[CONTRIBUTION FROM THE SAMUEL C. HOOKER LABORATORY OF THE DEPARTMENT OF CHEMISTRY OF WAYNE UNIVERSITY]

Studies in Organic Sulfur Compounds. VI.[1] Cyclic Ethylene and Trimethylene Hemithioketals

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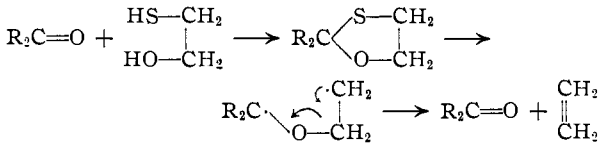
A number of steroidal as well as non-steroidal ketones have been converted into the corresponding cyclic ethylene (1,3-oxathiolane) and trimethylene (1,3-oxathiane) hemithioketals by employing either azeotropic distillation or an exchange method with the corresponding hemithioketal of acetone and continuous removal of acetone. Formation of the hemithioketals of Δ^4-3-ketosteroids appears to be accompanied by a shift of the 4,5-double bond to the 5,6-position. Sulfone and sulfoxide derivatives of the hemithioketals have also been prepared. A pronounced infrared band near 9.3 μ is characteristic of the hemithioketal grouping.

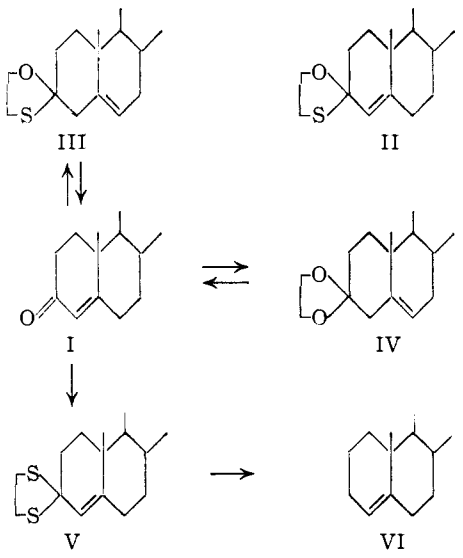
In an earlier study,[3] limited to certain steroidal ketones, it was reported that such ketones condense readily with β-mercaptoethanol to furnish cyclic hemithioketals which upon desulfurization with Raney nickel regenerate the parent ketone. It was suggested that this latter reaction may proceed *via* a 1,4-diradical



It appeared of interest to investigate further the scope and mechanism of this reaction for the following reasons. The facile removal of the hemithioketal grouping under essentially neutral conditions with Raney nickel represents potentially a very useful tool in organic synthesis since it is thus possible to protect a carbonyl function in a manner which does not involve ultimate cleavage with acids as is the case with ketals, semicarbazones, etc. Furthermore, if the 1,4-diradical mechanism proposed above is indeed correct, then the corresponding six-membered trimethylene hemithioketals upon similar treatment with Raney nickel should lead to propyl ethers or spirans in which the carbon atom adjacent to the sulfur should still be asymmetric, provided an unsymmetrical ketone is employed. Finally, conversion of the sulfide linkage to a sulfone followed by desulfurization might lead to interesting results in view of the difference observed recently in the behavior of optically active sulfones[4] as compared to sulfides[4,5] when treated with Raney nickel.

In view of the fact that trimethylene hemithioketals appear not to have been recorded before and that the two generally applicable methods for ethylene hemithioketal formation involve hydrogen chloride[6] or zinc chloride[3] as condensing agents, two additional procedures were developed. A description of these methods and of the structures of some of the compounds formed constitutes the content of this paper.

The first method involved condensation of a ketone with β-mercaptoethanol or γ-mercaptopropanol in benzene solution in the presence of *p*-toluenesulfonic acid under conditions of azeotropic distillation employing a water separator. This procedure, which has been used frequently with ethylene glycol for the formation of ketals,[7] served very satisfactorily for the ethylene (Tables I and II) and trimethylene (Tables I and III) hemithioketals of saturated ketones,[8] but unsaturated ketones as exemplified by the Δ^4-3-ketosteroids (I) gave the desired products in only mediocre yields. In the earlier article[3] in which the hemithioketal of testosterone had been described, it was assumed that the double bond remained in the original 4,5-position (II), but recently[9,10] the hitherto neglected observation of Fernholz[11] was recalled which indicated that in the case of ethylene ketals the double bond shifts to the 5,6-position (IV). Additional confirmatory evidence for this shift recently has been presented.[9] On the other hand, Hauptmann[12] showed that formation of the corresponding ethyl-



(1) Paper V, C. Djerassi and A. L. Nussbaum, THIS JOURNAL, **75**, 3700 (1953).

(2) Schering Corporation Predoctorate Fellow in Organic Chemistry at Wayne University, 1952–1953.

(3) J. Romo, G. Rosenkranz and C. Djerassi, THIS JOURNAL, **73**, 4961 (1951).

(4) W. A. Bonner, *ibid.*, **74**, 1034 (1952).

(5) H. Hauptmann, B. Wladislaw, L. L. Nazario and W. F. Walter, *Ann.*, **576**, 45 (1952), and earlier papers cited therein.

(6) F. Kipnis and J. Ornfelt, *ibid.*, **71**, 3555 (1949).

(7) For a recent example, see E. P. Oliveto, T. Clayton and E. B. Hershberg, *ibid.*, **75**, 486 (1953).

(8) Benzophenone was recovered unchanged.

(9) G. I. Poos, G. E. Arth, R. E. Beyler and L. H. Sarett, THIS JOURNAL, **75**, 422 (1953). *Cf.* footnote 5.

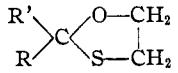
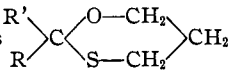
(10) R. Antonucci, S. Bernstein, R. Littell, K. J. Sax and J. H. Williams, *J. Org. Chem.*, **17**, 1341 (1952).

(11) E. Fernholz, U. S. 2,356,154 (1944), 2,378,918 (1945); E. Fernholz and H. E. Stavely, Abstracts, p. 39M, A. C. S. meeting, Atlantic City, Sept. 1941.

(12) H. Hauptmann, THIS JOURNAL, **69**, 562 (1947).

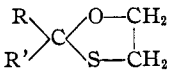
TABLE I

LIQUID HEMITHIOKETALS

No.	Ketone	Yield,[a] %	B.p., °C.	$n^{24}D$	d^{24}_4	(M) Calcd.	(M) Obsd.	Infrared band[b]	Formula	Analyses Calcd.	Found
	A. Ethylene hemithioketals 										
1	Acetone	85	70 (65 mm.)	1.4742	1.0105	32.70	32.83	9.48	$C_5H_{10}OS$	C 50.83	50.60
										H 8.53	8.75
2	Methyl ethyl ketone	79	42 (8 mm.)	1.4751	0.9776	37.32	37.20	9.40	$C_6H_{12}OS$	C 54.53	54.66
										H 9.15	9.57
3	Methyl isobutyl ketone[c]	70	41 (2 mm.)	1.4730	0.9696	46.56	46.34	9.30			
4	Cyclohexanone	62	47 (0.6 mm.)	1.5155	1.0811	44.36	44.16	9.33	$C_8H_{14}OS$	C 60.47	60.34
										H 8.92	8.87
5	Ethyl acetoacetate	77	117 (20 mm.)	1.4790	1.1118	48.21	48.13	9.08	$C_8H_{14}O_3S$	C 50.52	50.48
										H 7.42	7.19
6	Acetophenone	78	96 (2 mm.)	1.5663	1.1232	52.19	52.34	9.38	$C_{10}H_{12}OS$	C 66.65	66.44
										H 6.71	6.86
	B. Trimethylene hemithioketals 										
1	Acetone	81	49 (18 mm.)	1.4880	1.0216	37.32	37.27	9.33	$C_6H_{12}OS$	C 54.53	54.70
										H 9.15	8.96

[a] Water separator method. [b] Characteristic band in the 9–10μ region. [c] Already reported in ref. 20.

TABLE II

SOLID ETHYLENE HEMITHIOKETALS 

No.	Ketone	Yield, % Proced. A[a]	Yield, % Proced. B[b]	M.p., °C.	$[\alpha]^{20}D$ ($CHCl_3$)	Recrystal. solv.	Infrared band[c]	Formula	Analyses Calcd.	Found
1	Dibenzyl ketone	90		42–43		Et_2O–MeOH	9.24	$C_{17}H_{18}OS$	C 75.53	75.26
									H 6.71	6.66
2	Androstan-17-one	93	90	119–121	−40°	Et_2O–MeOH	9.28	$C_{21}H_{34}OS$	C 75.40	75.13
									H 10.25	10.30
3	Δ^6-Androsten-3β-ol-17-one acetate[d]	90	85	172–174	−99°	Et_2O–MeOH	9.28			
4	Cholestan-3-one	89		135–136	+25°	Me_2CO–MeOH	9.40	$C_{29}H_{50}OS$	C 77.97	77.76
									H 11.28	11.48
5	22a-5α-Spirostan-3β-ol-12-one acetate	62		224–225	−77°	CH_2Cl_2–MeOH	[f]	$C_{31}H_{48}O_5S$	C 69.89	69.66
									H 9.08	9.16
6	Testosterone[d]	22		192–194[e]	−30°	CH_2Cl_2–MeOH	9.26			
7	Δ^4-Pregnen-3-one-20β-ol acetate	30		183–185[e]	−31°	Et_2O–Hexane	9.33	$C_{35}H_{38}O_3S$	C 71.74	71.97
									H 9.15	9.23
8	Δ^4-22a-Spirosten-3-one	65	34	240–242[e]	−146°	$CHCl_3$–MeOH	[f]	$C_{29}H_{44}O_3S$[g]	C 73.69	73.91
									H 9.38	8.94

[a] Water separator method. [b] Exchange method. [c] Characteristic band in the 9–10 μ region. [d] Reported in ref. 3. [e] No selective absorption at 240 mμ. [f] Band obscured by spiroketal side-chain. [g] Calcd.: S, 6.77. Found: S, 6.84.

ene mercaptal (V) apparently did not involve a shift of the double bond since desulfurization led to the Δ^4-unsaturated hydrocarbon.

A consideration of the molecular rotations and a plausible reaction mechanism indicates that a shift of the double bond is indeed involved in the formation of the hemithioketal (III). Thus in the Δ^4-cholesten-3-one series, the change in molecular rotation on going to the mercaptal is positive (ΔM_D I → V = +193) while the corresponding change (I → IV) in the ketals of cholestenone[9,11] and testosterone acetate[10] is strongly negative (−469 and −495), a change characteristic of the 5,6-double bond.[13] Similar calculations (I → III) for the four hemithioketals reported in this paper (No. 6, 7, 8, Table II; No. 5, Table III) yield ΔM_D values of −431, −651, −616 and −696. The levorotatory change is thus strongly suggestive of a shift of the double bond to the 5,6-position (III) and the fact that these rotation changes are even more pronounced than in the case of the ketals (IV) may be due to the effect of the new asymmetric center generated at C-3. In order to rationalize the fact that a shift of the double bond is observed in the ketals (IV) and hemithioketals (III) but not mercaptals (V), it seems important to consider the primary intermediate in all three reactions.[14]

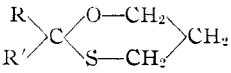
In the case of the ketals or hemithioketals, the

(13) *Cf.* D. H. R. Barton and W. Klyne, *Chemistry & Industry*, 755 (1948).

(14) Theoretically, intermediate A in the hemithioketals could involve the alternate structure with Y = O and a free thiol group. However, such a structure is *a priori* unlikely because of the greater nucleophilic character of sulfur and structure A has indeed been established by the isolation of a β-hydroxyethylthioenol ether in the reaction of β-mercaptoethanol and Δ^4-androstene-3,17-dione (G. Rosenkranz, S. Kaufmann and J. Romo, THIS JOURNAL, 71, 3689 (1949)).

TABLE III

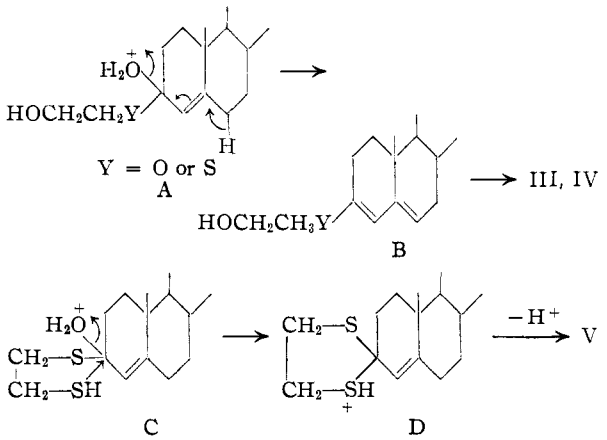
SOLID TRIMETHYLENE HEMITHIOKETALS



No.	Ketone	Yield, % Proced. A[a]	Proced. B[b]	M.p., °C.	$[\alpha]^{20}D$ $CHCl_3$	Recrystal. solv.	Infrared band[c]	Formula	Analyses	Calcd.	Found
1	Dibenzyl ketone	65		70–71		MeOH	9.28	$C_{18}H_{20}OS$	C	76.03	76.34
									H	7.09	7.11
2	Androstan-17-one	68	60	150–152		Et_2O–MeOH	9.22	$C_{22}H_{36}OS$	C	75.81	76.27
									H	10.41	10.70
									S	9.18	9.26
3	Δ^5-Androsten-3β-ol-17-one acetate	88		176–178	−98°	Me_2CO–MeOH	9.22	$C_{24}H_{36}O_3S$	C	71.25	70.91
									H	8.97	8.66
									S	7.91	7.92
4	22a-5α-Spirostan-3β-ol-12-one acetate	52		205–207	−65°	Et_2O–MeOH	[e]	$C_{32}H_{50}O_5S$	C	70.30	70.17
									H	9.22	9.35
									S	5.86	6.01
5	Δ^4-22a-Spirosten-3-one	43		145–147[d]	−187°	Me_2CO	[e]	$C_{30}H_{46}O_3S$	C	74.03	73.65
									H	9.53	9.32

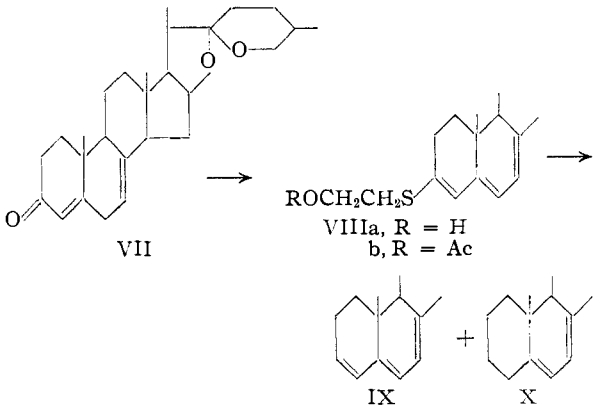
[a] Water separator method. [b] Exchange method. [c] Characteristic band in the 9–10μ region. [d] No selective absorption at 240μ. [e] Band obscured by spiroketal sidechain.

intermediate A can undergo either nucleophilic attack by the primary hydroxyl group to furnish the *unrearranged* derivative (*e.g.*, II) or first undergo dehydration to B[9] (stable $\Delta^{3,5}$-diene system) followed by 1,2-addition to the 3,4-double bond to furnish the *rearranged* derivatives (III, IV). Evidently the driving force to form the conjugated diene B is greater and the latter process occurs. On the other hand in the case of the mercaptal intermediate C, S_N2 attack to D by the more powerful nucleophilic attacking agent sulfur predominates over dehydration and the unrearranged mercaptal (V) is obtained.



The chemical proof[9,11] for the migration of the 4,5-double bond during ketal formation (I → IV) involves epoxidation of the double bond and is thus not readily applicable to the hemithioketals (III) because of rapid reaction with peracid to the corresponding sulfone (*vide infra*). Antonucci and co-workers[10] have provided indirect evidence for the double bond shift by demonstrating that the reaction of $\Delta^{4,7}$-3-ketosteroids with ethylene glycol (benzene solution, *p*-toluenesulfonic acid, azeotropic distillation) led to the $\Delta^{5,7}$-3-ethylene ketal but they were unable to detect $\Delta^{5,7}$-diene formation with β-mercaptoethanol. We had independently studied this sequence with β-mercaptoethanol and were able to clarify the course of the reaction.

Treatment of $\Delta^{4,7}$-22a-spirostadien-3-one (VII)[15] with β-mercaptoethanol in benzene solution in the presence of *p*-toluenesulfonic acid furnished in about 26% yield a crystalline substance, the infrared spectrum of which showed the presence of a free hydroxyl group and the absence of a carbonyl function. The characteristic ultraviolet absorption spectrum with maxima at 322, 334 and 352 mμ clearly established the structure of the compound as the thioenol ether VIIIa since the corresponding enol acetate[15] possesses maxima at 302, 314 and 330 mμ, characteristic of the $\Delta^{3,5,7}$-triene system,[16] and it is known that substitution of oxygen by sulfur involves a bathochromic shift of *ca.* 20 mμ.[14,17] As was to be expected,[17] the thioenol ether was formed in much better yield with pyridine hydrochloride as the condensing agent and the structure of the ether was supported further by conversion to the acetate (VIIIb) and by desulfurization to the $\Delta^{3,5,7}$-triene IX, admixed by some $\Delta^{5,7}$-diene X apparently formed from IX by reduction during the desulfurization process. This reaction sequence again[14] demonstrates that initial attack on the carbonyl group



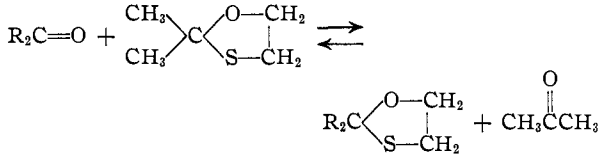
(15) R. Yashin, G. Rosenkranz and C. Djerassi, THIS JOURNAL, **73**, 4654 (1951).

(16) *Cf.* D. H. Gould, K. H. Schaaf and W. L. Ruigh, *ibid.*, **73**, 1263 (1951).

(17) J. Romo, M. Romero, C. Djerassi and G. Rosenkranz, *ibid.*, **73**, 1528 (1951).

proceeds *via* the SH rather than the OH function of β-mercaptoethanol. This also appears to be the explanation why only one isomer is isolated in the reaction of the saturated 3- and 17-ketosteroids with β-mercaptoethanol (Table II) and γ-mercaptopropanol (Table III) in spite of the fact that two isomers are possible. Evidently in all cases, initial attack by sulfur occurs from the unhindered rear (α) side so that all of the hemithioketals have the C–S (α) and C–O (β) configurations.

The second method for the formation of the hemithioketals involves an adaptation of the elegant exchange method developed recently for ketals,[18] in which a non-volatile ketone is refluxed in benzene solution with ethyl methyl dioxolane in the presence of *p*-toluenesulfonic acid, the equilibrium being displaced by the continuous distillation of ethyl methyl ketone as it is formed. In attempts to adapt this procedure to hemithioketal formation, it was found preferable to employ the corresponding acetone (2,2-dimethyl-1,3-oxathiolane and 2,2-dimethyl-1,3-oxathiane) rather than methyl ethyl ketone derivatives.



The reaction proceeded in essentially the same yield as by the first procedure and details are given in the experimental section and in the tables. It is pertinent to mention at this point that an exchange reaction between a steroid ketone and the ethylene mercaptal of acetone failed.[19]

For reasons pointed out in the beginning of this discussion, a study of the desulfurization of hemithioketals should also include the corresponding sulfones and a few representative types are described in the experimental section. The sulfones are readily prepared by oxidation with monoperphthalic acid while the corresponding sulfoxides are best synthesized by brief oxidation with hydrogen peroxide. The remarkable levorotatory effect of the introduction of a hemithioketal grouping upon the rotation of 17-ketosteroids has been remarked upon earlier[3] (*cf.* Tables II and III) and is also noticeable in the 12-ketosteroid reported in the present study (No. 5 in Table II, No. 4 in Table III). This is apparently due to the fact that a new asymmetric center is generated next to C-13 and thus produces a very considerable vicinal effect through the entire chain of asymmetric centers (13, 14, 8, 9, 10, 5). It is also of interest to note that while the rotation of a hemithioketal and the corresponding sulfone differ only slightly, an appreciable change is produced in the case of the sulfoxide and this again may be a reflection of the production of a new asymmetric center directly connected to seven other asymmetric carbon atoms. Thus in the case of androstan-17-one the following specific rotations are observed: ketone +113°, hemithioketal −40°, sulfone −38° and sulfoxide +49°.

The infrared absorption spectra of all of the hemithioketals reported in this paper have been measured in chloroform solution and as shown in the appropriate column in Tables I, II and III, a strong band near 9.3 μ appears to be characteristic of the hemithioketal grouping.[20]

Desulfurization studies of the presently described hemithioketals are now in progress and will be reported in a future communication.

Experimental[21]

Synthesis of Hemithioketals (*cf.* **Tables I–III**). **Procedure A. Water Separator Method.**—A mixture of 0.55 mole of the ketone, 0.5 mole of β-mercaptoethanol or γ-mercaptopropanol[22] and 100 cc. of anhydrous benzene containing 0.8 g. of *p*-toluenesulfonic acid monohydrate was refluxed in a round-bottomed flask connected to a Dean-Stark water separator[23] until no more water appeared in the separator (2–3 hours). In the case of steroidal ketones,[24] the proportions were varied in that for each g. of steroid, there was employed 1.0 g. of the mercapto alcohol, 30–50 mg. of *p*-toluenesulfonic acid and 40–50 cc. of benzene.

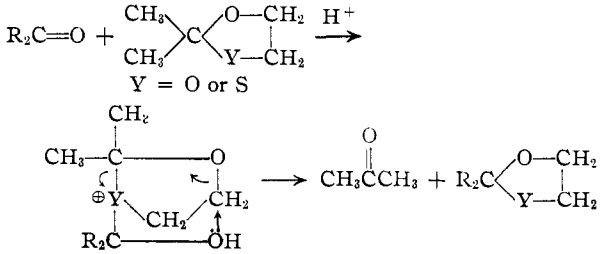
The benzene solution was cooled, washed with sodium bicarbonate solution and water, dried, evaporated and the residual hemithioketal was purified by distillation or crystallization.

Procedure B. Exchange Method.—A solution of the non-volatile ketone, a tenfold excess (by weight) of acetone ethylene- or trimethylene-hemithioketal, and *p*-toluenesulfonic acid (10% by weight of ketone) in benzene solution was concentrated over a period of 5 hours by slow distillation through a Vigreux column to one-half its volume. The original volume was restored by the addition of fresh benzene, an additional 10% of *p*-toluenesulfonic acid was added and the slow distillation was repeated. The benzene solution was then treated as in Procedure A and the desired hemithioketal was crystallized from methanol.

Stability of Hemithioketals toward Acidic Reagents.—Ethylene ketals are readily reconverted to the parent ketone

(18) H. J. Dauben, B. Loken and H. J. Ringold, in press; *cf. Chem. Eng. News*, **29**, 2747 (1951). We are indebted to these authors for advance information on their "*trans*-ketalization" method.

(19) A possible mechanism for this exchange reaction is indicated below.



As a consequence, this implies that the oxygen atom in the final derivative is that originally present in the non-volatile ketone and that in the case of hemithioketals, initial attack has to proceed *via* the sulfur atom (Y = S) since otherwise a ketal would be produced. Finally, it should be noted that if the exchange reaction had been successful with acetone ethylene mercaptal, the resulting products would have been a hemithioketal (rather than a mercaptal) and thioacetone, the monomer of which has never been described (*cf.* E. Campaigne, *Chem. Revs.*, **39**, 1 (1946)).

(20) E. D. Bergmann, E. Merron, Y. Hirshberg and S. Pinchas, *Rec. trav. chim.*, **71**, 200 (1952) have made the same observation with two aliphatic oxathiolanes.

(21) All melting points are uncorrected. Rotations were measured in chloroform and ultraviolet absorption spectra in absolute ethanol solution. The infrared spectra were obtained with a Baird Associates double beam recording infrared spectrophotometer employing a cell thickness of 0.1 mm. We are indebted to Messrs. M. Papo and R. Mullins (Wayne University) and Mr. Joseph F. Alicino (Metuchen, N. J.) for the microanalyses.

(22) Obtained by lithium aluminum hydride reduction (ether, solution, 2 hours refluxing) of commercially available β-mercaptopropionic acid.

(23) *Cf. Organic Syntheses*, **23**, 38 (1943).

(24) A number of the steroid ketones employed in this study were generously supplied by Syntex, S. A., Mexico City, D. F.

by an exchange reaction in acetone solution in the presence of *p*-toluenesulfonic acid.[25] In order to examine the behavior of a hemithioketal under these conditions, 0.2 g. of Δ^5-androsten-3β-ol-17-one 3-acetate 17-ethylene hemithioketal was allowed to stand at room temperature for 24 hours in 15 cc. of acetone with 50 mg. of *p*-toluenesulfonic acid. After working up in the usual manner, there was recovered 0.19 g. of unchanged hemithioketal.

It had been demonstrated earlier[3] that ethylene hemithioketals can be hydrolyzed to the original ketone by refluxing with ethanolic hydrochloric acid. In order to show that the six-membered hemithioketals behave similarly, 0.2 g. of Δ^5-androsten-3β-ol-17-one 3-acetate 17-trimethylene hemithioketal was refluxed for 3 hours with 0.8 cc. of concd. hydrochloric acid, 2 cc. of water and 40 cc. of ethanol. The crude reaction product was reacetylated with acetic anhydride–pyridine yielding *ca.* 70% of Δ^5-androsten-3β-ol-17-one acetate with m.p. 167–169°.

In certain instances, it may be desirable to test a mixture, containing a hemithioketal, with Girard reagent for the presence of ketonic material. This necessitated an experimental demonstration of the stability of the hemithioketal grouping toward conditions prevailing in such a separation. When the above-mentioned hemithioketal (No. 3, Table II) was refluxed for 1 hour in ethanol solution with an equal amount of Girard reagent T and glacial acetic acid, there was recovered 90% of unchanged hemithioketal and no ketonic cleavage product was observed.

$\Delta^{3,5,7}$-22a-3-(β-Hydroxyethylmercapto)-spirostatriene (VIIIa). (a) With Pyridine Hydrochloride.—A mixture of 2.0 g. of $\Delta^{4,7}$-22a-spirostadien-3-one (VII),[15] 2.0 g. of β-mercaptoethanol, 0.2 g. of pyridine hydrochloride, 10 cc. of ethanol and 150 cc. of benzene was refluxed for 3 hours, cooled, washed with bicarbonate solution and water, dried and evaporated to dryness. Recrystallization from acetone–methanol yielded 1.6 g. of pale yellow crystals of the thioenol ether with m.p. 176–178°, $[\alpha]^{20}D$ −138°, λ_{max}^{EtOH} 322, 334 and 352 mμ, log ϵ 4.53, 4.65 and 4.54: the infrared spectrum showed a hydroxyl band at 2.80 μ but no carbonyl band.

Anal. Calcd. for $C_{29}H_{42}O_3S$: C, 74.01; H, 9.00; S, 6.80. Found: C, 74.18; H, 9.30; S, 6.88.

(b) **With *p*-Toluenesulfonic Acid.**—When 1.0 g. of the $\Delta^{4,7}$-3-ketone VII was subjected to the water-separator method (Procedure A, *vide supra*) with 1.0 g. of β-mercaptoethanol, 80 mg. of *p*-toluenesulfonic acid and 60 cc. of benzene, there was obtained 0.7 g. of light brownish solid with m.p. 140–160°. Repeated recrystallization from acetone–methanol led to 0.3 g. (26%) of light yellowish crystals of the thioenol ether with m.p. 176–178°, undepressed upon admixture with a sample prepared according to (a) and further identified by its ultraviolet and infrared absorption spectrum.

The $\Delta^{3,5,7}$-22a-3-(β-Acetoxyethylmercapto)-spirostatriene (VIIIb).—The above β-hydroxyethylthioenol ether VIIIa (0.37 g.) was acetylated with acetic anhydride–pyridine at room temperature. Dilution with water, collection of the precipitate and recrystallization from acetone–methanol furnished 0.26 g. of the pale yellow acetate with m.p. 136–137°, $[\alpha]^{20}D$ −135°, λ_{max}^{EtOH} 321, 334 and 351 mμ, log ϵ 4.45, 4.58 and 4.46, $\lambda_{max}^{CHCl_3}$ 5.75 μ.

Anal. Calcd. for $C_{31}H_{44}O_4S$: C, 72.62; H, 8.65; S, 6.24. Found: C, 72.88; H, 8.89; S, 5.80.

***Desulfurization of* $\Delta^{3,5,7}$-22a-3-(β-Hydroxyethylmercapto)-spirostatriene (VIIIa).**—A solution of 1.0 g. of the thioenol ether VIIIa in 50 cc. of acetone was added to a suspension of 10 g. of W-2 Raney nickel in 100 cc. of acetone (which had been refluxing for 2 hours), and the mixture was refluxed for 3 hours. Filtration of the catalyst, evaporation of the filtrate to dryness and crystallization from methyl ethyl ketone furnished 0.77 g. of crystals with m.p. 139–141° which upon further recrystallization led to 0.40 g. of material with constant melting point 149–150°, $[\alpha]^{20}D$ −218°, λ_{max}^{EtOH} 273, 282, 296, 315 and 330 mμ, log ϵ 4.02, 4.09, 4.07, 4.07, 3.90. The rotatory and spectral data[16] show that this is a mixture of $\Delta^{3,5,7}$-22a-spirostatriene (IX) and the corresponding $\Delta^{5,7}$-diene (X), evidently formed by partial reduction of the triene during the desulfurization. The first two maxima correspond to those of the diene and the last two to the triene while the maximum at 296 mμ is evidently due to the superimposition of the 292 mμ maximum of the diene and the 302 mμ maximum[16] of the triene.

Anal. Calcd. for $C_{27}H_{38}O_2$: C, 82.18; H, 9.71. Found: C, 82.39; H, 10.04.

The same result was obtained when the acetate VIIIb was desulfurized.

Dibenzyl Ketone Ethylene Hemithioketal Sulfone (3,3-Dioxo-2,2-dibenzyl-1,3-oxathiolane).—A solution of 1.0 g. of dibenzyl ketone ethylene hemithioketal in 200 cc. of ether was treated overnight with an excess (0.012 mole) of monoperphthalic acid in the same solvent. After washing with bicarbonate and water, the solvent was removed and the residue was recrystallized from ether–pentane furnishing 0.78 g. of the sulfone with m.p. 76–78°, characteristic[26] infrared sulfone peaks (chloroform solution) at 7.67 and 8.85 μ.

Anal. Calcd. for $C_{17}H_{18}O_3S$: C, 67.54; H, 6.00. Found: C, 67.50; H, 6.08.

Dibenzyl Ketone Trimethylene Hemithioketal Sulfone.—An ethereal solution of 0.2 g. of dibenzyl ketone trimethylene hemithioketal (No. 1, Table III) was treated with an excess of monoperphthalic acid as described above for the 5-membered analog. Crystallization from pentane–acetone afforded 0.19 g. of the colorless sulfone with m.p. 108–110° and characteristic infrared sulfone bands[26] at 7.66 and 8.86 μ.

Anal. Calcd. for $C_{18}H_{20}O_3S$: C, 68.34; H, 6.37. Found: C, 68.11; H, 6.16.

Androstan-17-one Ethylene Hemithioketal Sulfone.—Androstan-17-one ethylene hemithioketal (1.0 g.) was oxidized with monoperphthalic acid as indicated above. Crystallization from acetone furnished 0.42 g. of the sulfone with m.p. 193–195°, while from the filtrate upon concentration there was isolated 0.39 g. of androstan-17-one (m.p. 110–115°, $\lambda_{max}^{CHCl_3}$ 5.78 μ) evidently arising from acid hydrolysis of the hemithioketal. Further recrystallization from acetone yielded the analytical sample of the sulfone with m.p. 199–200°, $[\alpha]^{20}D$ −38°, $\lambda_{max}^{CHCl_3}$ 7.66 μ. The identical sulfone was obtained when the hemithioketal was oxidized with ruthenium tetroxide[27] in carbon tetrachloride solution.

Anal. Calcd. for $C_{21}H_{34}O_3S$: C, 68.82; H, 9.35. Found: C, 69.31; H, 9.62.

Androstan-17-one Ethylene Hemithioketal Sulfoxide.—The oxidation procedure is similar to that employed for sulfoxidoenol ethers.[17]

To a solution of 0.9 g. of the ethylene hemithioketal in 60 cc. of ethanol and 20 cc. of dioxane was added 5 cc. of a saturated sodium carbonate solution followed by 10 cc. of 30% hydrogen peroxide. After 10 minutes on the steam-bath and 2 hours at room temperature, the sulfoxide was precipitated by the addition of water, filtered and recrystallized from acetone; yield 0.39 g., m.p. 164–166°, $[\alpha]^{20}D$ +49°, characteristic[28] infrared sulfoxide band (chloroform solution) at 9.57 μ.

Anal. Calcd. for $C_{21}H_{34}O_2S$: C, 71.96; H, 9.78. Found: C, 71.60; H, 9.89.

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