up (see above under VIIIb) followed by recrystallization from chloroform–methanol yielded 3.1 g. of the desired hemithioketal with m.p. 190–192.5°, $[\alpha]^{20}\mathrm{D}$ +77.4°, ultraviolet absorption maximum at 242 mμ (log ϵ 4.31).

Anal. Calcd. for $C_{23}H_{34}O_2S$: C, 73.75; H, 9.15; S, 8.54. Found: C, 73.70; H, 8.97; S, 8.45.

Acid hydrolysis gave pure progesterone (VIa) in 48% yield with m.p. 126–127°, $[\alpha]^{20}\mathrm{D}$ +189° (chloroform), ultraviolet absorption maximum at 240 mμ (log ϵ 4.30).

General Procedure for Preparation of Ethylenehemithioketals of α,β-Unsaturated Ketones.—A solution of 8 g. of the steroid ketone in 100 cc. of benzene was refluxed for 5–7 hours with 12–15 g. of β-mercaptoethanol and 1.5 g. of *p*-toluenesulfonic acid.[11] After washing with sodium carbonate solution and water, the benzene was dried and evaporated. The product was purified by crystallization.

Δ^4-Androstene-3,17-dione 3,17-Bisethylenehemithioketal (IXa).—Direct crystallization from acetone–methanol gave 1.0 g. of the bis-hemithioketal IXa and 3.0 g. of impure solid, which was subjected to a Girard separation. From the non-ketonic fraction there was isolated 1.6 g. of bis-hemithioketal, raising the total yield of IXa to 23%, while from the ketonic fraction there was obtained 0.9 g. (9%) of the 17-monoethylenehemithioketal VIIIb. The analytical sample of the bis-ethylenehemithioketal IXa was crystallized from acetone–methanol, whereupon it showed m.p. 202–204°, $[\alpha]^{20}\mathrm{D}$ −60°, no selective absorption in the ultraviolet and no infrared carbonyl band.

Anal. Calcd. for $C_{23}H_{34}O_2S_2$: C, 67.95; H, 8.43; S, 15.74. Found: C, 68.24; H, 8.62; S, 15.70.

Raney nickel desulfurization in acetone solution proceeded in markedly poorer yield (22%) and the resulting Δ^4-androstene-3,17-dione (VIIIa) had to be purified by chromatography. On the other hand, acid hydrolysis (5 hours) occurred in the usual fashion and yielded 60% of Δ^4-androstene-3,17-dione (VIIIa).

Testosterone 3-Ethylenehemithioketal (IXb).—Colorless prisms (18%) from methanol, m.p. 192–193°, $[\alpha]^{20}\mathrm{D}$ −19°, no selective absorption in the ultraviolet.

Anal. Calcd. for $C_{21}H_{32}O_2S$: C, 72.36; H, 9.25; S, 9.19. Found: C, 72.59; H, 9.22; S, 9.18.

Testosterone Acetate 3-Ethylenehemithioketal (IXc).—15% yield after recrystallization from methanol in m.p. 200–202°, $[\alpha]^{20}\mathrm{D}$ −15°, no selective absorption in the ultraviolet.

Anal. Calcd. for $C_{23}H_{34}O_3S$: C, 70.73; H, 8.77; S, 8.19. Found: C, 71.23; H, 8.69; S, 7.79.

Δ^4-Pregnen-3-ol-one 20-Ethylenehemithioketal (IXd).—A solution of 4.0 g. of progesterone 20-ethylenehemithioketal (VIb) in 60 cc. of dry tetrahydrofuran was added dropwise to a mixture of 3.0 g. of lithium aluminum hydride in 25 cc. of the same solvent. After refluxing for 15 minutes and decomposing with ice-water, the solution was adjusted to *p*H 6 and the product was extracted with chloroform. Washing, drying and evaporation followed by recrystallization from methanol–chloroform gave 3.1 g. (78%) of the unsaturated alcohol IXd with m.p. 156–158°, $[\alpha]^{20}\mathrm{D}$ + 36°, which showed no selective absorption in the ultraviolet.

Anal. Calcd. for $C_{23}H_{36}O_2S$: C, 73.36; H, 9.63; S, 8.49. Found: C, 73.87; H, 9.77; S, 8.21.

16-β-Hydroxyethylmercapto-Δ^5-pregnen-3β-ol-20-one 3-Acetate (Xa).—A solution of 5 g. of $\Delta^{5,16}$-pregnadiene-3β-ol-20-one 3-acetate in 150 cc. of benzene was refluxed with 5 g. of β-mercaptoethanol and 6 cc. of piperidine for 5 hours and then allowed to stand for 20 hours at room temperature. After washing with dilute acid and water, the solution was dried and evaporated. Recrystallization of the residue from ether–pentane afforded the 16-β-hydroxyethylmercapto derivative Xa in over 90% yield, m.p. 91–93°, $[\alpha]^{20}\mathrm{D}$ −24.5°, no selective absorption in the ultraviolet.

Anal. Calcd. for $C_{25}H_{38}O_4S$: C, 69.09; H, 8.81; S, 7.36· Found: C, 69.08; H, 8.93; S, 7.11

Raney nickel desulfurization in acetone solution gave 52% of Δ^5-pregnen-3β-ol-20-one 3-acetate (Va) with m.p. 147–148°, $[\alpha]^{20}\mathrm{D}$ −14° (chloroform).

16-β-Benzoyloxyethylmercapto-Δ^5-pregnen-3β-ol-20-one 3-acetate (Xb) was obtained in nearly quantitative yield upon benzoylation (benzoyl chloride–pyridine) of Xa and recrystallization from methanol; m.p. 123–125°, $[\alpha]^{20}\mathrm{D}$ −12°, ultraviolet absorption maximum (due to benzoate group) at 230 mμ (log ϵ 4.18).

Anal. Calcd. for $C_{32}H_{42}O_5S$: C, 71.34; H, 7.85; S, 5.94. Found: C, 71.32; H, 7.88; S, 5.86.

16-(β-Hydroxyethylmercapto)-progesterone (XIIa).—The addition of β-mercaptoethanol to $\Delta^{4,16}$-pregnadiene-3,-20-dione (XI) was carried out exactly as described in the preceding experiment; yield 92%, m.p. 72–74° (after recrystallization from dilute methanol), $[\alpha]^{20}\mathrm{D}$ +84°, ultraviolet absorption maximum at 240 mμ (log ϵ 4.31).

Anal. Calcd. for $C_{23}H_{34}O_3S$: S, 8.19. Found: S, 8.35.

Treatment with Raney nickel in acetone solution led in 60% yield to progesterone (VIa), m.p. 127–128°.

16-(β-Benzoyloxyethylmercapto)-progesterone (XIIb), after recrystallization from acetone–hexane, showed m.p. 129–130°, $[\alpha]^{20}\mathrm{D}$ + 72°, ultraviolet absorption maximum at 234 mμ (log ϵ 4.58). The high extinction coefficient is due to the cumulative effect of the Δ^4-3-keto and the benzoate absorption.

Anal. Calcd. for $C_{30}H_{38}O_4S$: C, 72.84; H, 7.74; S, 6.46. Found: C, 73.05; H, 7.75; S, 5.99.

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[11] It was reported earlier (ref. 3) that in a similar condensation with Δ^4-androstene-3,17-dione where only a slight excess of β-mercaptoethanol was employed, the 17-monoethylenehemithioketal (VIIIb) (*cf.* footnote 4) could be isolated. By mistake, the catalyst (*p*-toluenesulfonic acid) was not specified.