[Chem. Pharm. Bull. 17(10)2110—2119(1969)]

UDC 547.92.07

Thiosteroids. XXI.[1] Episulfide Formation from Vicinal Thiocyanatohydrins and Their Acetates

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(Received May 19, 1969)

Each epimers of 2,3-episulfides of 5β,25D-spirostane and 17β-hydroxy-5α-androstanes having a methyl group at C-1α, C_2, or C_3 were synthesized *via* the corresponding vicinal diaxial thiocyanatohydrins. In addition the formation of both episulfides and oxides from the vicinal diaxial thiocyanatohydrin acetates was discussed on the basis of the natures of the substituents.

In our continuing studies of steroidal episulfides,[3-9] direct formation of episulfides from the vicinal *trans* diaxial thiocyanatohydrins with alkali was successfully achieved only when the substituents were situated at C–2 and C–3 in 5α-steroids.[7,9] Under similar conditions the diaxial thiocyanatohydrins at C–3:C–4,[9] C–5:C–6,[5] C–11:C–12,[3] and C–16:C–17[6,10] were regenerated completely to the parent oxides. It was therefore assumed that the direct formation of episulfides proceeds by the same mechanism postulated and established by van Tamelen[11] through the 5-membered intermediate, 2-imino-1,3-oxathiolane. In fact we observed[9] that treatment of the 2β,3α-thiocyanatohydrins with Florisil afforded the 2-carbamoylimino-1,3-oxathiolanes together with episulfides as the result of disproportionation of the 5-membered intermediates and that the diaxial 2β,3α-mercapto-ols were condensed easily with acetone to yield the corresponding acetonides but 3α,4β-mercapto-ols were not.[9,12]

The present paper deals with the formation of episulfides from diaxial 2,3-thiocyanatohydrins in 5β-steroids and from those having a methyl group(s) in their neighborhood in 5α-androstane, where the introduced methyl group would be anticipated to cause a significant steric hindrance in such intermediates.

Treatment of 2β,3β-epoxy-5β,25D-spirostane (**1**) derived from Yonogenin[13] with thiocyanic acid gave 2α-thiocyanato-3β-ol (**2a**), and 2α,3α-epoxy-5β,25D-spirostane (**4**) yielded 3β-thiocyanato-2α-ol (**5a**). Treatment of both thiocyanatohydrins with potassium hydroxide in methanol provided preferential formation of the corresponding episulfides (2α,3α-episulfide

1) Part XX: C. Djerassi, D.A. Lightner, D.A. Schooley, K. Takeda, T. Komeno, and K. Kuriyama, *Tetrahedron*, **24**, 6913 (1969).
2) Location: *Fukushima-ku, Osaka.*
3) K. Takeda, T. Komeno, and J. Kawanami, *Chem. Pharm. Bull.* (Tokyo), **8**, 621 (1960).
4) T. Komeno, *Chem. Pharm. Bull.* (Tokyo), **8**, 668 (1960).
5) T. Komeno, *Chem. Pharm. Bull.* (Tokyo), **8**, 672 (1960).
6) T. Komeno, *Chem. Pharm. Bull.* (Tokyo), **8**, 680 (1960).
7) K. Takeda, T. Komeno, *Chem. Ind.* (London), **1962**, 1793.
8) K. Tori, T. Komeno, and T. Nakagawa, *J. Org. Chem.*, **29**, 1136 (1964).
9) K. Takeda, T. Komeno, J. Kawanami, S. Ishihara, H. Kadokawa, H. Tokura, and H. Itani, *Tetrahedron*, **21**, 329 (1965).
10) The similar situation was recently observed by E. Yoshida and F. Watanabe in this Laboratory in the hydrolysis of 1α,2β-thiocyanatohydrins of A-nor-5α-androstan-17β-ol, *Chem. Pharm. Bull.* (Tokyo), **15**, 1966 (1967).
11) E.E. van Tamelen, *J. Am. Chem. Soc.*, **73**, 3444 (1951).
12) T. Komeno, K. Tori, and K. Takeda, *Tetrahedron*, **21**, 1635 (1965).
13) K. Takeda, T. Okanishi, and A. Shimaoka, *Chem. Pharm. Bull.* (Tokyo), **6**, 532 (1958); **7**, 942 (1959).

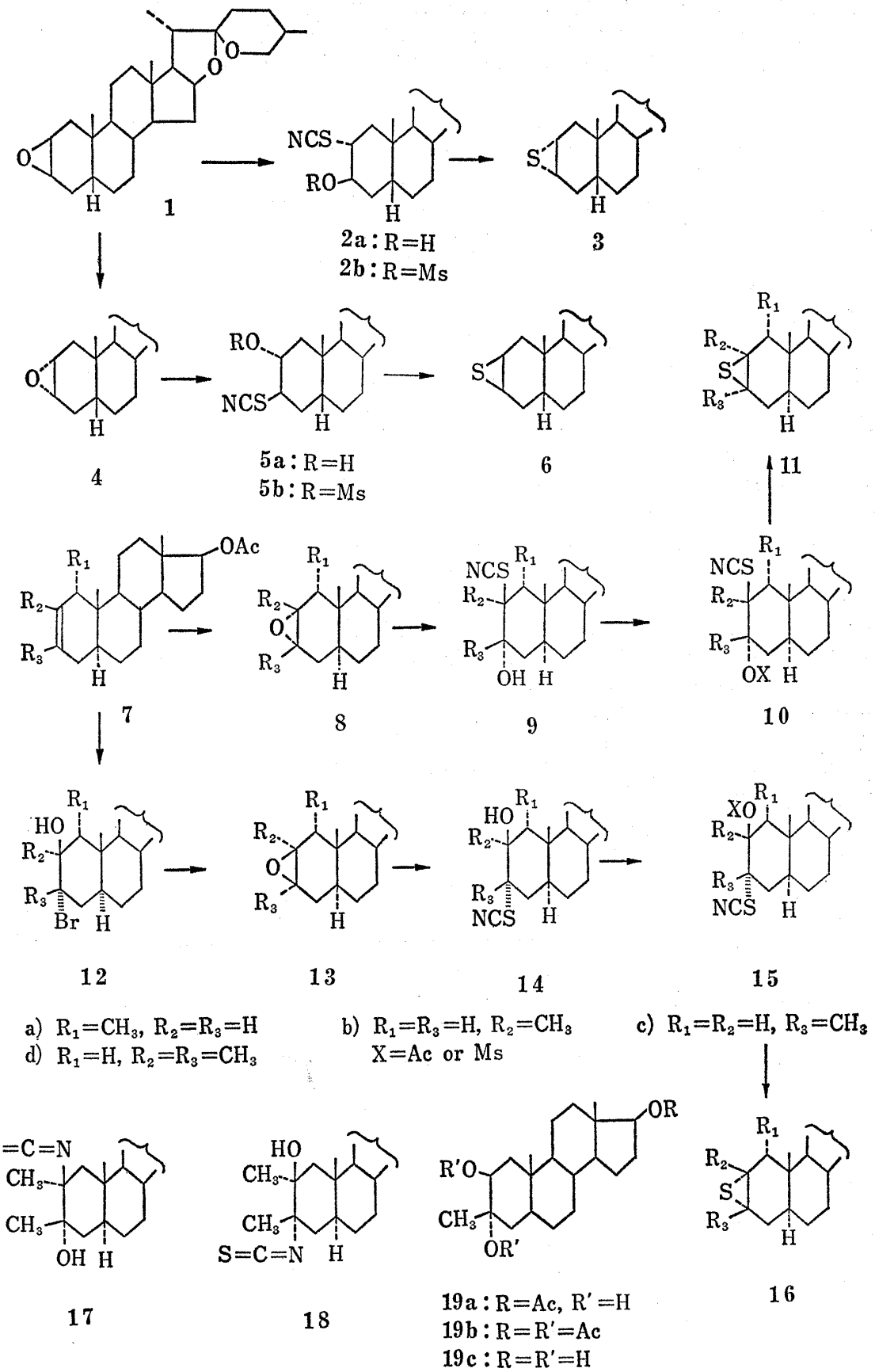


Chart 1

(**3**): 81% and 2β,3β-episulfide (**6**): 95%) and a very small amount of the parent oxides. The mesylate of both thiocyanatohydrins were treated with alkali to give only the episulfides.

The starting material, 2β,3α-thiocyanatohydrins having 1α,2α,3β-methyl groups or 2α,3β-dimethyl groups were synthesized as follows. 2β-Thiocyanato-3α-ols (**9a—9d**) were obtained by epoxidation of the olefins (**7a—7d**) with *m*-chloroperbenzoic acid, followed by treatment with thiocyanic acid. The structure of these compounds was confirmed by their behavior on acetylation and by the nuclear magnetic resonance (NMR) spectra (see Experimental). On the other hand, the olefins (**7a—7d**) were treated with N-bromosuccinimide in the presence of perchloric acid to give 3α-bromo-2β-ols (**12a—12d**). Of particular interest was that a considerable amount of 2β-bromo-3α-ol was isolated in the case of 3-methyl olefin (**7c**). The structure of this compound was established by conversion to 2α,3α-oxide (**8c**) with base and by the NMR spectrum, which shows the deshielded chemical shift for the 19-methyl group at 8.89 τ. Treatment of 2β,3β-oxides (**13a—13d**), obtained from 3α-bromo-2β-ols (**12a—12d**), with thiocyanic acid afforded 3α-thiocyanato-2β-ols (**14a—14d**). While the reaction of 2β,3α-thiocyanatohydrins having no methyl group with alkali gave only the episulfide, 2-methyl compounds (**9b**, **14b**), 3-methyl compounds (**9c**, **14c**), and 2,3-dimethyl compounds (**9d**, **13d**) regenerated completely the parent oxides. However, the 1α-methyl compound (**9a**) yielded the episulfide (**11a**) predominating over the oxide (**8a**) in a ratio of 8.5:1. These results are in harmony with the findings from an examination of a Dreiding model, which suggested that both 2α- and 3β-methyl groups give rise to a non-bonded interaction making the formation of the 5-membered intermediates unfavourable, and that the effect of 1α-methyl group is not so severe. The synthesis of the episulfides was carried out as follows. The thiocyanatohydrins having a secondary hydroxyl group (**9a**, **9b**, **14a**, **14c**) were converted to the mesylates, followed by treatment with base and those having a tertiary hydroxyl group (**9c**, **9d**, **14b**, **14d**) were converted to the acetates by forced acetylation in the presence of *p*-toluene sulfonic acid, followed by treatment with base as before.

It is noteworthy that in the reaction of 2,3-dimethyl oxide (**8d**, **13d**) with thiocyanic acid a considerable amount of the isothiocyanatohydrins (**17**, **18**) was isolated besides the normal product (**9d**, **14d**).

The NMR data of the episulfides[14] and the oxides obtained herein are summarized in Table I and II. In 5β-steroids the signals for 19-methyl group were unaffected by introduction of the β-episulfide, α-, and β-oxide groups, whereas that of the α-episulfide was deshielded by 0.05 ppm. In all cases of the series of methylated 5α-androstanes the signals for the 19-methyl group of the β-substituted compounds are more deshielded than those of the α-isomers by 0.08—0.18 ppm. The same effect was observed with the compounds having no methyl group (0.08—0.11 ppm).[8] The solvent effect was also found (see Table II). Therefore it is obvious that this effect is attributable to the spatial proximity of the substituents to 19-methyl group and hence supports their configuration as assigned.

Table I. NMR Data of 25D,5β-Spirostan-2,3-oxides and Episulfides (τ) in $CDCl_3$ Solution

Compound	18-H	19-H
25D-5β-Spirostane	9.24	9.08
25D-5β-Spirostane-2β,3β-oxide	9.23	9.09
25D-5β-Spirostane-2α,3α-oxide	9.27	9.07
25D-5β-Spirostane-2β,3β-episulfide	9.23	9.08
25D-5β-Spirostane-2α,3α-episulfide	9.27	9.03

14) The optical rotatory dispersion (ORD) and circular dichroism (CD) data of the episulfides, which supported the configuration, were already reported, K. Kuriyama, T. Komeno, and K. Takeda, *Tetrahedron*, **22**, 1039 (1966).

Table II. NMR Data of Methylated 5α-Androstan-2,3-oxides and -episulfides (τ)

Substituent			in $CDCl_3$			in C_6H_6		
Me	2,3-	17β-	18-H	19-H	Me	18-H	19-H	Me
1α-Me	α-O	OAc	9.22	9.20	9.07	9.22	9.38	9.30
1α-Me	β-O	OAc	9.22	9.07	9.07	9.23	8.97	9.28
1α-Me	α-S	OH	9.27	9.14	8.97	9.28	9.35	8.95
1α-Me	β-S	OH	9.27	8.98	8.88	9.32	8.95	9.11
2-Me	α-O	OH	9.28	9.26	8.71	9.28	9.43	8.80
2-Me	β-O	OH	9.28	9.15	8.74	9.30	9.06	8.83
2-Me	α-S	OH	9.28	9.21	8.42	9.31	9.45	8.54
2-Me	β-S	OH	9.29	9.09	8.44	9.32	9.03	8.54
3-Me	α-O	OH	9.28	9.26	8.71	9.28	9.41	8.83
3-Me	β-O	OH	9.28	9.17	8.70	9.33	9.08	8.81
3-Me	α-S	OH	9.28	9.27	8.40	9.30	9.43	8.53
3-Me	β-S	OH	9.28	9.11	8.40	9.32	9.06	8.52
2,3-DiMe	α-O	OAc	9.23	9.28	8.73	9.21	9.41	8.81, 8.79
2,3-DiMe	β-O	OAc	9.24	9.17	8.76, 8.72	9.23	9.06	8.83, 8.80
2,3-DiMe	α-S	OAc	9.23	9.28	8.40, 8.35	9.22	9.45	8.49, 8.46
2,3-DiMe	β-S	OAc	9.23	9.10	8.41, 8.38	9.23	9.03	8.50, 8.48

The reaction of the vicinal *trans* diaxial thiocyanatohydrin acetate with base was carried out, since it is anticipated that in this case the reaction takes a different path from that of the thiocyanatohydrin. A generally possible path of the reaction shown in the Chart is plausible. There are two types of reactions possible depending upon the position where the base attacks. a) If initial attack of the base occurs at the acetoxyl carbonyl to yield the O-anion, two kinds of products are expected; in case the anion attacks the carbon bearing the thiocyanate and pushs this group away in SN_2 manner, epoxide is formed. On the other hand, when the anion attacks the thiocyanate carbon giving the 5-membered intermediate, episulfide yields. b) Contrary, if initial attack occurs at the sulfur atom of the thiocyanate group, the S-anion forms, giving the episulfide in a similar manner. For example, treatment of 3α-thiocyanato-5α-cholestan-4β-ol acetate[9] and 12α-thiocyanato-5α-pregnane-3β,11β,20β-triol triacetate[15] with base afforded exclusively the corresponding episulfides, while the free thiocyanatohydrins regenerated the parent oxides, because 5-membered cyclic intermediate can not be formed. It is assumed that the reaction with these compounds having both secondary thiocyanate and secondary acetoxyl group proceeds through the path (b). When the methylated thiocyanatohydrin acetate (**10c**, **10b**, **15c**, **10d**, **15d**) were treated with alkali, both episulfides and oxides were obtained as shown in Table III.

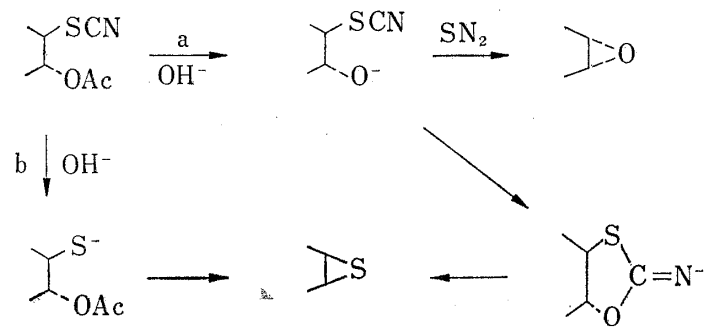
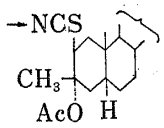
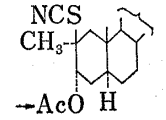
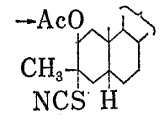
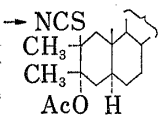
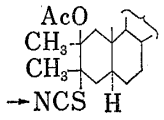
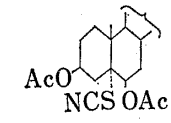


Chart 2

The compound, (**10b**) and (**15c**), having a tertiary thiocyanate and a secondary acetoxyl group afforded predominantly oxides over episulfides. The compounds (**10d**) and (**15d**) having

15) C. Djerassi, D.A. Lightner, D.A. Schooley, K. Takeda, T. Komeno, and K. Kuriyama, *Tetrahedron*, **24**, 6913 (1968).

Table III. The Yields (%) of the Products obtained by Treatment of Thiocyanatohydrin Acetates with KOH–EtOH

	Yield of episulfide	Yiled of epoxide
 (10c)	81.5	2.9
 (10b)	9.3	88.3
 (15c)	36.4	60.1
 (10d)	52.1	45.2
 (15d)	86.7	9.0
	13.5	65.5

both tertiary thiocyanate and acetoxyl group gave preferentially episulfides over oxides. These results indicate that here two types (a and b) of reactions are competitive and that there is an order of facility of the S- and the O-anion formation as follows,

sec-SCN>*sec*-OAc>*tert*-SCN>*tert*-OAc

However, in two pairs of isomers having similar situation (**10b** *vs.* **15c** and **10d** *vs.* **15d**) a marked difference was observed between the yield of the episulfide and that of the oxide. This fact may be attributable to a steric factor. Fürst and Plattner[16] reported that the hydrolyses of 2β- and 3α-alcohol acetate under the standard conditions proceeded to 11 and 34%, respectively. In agreement with this fact, 3β-methyl-3α-thiocyanato-2β-ol acetate (**15c**) gave relatively less oxide than **10b** and consequently relatively more episulfide was obtained. Similarly, 2α,3β-dimethyl-3α-thiocyanato-2β-ol acetate (**15d**) afforded relatively more episulfide than **10d**.

Experimental[17]

General Procedure of Epoxide with Peracid——To a solution of 10 mmole of an olefin in 50 ml of methylene-chloride 13 mmole of *m*-chloroperbenzoic acid was added under cooling and the mixture was kept at room

16) A. Fürst, Pl. A. Plattner, *Helv. Chim. Acta*, **32**, 275 (1949).

17) All melting points were measured on a Kofler hot-stage apparatus and are uncorrected. Optical rotations were determined in 1% EtOH–$CHCl_3$ with a Perkin–Elmer Polarimeter, type 141. Unless otherwise stated, IR spectra were recorded in Nujol mulls with a Nihon Bunko Infrared Spectrophotometer Model DS–201B. NMR spectra were run in deuterated chloroform solution on a Varian A–60 spectrometer, tetramethylsilane serving as internal standard. For preparative TLC silica gel G (Merck Co.) was used as an adsorbent.

temp overnight. The reaction mixture was washed with Na_2CO_3 aq. and water, dried over Na_2SO_4, and evaporated *in vacuo*. Recrystallization from appropriate solvents gave the corresponding epoxide.

1α-Methyl-17β-acetoxy-5α-androstan-2α,3α-epoxide (8a)——64.8% yield from **7a**[18] (aq. MeOH), mp 104—107°, $[\alpha]_D^{23.5}$ 58.3±2° (c=1.037). *Anal.* Calcd. for $C_{22}H_{34}O_3$: C, 76.26; H, 9.89. Found: C, 76.25; H, 10.00. IR ν_{max} cm^{-1}: 1732, 1254 (OAc), 1028, 825, 817.

2β-Methyl-17β-acetoxy-5α-androstan-2α,3α-epoxide (8b)——82.8% yield from **7b**[19] (acetone), mp 208—210°, $[\alpha]_D^{24}$ 10.6±2° (c=1.073). *Anal.* Calcd. for $C_{22}H_{34}O_3$: C, 76.26: H, 9.89. Found: C, 76.23; H, 9.90. IR ν_{max} cm^{-1}: 1732, 1242 (OAc), 1043, 1031, 809, 791.

3β-Methyl-17β-acetoxy-5α-androstan-2α,3α-epoxide (8c)——88.8% yield from **7c**[19] (hexane), mp 134—136°, $[\alpha]_D^{23}$ 22.1±2° (c=0.989). *Anal.* Calcd. for $C_{22}H_{34}O_3$: C, 76.26: H, 9.89. Found: C, 76.21; H, 9.92. IR ν_{max} cm^{-1}: 1739, 1252, 1238 (OAc), 1044, 1035, 959, 895, 875, 843, 812, 803.

2β,3β-Dimethyl-17β-acetoxy-5α-androstan-2α,3α-epoxide (8d)——83.8% yield from **7d** (acetone). $[\alpha]_D^{23}$ 18.5±2° (c=1.046). *Anal.* Calcd. for $C_{23}H_{36}O_3$: C, 76.62; H, 10.06. Found: C, 76.82; H, 10.13. IR ν_{max} cm^{-1}: 1732, 1240, 1219 (OAc), 1041, 1030, 846.

2,3-Dimethyl-5α-androst-2-en-17β-ol acetate (**7d**) was obtained from 2α-methyl-5α-androstan-3-one by Grignard reaction with CH_3MgI, followed by treatment with $HClO_4$ in acetic acid. 69.9% overall yield, mp 155—157° (acetone), $[\alpha]_D^{23}$ 63.8±2° (c=1.009). *Anal.* Calcd. for $C_{23}H_{36}O_2$: C, 80.18; H, 10.53. Found: C, 80.22; H, 10.64. NMR: 9.29 (18-H), 9.20 (19-H), 8.42 (2-, 3-CH_3), 7.98 (OAc), 5.38t (17α-H).

1α-Methyl-17β-acetoxy-5α-androstan-2β,3β-oxide (13a)——To a solution of 7.152 g (20.7 mmole) of **7a** in 100 ml of 80% dioxane 5.02 g (26.9 mmole) of N-bromosuccinimide (NBS) and 1.8 ml of 70% $HClO_4$ was added subsequently. The mixture was stirred at room temp. for 5.5 hr, then poured into 300 ml of ice water, and extracted with ether. The ether solution was washed with Na_2CO_3 aq. and water, dried over Na_2SO_4, and evaporated to dryness *in vacuo*. A solution of the residue (9.26 g) and anhydrous AcOK in abs EtOH (135 ml)was heated under reflux for 1.5 hr, poured into 400 ml of water, and extracted with ether. The etheral solution was washed with water, dried over Na_2SO_4, and evaporated to dryness under reduced pressure. The residue (7.6 g) was dissolved in pet. ether and subjected to chromatography over 150 g of standardized Al_2O_3 (Grade II). The eluate with pet. ether was crystallized from ether and recrystallized from hexane to yield 2.606 g of **13a**. 34.6% yield, mp 162—164°, $[\alpha]_D^{24}$ 69.1±2° (c=0.990). *Anal.* Calcd. for $C_{22}H_{34}O_3$: C, 76.26; H, 9.89. Found: C, 76.04; H, 9.98. IR ν_{max} cm^{-1}: 1732, 1253 (OAc), 1045, 813, 801.

2α-Methyl-17β-hydroxy-5α-androstan-2β,3β-epoxide (13b)——To a solution of 7.038 g of **7b** in 87% dioxane (115 ml) 4.41 g of N-bromoacetoamide (NBA) and 3.05 ml of 70% $HClO_4$ were added. The mixture was stirred at room temp. for 1.5 hr, and treated as described above. The residue was recrystallized from acetone–hexane to give 3.66 g of 2α-methyl-3α-bromo-5α-androstane-2β,17β-diol 17-monoacetate (**12b**). 40.2% yield. mp 161—163°. $[\alpha]_D^{28}$ 54.6±2° (c=0.961). *Anal.* Calcd. for $C_{22}H_{35}O_3Br$: C, 61.82; H, 8.25. Found: C, 61.70; H, 8.38. IR ν_{max} cm^{-1}: 3538, 3510, 3406 (OH), 1739, 1712, 1275, 1263, 1248 (OAc), 1047, 1038, 1028, 960, 895. NMR :9.20 (18-H), 8.98 (19-H), 8.60 (2α-CH_3), 7.97 (AcO), 5.39t (17α-H), 5.83 (3β-H). This substance was acetylated in the presence of p-TsOH·H_2O to yield 2,17-diacetate, which was recrystallized from acetone–hexane, mp 147.5—148.5°, $[\alpha]_D^{25}$ 46.7±2° (c=1.064). *Anal.* Calcd. for $C_{24}H_{37}O_4Br$: C, 61.40; H, 7.94: Br, 17.02. Found: C, 61.48; H, 8.13; Br, 17.12. IR ν_{max} cm^{-1}: 1737, 1257, 1242 (OAc), 1050, 1037. NMR: 9.22 (18-H), 9.08 (19-H), 8.35 (2α-CH_3), 8.02, 7.97 (AcO), 5.41 t (17α-H), 5.28 (3β-H). To a solution of 2.922 g of bromohydrin (**12b**) in 65 ml of iso-PrOH 3 g of KOH was added. The resulting mixture was heated under reflux for 3 hr, poured into 200 ml of ice water, and extracted with CH_2Cl_2. The CH_2Cl_2 layer was washed with water, dried over Na_2SO_4, and evaporated to dryness *in vacuo*. The residue was recrystalllized from acetone–hexane to give 1.973 g (95.0%) of 2α-methyl-17β-hydroxy-5α-androstan-2β,3β-epoxide, mp 171.5—173.5°, $[\alpha]_D^{27.5}$ 56.7±2° (c=0.991). *Anal.* Calcd. for $C_{20}H_{32}O_2$: C, 78.89; H, 10.59. Found: C, 78.67; H, 10.81.

3α-Methyl-17β-acetoxy-5α-androstan-2β,3β-epoxide (13c)——To a solution of 27.0 g of (**7c**) in 330 ml of 82% dioxane 17 g of NBA and 5.8 ml of 70% $HClO_4$ were added under cooling. The mixture was strried for 30 min and poured into 2 liter of ice water. The appeared precipitates were collected by filtration, washed with Na_2CO_3 aq. and water, dried, and triturated in ether.

a) The appeared crystals, collected by filtration, were recrystallized from $CHCl_3$–AcOEt to give 8.4 g (24.1%) of 3β-methyl-2β-bromo-5α-androstane-3α,17β-diol 17-monoacetate, mp 190—192°, $[\alpha]_D^{23.5}$ 31.6±2° (c=1.033). *Anal.* Calcd. for $C_{22}H_{35}O_3Br$: C, 61.82; H, 8.25; Br, 18.70. Found: C, 61.62; H, 8.41; Br, 18.79. IR ν_{max} cm^{-1}: 3544 (OH), 1719, 1263 (OAc), 1039, 1031, 857. NMR: 9.20 (18-H), 8.89 (19-H), 8.56 (3β-CH_3), 7.98 (OAc), 5.42t (17α-H), 5.85 (2α-H). This substance was recovered by acetylation with pyridine and acetic anhydride, but was treated with acetic anhydride and acetic acid in the presence of p-TsOH·H_2O to yield two products. These were separated by TLC technique and provided 39.9% of 3β-methyl-2β-bromo-5α-androstane-3α,17β-diol 3,17-diacetate, mp 122—123°, $[\alpha]_D^{24}$ 46.6±2° (c=1.018). *Anal.* Calcd. for $C_{24}H_{37}O_4Br$: C,

18) B. Pelc, *Collection Czech. Chem. Commun.*, **30**, 3468 (1965).
19) A.D. Cross, J.A. Edwards, J.C. Orr, B. Berköz, L. Cervantes, M.C. Calzada, and A. Bowers, *J. Med. Chem.*, **6**, 162 (1963).

61.40; H, 7.94; Br, 17.02. Found: C, 61.47; H, 7.98; Br, 17.30. IR ν_{max} cm^{-1}: 1740, 1731, 1251, 1236 (OAc), 1039, 1033. NMR: 9.21 (18-H), 8.86 (19-H), 8.36 (3β-CH_3), 7.98 (OAc), 5.42t (17α-H), 5.23 (2α-H) and 16.0% of 3-methyl-2β-bromo-5α-androst-3-en-17β-ol acetate, which was not identified but assumed by the following data, mp 157—158.5°. *Anal.* Calcd. for $C_{22}H_{33}O_2Br$: C, 64.54; H, 8.12; Br, 19.52. Found: C, 64.31; H, 8.28; Br, 19.33. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1737, 1248 (OAc), 1670 (Δ), 1044, 1030, 871. Treatment of crystallized bromohydrin, mp 190—192°, with KOH–iso-PrOH, followed by acetylation with pyridine and acetic anhydride afforded single crystals, mp 134—136°, which were identified as 2α,3α-epoxide (**8c**) by means of mixed mp and IR spectrum.

b) The ethereal mother liquor was evaporated to dryness *in vacuo* and dissolved in 660 ml of 5% KOH–iso-PrOH. The mixture was heated under reflux for 1.5 hr, concentrated under reduced pressure, poured into water, and extracted with ether. The ethereal solution was washed with water, dried over Na_2SO_4, and concentrated to a small volume. The appeared crystals were collected by filtration to give 7.4 g of 3α-methyl-17β-hydroxy-5α-androstan-2β,3β-epoxide. Recrystallization from CH_2Cl_2–acetone afforded the pure sample, mp 193—194°. $[\alpha]_D^{23.5}$ 46.5±2° (c=1.014). *Anal.* Calcd. for $C_{20}H_{32}O_2$: C, 78.89; H, 10.59. Found: C, 78.61; H, 10.63. IR ν_{max} cm^{-1}: 3398 (OH), 1082, 1061, 1054, 1040, 932, 905, 851, 839, 786, 693. The ethereal mother liquor was evaporated *in vacuo* and chromatographed over 280 g of Florisil. The eluate with benzene gave the less polar mixture (3.69 g). The eluates with a mixture of benzene and CH_2Cl_2 (9:1—1:1) were combined and evaporated. The residue was recrystallized from CH_2Cl_2–acetone to yield 1.106 g of the above 2β,3β-epoxide, total yield: 34.2%. Acetylation of this substance was effected with pyridine and acetic anhydride to give 17-acetate (**13c**), mp 182—184°. $[\alpha]_D^{24}$ 37.2±2° (c=1.014). *Anal.* Calcd. for $C_{22}H_{34}O_3$: C, 76.26; H, 9.89. Found: C, 76.41; H, 10.02. IR ν_{max} cm^{-1}: 1731, 1253 (OAc), 1050, 1035, 935, 914, 907, 891, 847, 704.

2α,3α-Dimethyl-17β-acetoxy-5α-anhdrostan-2β,3β-epoxide (13d)——To a solution of 3.960 g of **7d** in 100 ml of 80% dioxane 2.67 g of NBS and 1 ml of 60% $HClO_4$ were added under cooling. The mixture was stirred for 1 hr, then poured into water. The precipitates were collected by filtration, washed with water, dried, and crystallized from ether to yield 3.094 g (60.8% yield) of 2α,3β-dimethyl-3α-bromo-5α-androstane-2β,17β-diol 17-monoacetate (**12d**). Recrystallization from acetone afforded the pure sample, mp 170—172°. $[\alpha]_D^{23}$ 60.1±2° (c=1.066). *Anal.* Calcd. for $C_{23}H_{37}O_3Br$: C, 62.58; H, 8.45. Found: C, 62.83; H, 8.67. IR ν_{max} cm^{-1}: 3520 (OH), 1714, 1267, 1262, 1247 (OAc), 1063, 1034. NMR: 9.22 (18-H), 9.00 (19-H), 8.56, 8.19 (2α-, 3β-CH_3), 7.98 (OAc), 5.42t (17α-H). Acetylation of this substance with acetic anhydride and acetic acid in the presence of p-TsOH·H_2O gave 2,17-diacetate, mp 142—144° (56% yield). $[\alpha]_D^{23}$ 54.2±2° (c=1.031). *Anal.* Calcd. for $C_{25}H_{39}O_4Br$: C, 62.10; H, 8.13; Br, 16.53. Found: C, 62.32; H, 8.26; Br, 16.75. NMR: 9.24 (18-H), 9.16 (19-H), 8.27, 8.19 (2α-, 3β-CH_2), 8.05, 7.98 (OAc), 5.43t (17α-H). A mixture of 1.866 g of the bromohydrin, mp 170—172°, and 1.9 g of anhydrous AcOK in 30 ml of abs. EtOH was heated under reflux for 1 hr. After working up as usual, recrystallization from acetone gave 1.262 g (82.9% yield) of (**13d**), mp 182—184°. $[\alpha]_D^{23}$ 40.7±2° (c=0.972). *Anal.* Calcd. for $C_{23}H_{36}O_3$: C, 76.62; H, 10.06. Found: C, 76.35; H, 10.03. IR ν_{max} cm^{-1}: 1732, 1243, 1233 (OAc), 1043, 842.

Attempted Synthesis of 3α-Methyl-17β-hydroxy-5α-androstan-3β-oxide from 2α,3α-Epoxide (8c)—— A solution of 373 mg of 2α,3α-epoxide (**8c**) in a mixture of CH_2Cl_2 (10 ml), acetone (10 ml) and H_2O (2.7 ml) 0.2 ml of 60% $HClO_4$ was added. The resulting mixture was agitated for 1.5 hr, poured into water, and extracted with $CHCl_3$. The $CHCl_3$ solution was washed with Na_2CO_3 aq. and water, dried over Na_2SO_4, and evaporated to dryness. The residue was recrystallized from acetone–hexane to give 3β-methyl-5α-androstane-2β,3α,17β-triol 17-monoacetate (**19a**), mp 213—214°. $[\alpha]_D^{22}$ 24.7±2° (c=1.037). *Anal.* Calcd. for $C_{22}H_{36}O_4$: C, 72.49; H, 9.96. Found: C, 72.72; H, 10.08. IR ν_{max} cm^{-1}: 3516, 3326 (OH), 1724, 1708, 1280, 1266 (OAc), 1048, 1034. NMR: 9.22 (18-H), 9.02 (19-H), 8.74 (3β-CH_3), 7.98 (OAc), 5.40t (17α-H), 6.38 (2α-H). Forced acetylation of (**19a**) in the presence of p-TsOH·H_2O gave triacetate (**19b**) 70.0% yield (MeOH), mp 175—176.5°. $[\alpha]_D^{25}$ 56.8±2° (c=1.031). *Anal.* Calcd. for $C_{26}H_{40}O_6$: C, 69.61; H, 8.99. Found: C, 69.63; H, 9.08. IR ν_{max} cm^{-1}: 1739, 1251 (OAc), 1048. NMR: 9.23 (18-H), 9.10 (19-H), 8.57 (3β-CH_3), 7.98, 7.96 (OAc), 5.41 (17α-H), 4.90 (2α-H). Heating of triacetate (**19b**) with KOH–EtOH for 1.5 hr afforded no 2β,3β-epoxide but triol (**19c**) quantitatively. Forced acetylation of triol (**19c**) regenerated triacetate (**19b**).

General Procedure of Thiocyanatohydrins——To a mixture of 3 g of KSCN dissolved in a small volume of ice water and 10 ml of ether, 4.5 g of H_3PO_4 was added in small portions and shaken to extract HSCN formed into ether layer. The pink colored HSCN–ether solution was dried over Na_2SO_4 and added to a solution of 1 mmole of the epoxide in 5 ml of ether or methylenechloride. The reaction mixture was allowed to stand at room temp. overnight. The solution was washed with Na_2CO_3 aq. and water, dried over Na_2CO_3, and evaporated to dryness under reduced pressure. Recrystallization from appropriate solvents gave the corresponding thiocyanatohydrin. (a) That having a newly formed secondary hydroxyl group could be acetylated with pyridine and acetic anhydride and mesylated with pyridine and mesyl chloride as usual. (b) When the thiocyanatohydrin have a teritary hydroxyl group, it was subjected to forced acetylation. To a solution of 1 mmole thiocyanatohydrin in 3 ml of AcOH, were added 1 ml of Ac_2O and 0.1—0.2 mmole of p-TsOH·H_2O. The reaction mixture was kept at room temp. overnight. After usual working up the acetate was obtained.

2α-Thiocyanato-5β,25D-spirostan-3β-ol (2a)——Yield: 77.7% (acetone–hexane), mp 180—183°, $[\alpha]_D^{25}$ −55.2±2° (c=1.125). *Anal.* Calcd. for $C_{28}H_{42}O_3NS$: C, 70.99; H, 9.15; N, 2.96; S, 6.77. Found: C, 70.86; H, 9.22; N, 2.98; S, 6.50. IR ν_{max} cm^{-1}: 3393 (OH), 2154 (SCN), 979, 897, 862. A solution of this compound (25 mg) in 0.5 ml of dioxane was treated with 5% KOH–MeOH (0.5 ml) for 2 hr. The products were separateded by preparative TLC to yield 80.8% of 2α,3α-episulfide (3) and 4.6% of 2β,3β-epoxide (1).

3β-Mesylate (2b)——Method (a) Yield: 98.8% (ether–pet. ether), mp 145—148°, $[\alpha]_D^{25}$ −63.7±2° (c=1.062). *Anal.* Calcd. for $C_{29}H_{45}O_5NS_2$: C, 63.13; H, 8.22; N, 2.54; S, 11.61. Found: C, 63.36; H, 8.41; N, 2.62; S, 11.32. IR ν_{max} cm^{-1}: 2142 (SCN), 1185 (OMs).

3β-Thiocyanato-5β-25D-spirostan-2α-ol (5a)——Yield: 96.4% (ether–pet. ether), mp 217—220°, $[\alpha]_D^{24}$ −76.1±2° (c=0.965). *Anal.* Calcd. for $C_{28}H_{42}O_3NS$: C, 70.99; H, 9.15; N, 2.96; S, 6.77. Found: C, 70.92; H, 9.28; N, 3.09; S, 6.70. IR ν_{max} cm^{-1}: 3368 (OH), 2142 (SCN), 1059, 963, 928, 893. Treatment of this compound with KOH–MeOH as described above provided 95.1% of 2β,3β-episulfide (6) and 2.9% of 2α, 3αepoxide (4).

2α-Mesylate (5b)——Method (a) Yield: 87.2% (hexane), mp 141—144°. $[\alpha]_D^{24}$ −80.9±2° (c=1.021). *Anal.* Calcd. for $C_{29}H_{45}O_5NS_2$: C, 63.13; H, 8.22; N, 2.54; S, 11.61. Found: C, 62.83; H, 8.32; N, 2.58; S, 11.76. IR ν_{max} cm^{-1}: 2156 (SCN), 1193 (OMs), 1078, 1060, 979, 965, 913, 880.

1α-Methyl-2β-thiocyanato-5α-androstane-3α,17β-diol 17-Monoacetate (9a)——Yield: 56.9% (acetone), mp 205—208°, $[\alpha]_D^{23}$ 28.1±2° (c=1.003). *Anal.* Calcd. for $C_{23}H_{35}O_3NS$: C, 68.12; H, 8.70; N, 3.45; S, 7.91. Found: C, 67.85; H, 8.79; N, 3.43; S, 7.89. IR ν_{max} cm^{-1}: 3400 (OH), 2154 (SCN), 1704, 1276 (OAc), 1046, 1031, 781.

3-Mesylate (10a)——Method (a) no isolated.

1α-Methyl-3α-thiocyanato-5α-androstane-2β,17β-diol 17-Monoacetate (14a)——Yield: 92.2% (acetone–hexane), mp 155—158°, $[\alpha]_D^{23.5}$ 81.8±2° (c=1.084). *Anal.* Calcd. for $C_{23}H_{35}O_3NS$: C, 68.12; H, 8.70; N, 3.45; S, 7.91. Found: C, 68.26; H, 8.97; N, 3.46; S, 7.79. IR ν_{max} cm^{-1}: 3532 (OH). 2144 (SCN), 1714, 1270 (OAc), 1040.

2-Mesylate (15a, X=Ms)——Method (a) Yield: 90.8% (acetone–hexane), mp 163—164°, $[\alpha]_D^{23.5}$ 54.1±2° (c=1.011). *Anal.* Calcd. for $C_{24}H_{37}O_5NS_2$: C, 59.60; H, 7.71; N, 2.90; S, 13.26. Found: C, 59.72; H, 7.85; N, 3.02; S, 13.13, IR ν_{max} cm^{-1}: 2158 (SCN), 1734, 1249 (OAc), 1179 (OMs), 1050, 1043, 918, 850, 829.

2α-Methyl-2β-thiocyanato-5α-androstane-3α,17β-diol 17-Monoacetate (9b)——Yield: 74.4% (acetone–hexane), mp 182—183°. $[\alpha]_D^{24}$ 52.8±2° (c=1.114). *Anal.* Calcd. for $C_{23}H_{35}O_3NS$: C, 68.12; H, 8.70; N, 3.45; S, 7.91. Found: C, 68.18; H, 8.81; N, 3.52; S, 7.75. IR ν_{max} cm^{-1}: 3444 (OH), 2164 (SCN), 1735, 1249 (OAc), 1049, 1043, 1026. NMR: 9.23 (18-H), 9.03 (19-H), 8.35 (2α-CH_3), 7.98 (AcO), 5.40t (17α-H), 6.03 (3β-H).

3-Mesylate (10b, X=Ms)——Method (a) Yield: 77.6% (acetone–hexane), mp 119.5—121.5°, $[\alpha]_D^{24}$ 70.5±2° (c=1.102). *Anal.* Calcd. for $C_{24}H_{37}O_5NS_2$: C, 59.60; H, 7.71; N, 2.90; S, 13.26. Found: C, 59.75; H, 7.81; N, 2.97; S, 13.31. IR ν_{max} cm^{-1}: 2168 (SCN), 1730, 1253, 1238 (OAc), 1176 (OMs), 893, 812.

3,17-Diacetate (10b, X=Ac)——Method (a) Yield: 95.0% (acetone–hexane), mp 187—189°, $[\alpha]_D^{24}$ 75.8±2° (c=1.105). *Anal.* Calcd. for $C_{25}H_{37}O_4NS$: C, 67.08; H, 8.33; N, 3.13; S, 7.16. Found: C, 67.04; H, 8.42; N, 3.30; S, 6.95. IR ν_{max} cm^{-1}: 2170 (SCN), 1755, 1733, 1243 (OAc), 1044. NMR: 9.22 (18-H), 9.00 (19-H), 8.43 (2α-CH_3), 7.98, 7.92 (OAc), 5.41t (17α-H), 4.92 (3β-H).

2α-Methyl-3α-thiocyanato-5α-androstane-2β,17β-diol (14b)——Yield: 72.9% (acetone), mp 218—220°, $[\alpha]_D^{30}$ 119.0±2° (c=1.066). *Anal.* Calcd. for $C_{21}H_{33}O_2NS$: C, 69.37; H, 9.15; N, 3.85; S, 8.82. Found: C, 69.55; H, 9.22; N, 3.94; S, 8.65. IR ν_{max} cm^{-1}: 3480, 3372 (OH), 2155 (SCN), 1043.

17-Monoacetate (14b)——Method (a) Yield: 80.5% (acetone–hexane), mp 187—189°, $[\alpha]_D^{24}$ 107.7±2° (c=1.065). *Anal.* Calcd. for $C_{23}H_{35}O_3NS$: C, 68.12; H, 8.70; N, 3.45; S, 7.91. Found: C, 68.13; H, 8.76; N, 3.64; S, 7.78. IR ν_{max} cm^{-1}: 3450 (OH), 2177 (SCN), 1725, 1253, 1225 (OAc), 1049, 1037. NMR: 9.23 (18-H), 8.98 (19-H), 8.63 (2α-CH_3), 7.98 (OAc), 5.41t (17α-H), 6.42 (3β-H).

2,17-Diacetate (15b, X=Ac)——Method (b) Yield: 80.0% (acetone–hexane), mp 163—164°, $[\alpha]_D^{29}$ 81.0±2° (c=0.974). *Anal.* Calcd. for $C_{25}H_{37}O_4NS$: C, 67.08; H, 8.33; N, 3.13; S, 7.16. Found: C, 66.97; H, 8.65; N, 3.23; ,S 7.01. IR ν_{max} cm^{-1}: 2160 (SCN), 1736, 1255, 1242 (OAc), 1037, 1017. NMR: 9.23 (18-H), 9.08 (19-H), 8.35 (2α-CH_3), 8.01, 7.98 (OAc); 5.40t (17α-H), 5.82 (3β-H).

3β-Methyl-2β-thiocyanato-5α-androstane-3α,17β-diol 17-Monoacetate (9c)——Yield: 88.9% (acetone–hexane), mp 168—170°, $[\alpha]_D^{23.5}$ 55.1±2° (c=0.970). *Anal.* Calcd. for $C_{23}H_{35}O_3NS$: C, 68.12; H, 8.70; N, 3.45; S, 7.91. Found: C, 68.37; H, 9.00; N, 3.45; S, 8.03. IR ν_{max} cm^{-1}: 3496, 3370 (OH), 2172 (SCN), 1713, 1278, 1265 (OAc), 1047, 1035. NMR: 9.23 (18-H), 9.11 (19-H), 8.51 (3β-CH_3), 7.98 (OAc), 5.40t (17α-H), 6.40 (2α-H).

3,17-Diacetate (10c, X=Ac)——Method (b) Yield: 77% (acetone–hexane), mp 177—178.5°, $[\alpha]_D^{24}$ 72.5±2° (c=1.077). *Anal.* Calcd. for $C_{25}H_{37}O_4NS$: C, 67.08; H, 8.33; N, 3.13; S, 7.16. Found: C, 67.22; H, 8.62; N, 3.25; S, 6.88. IR ν_{max} cm^{-1}: 2164 (SCN), 1730, 1251, 1243 (OAc), 1028, 1014. NMR: 9.23 (18-H), 9.10 (19-H), 8.28 (3β-CH_3), 7.99, 7.98 (OAc), 5.42t (17α-H), 5.72 (2α-H).

3β-Methyl-3α-thiocyanato-5α-androstane-2β,17β-diol 17-Monoacetate (14c)——Yield: 87.0% (acetone–hexane), mp 161—162.5°, $[\alpha]_D^{25}$ 54.9±2° (c=1.000). *Anal.* Calcd. for $C_{23}H_{35}O_3NS$: C, 68.12; H, 8.70; N,

3.45; S, 7.91. Found: C, 68.49; H, 9.01; N, 3.37: S, 7.97. IR ν_{max} cm^{-1}: 3516 (OH), 2156 (SCN), 1719, 1273 (OAc), 1044. NMR: 9.23 (18-H), 9.00 (19-H), 8.33 (3β-CH_3), 7.99 (OAc), 5.42 (17α-H), 6.08 (2α-H).

2,17-Diacetate (15c, X=Ac)——Method (a) Yield: 94.3% (acetone), mp 209.5—210.5°, $[\alpha]_D^{23.5}$ 58.0±2° (c=0.848). *Anal.* Calcd. for $C_{25}H_{37}O_4NS$: C, 67.08; H, 8.33; N, 3.13; S, 7.16. Found: C, 67.44; H, 8.52; N, 3.24; S, 7.14. IR ν_{max} cm^{-1}: 2150 (SCN), 1734, 1235 (OAc), 1040, 1025. NMR: 9.23 (18-H), 9.08 (19-H), 8.41 (3β-CH_2), 7.98, 7.95 (OAc), 5.40t (17α-H), 4.93 (2α-H).

2-Mesylate (15c, X=Ms)——Method (a) Yield: 61.6% (acetone–hexane), mp 124—126°, $[\alpha]_D^{24.5}$ 46.2±2° (c=1.023). *Anal.* Calcd. for $C_{24}H_{37}O_5NS_2$: C, 59.60; H, 7.71; N, 2.90; S, 12.36. Found: C, 59.37; H ,7.65; N, 2.89; S, 13.22. IR ν_{max} cm^{-1}: 2168 (SCN), 1727, 1258 (OAc), 1177 (OMs), 956, 878.

2α,3β-Dimethyl-2β-thiocyanato-5α-androstane-3α,17β-diol 17-Monoacetate (9d)——Yield: 70.5% (acetone), mp 187—189°, $[\alpha]_D^{23}$ 55.8±2° (c=1.008). *Anal.* Calcd. for $C_{24}H_{37}O_3NS$: C, 68.69; H, 8.89; N, 3.34; S, 7.64. Found: C, 68.95; H, 8.99; N, 3.60; S, 7.47. IR ν_{max} cm^{-1}: 3464 (OH), 2160 (SCN), 1715, 1276 (OAc), 1058, 845. NMR: 9.22 (18-H), 8.95 (19-H), 8.63, 8.37 (2α-, 3β-CH_3), 7.98 (OAc), 5.41t (17α-H).

3,17-Diacetate (10d, X=Ac)——Method (b) Yield: 73.9% (acetone–hexane), mp 203—205° (decomp.), $[\alpha]_D^{23}$ 74.1±2° (c=1.037). *Anal.* Calcd. for $C_{26}H_{39}O_4NS$: C, 67.64; H, 8.52; N, 3.03; S, 6.95. Found: C, 67.84; H, 8.63; N, 3.23; S, 6.92. IR ν_{max} cm^{-1}: 2155 (SCN), 1733, 1244 (OAc), 1053, 1044. NMR: 9.23 (18-H), 8.96 (19-H), 8.33 (2α-, 3β-CH_3), 7.98 (OAc), 5.42t (17α-H).

2α,3β-Dimethyl-3α-thiocyanato-5α-androstane-2β,17β-diol 17-Monoacetate (14d)——Yield: 61.4% (acetone), mp 183—185°, 218—220° (decomp.), $[\alpha]_D^{23}$ 97.8±2° (c=1.018). *Anal.* Calcd. for $C_{24}H_{37}O_3NS$: C, 68.69; H, 8.89; N, 3.34; S, 7.64. Found: C, 68.62; H, 8.91; N, 3.45; S, 7.86. IR ν_{max} cm^{-1}: 3492 (OH), 2154 (SCN), 1713, 1273 (OAc), 1065, 1047, 1030. NMR: 9.22 (18-H), 8.98 (19-H), 8.70, 8.37 (2α-, 3β-CH_3), 7.98 (OAc), 5.40t (17α-H).

2,17-Diacetate (15d, X=Ac)——Method (b) Yield: 51.0% (ether–pet. ether), mp 158—160°, $[\alpha]_D^{23}$ 76.2±2° (c=1.026). *Anal.* Calcd. for $C_{26}H_{39}O_4NS$: C, 67.64; H, 8.52; N, 3.03; S, 6.95. Found: C, 67.95; H, 8.63; N, 3.17; S, 7.11. IR ν_{max} cm^{-1}: 2258 (SCN), 1734, 1258, 1240 (OAc), 1055, 1048, 1027, 1018. NMR: 9.23 (18-H), 9.13 (19-H), 8.38, 8.32 (2α-, 3β-CH_3), 5.40t (17α-H).

In the reaction of 2,3-dimethylepoxide (**8d** and **13d**) with HSCN, a considerable amount of less polar substance in TLC-plate was appeared, respectively. These substances were isolated by means of TLC-technique and characterized as the isothiocyanate by IR spectrum.

2α,3β-Dimethyl-2β-isothiocyanato-5α-androstane-3α,17β-diol 17-Monoacetate (17)——Yield: 5% (acetone–hexane), mp 250—252°, $[\alpha]_D^{23}$ −22.8±2° (c=1.055). *Anal.* Calcd. for $C_{24}H_{37}O_3NS$: C, 68.69; H, 8.89; N, 3.34; S, 7.64. Found: C, 69.07; H, 9.10; N, 3.55; S, 7.67. IR ν_{max} cm^{-1}: 3516 (OH), 2160 (NCS), 1716, 1271 (OAc), 1045, 1030. NMR: 9.22 (18-H), 8.98 (19-H), 8.68, 8.56 (2α-, 3β-CH_3), 7.98 (OAc), 5.42t (17α-H).

2α,3β-Dimethyl-3α-isothiocyanato-5α-androstane-2β,17β-diol 17-Monoacetate (18)——Yield: 6.9% (acetone), mp 260—262°, $[\alpha]_D^{23}$ 84.5±2° (c=1.064). *Anal.* Calcd. for $C_{24}H_{37}O_3NS$: C, 68.69; H, 8.89; N, 3.34; S, 7.64. Found: C, 68.42; H, 8.82; N, 3.24; S, 7.79. IR ν_{max} cm^{-1}: 3531 (OH), 2158 (NCS), 1724, 1269, 1262 (OAc), 1078, 1047, 944, 896. NMR: 9.23 (18-H), 9.02 (19-H), 8.72, 8.59 (2α-, 3β-CH_3), 7.98 (OAc), 5.40t (17α-H).

Preparative Procedure of Episulfides——(a) From Thiocyanatohydrin Mesylate: To a solution of 1 mmole of thiocyanatohydrin mesylate in 17 ml of dioxane 10 ml of 5% KOH–MeOH was added. The resulting mixture was stirred at room temp overnight, poured into water, and extracted with CH_2Cl_2. The CH_2Cl_2 solution was washed with water, dried over Na_2CO_3, and evaporated to dryness under reduced pressure. The residue was chromatographed on Al_2O_3, if necessary. In most cases, recrystallization from suitable solvents gave a pure sample.

5β,25D-Spirostan-2α,3α-episulfide (3)[20]——77.0% yield from (**2b**) (CH_2Cl_2–acetone), mp 167—169°, $[\alpha]_D^{25}$ −68.7±2° (c=1.120). *Anal.* Calcd. for $C_{27}H_{41}O_2S$: C, 75.47; H, 9.62; S, 7.46. Found: C, 75.67; H, 9.89; S, 7.53. IR ν_{max} cm^{-1}: 1056, 1047, 981, 897, 866. UV: λ_{max}^{EtOH} mμ (ε): 264 (54).

5β,25D-Spirostan-2β,3β-episulfide (6)[20]——87.3% yield from (**5b**) (CH_2Cl_2–acetone), mp 168—170°, $[\alpha]_D^{24.5}$ −49.6±2° (c=1.027). *Anal.* Calcd. for $C_{27}H_{41}O_2S$: C, 75.47; H, 9.62; S, 7.46. Found: C, 75.50; H, 9.72; S, 7.70. IR ν_{max} cm^{-1}: 1052, 879, 898, 863.

1α-Methyl-17β-hydroxy-5α-androstan-2β,3β-episulfide[21]——54.3% yield from (**10a**, X=Ms) (aq.-MeOH) mp 131—134°. *Anal.* Calcd. for $C_{20}H_{32}OS$: S, 10.00. Found: S, 9.54. IR ν_{max} cm^{-1}: 3320 (OH), 1060, 957.

17-Acetate (11a)[21]——(Acetone), mp 156—158°, $[\alpha]_D^{24}$ 63.7 ±2° (c=1.024). *Anal.* Calcd. for $C_{22}H_{34}O_2S$: C, 72.88; H, 9.45; S, 8.84. Found: C, 72.72; H, 9.54; S, 8.79. IR ν_{max} cm^{-1}: 1731, 1261 (OAc), 1046, 1035, 957.

20) The ORD and CD data of these compounds were reported in K. Kuriyama, T. Komeno, and K. Takeda, *Shionogi Kenkyusho Nempo*, **17**, 66 (1967).

21) The ORD and CD data was cited in K. Kuriyama, T. Komeno, and K. Takeda, *Tetrahedron*, **22**, 1039 (1966).

1α-Methyl-17β-hydroxy-5α-androstan-2α,3α-episulfide[21]——79.4% yield from (**15a**, X=Ms) (acetone–hexane), mp 124—125.5°. $[\alpha]_D^{23.5}$ 136.0±2° (c=1.084). *Anal.* Calcd. for $C_{20}H_{32}OS$: C, 74.94; H, 10.06; S, 10.00. Found: C, 74.85; H, 10.12; S, 9.91. IR ν_{max} cm^{-1}: 3446 (OH), 1051, 959.

17-Acetate (16a)[21]——(MeOH), mp 107—109°. $[\alpha]_D^{23.5}$ 118.9±2° (c=1.019). *Anal.* Calcd. for $C_{22}H_{34}O_2S$: C, 72.88; H, 9.45; S, 8.84. Found: C, 72.89; H, 9.57; S, 8.78. IR ν_{max} cm^{-1}: 1734, 1253 (OAc), 1045, 1029, 1021, 959.

2α-Methyl-17β-hydroxy-5α-androstan-2β,3β-episulfide[21]——82.8% yield from (**10b**, X=Ms) (acetone–hexane), mp 155—157°. $[\alpha]_D^{24}$ 47.5±2° (c=1.046). *Anal.* Calcd. for $C_{20}H_{32}OS$: C, 74.94; H, 10.06; S, 10.00. Found: C, 74.65; H, 10.06; S, 9.87. IR ν_{max} cm^{-1}: 3470 (OH), 1062, 1004, 988, 938.

17-Acetate (11b)——(acetone–hexane), mp 147—149°, $[\alpha]_D^{24}$ 27.5±2° (c=0.969). *Anal.* Calcd. for $C_{22}H_{34}O_2S$: C, 72.88; H, 9.45; S, 8.84. Found: C, 72.92; H, 9.52; S, 8.72. IR ν_{max} cm^{-1}: 1730, 1250 (OAc), 1047, 1026, 914.

3β-Methyl-17β-hydroxy-5α-androstan-2α,3α-episulfide[21]——81.6% yield from (**15c**, X=Ms) (hexane), mp 126—128°. $[\alpha]_D^{25}$ 26.2±2° (c=1.075). *Anal.* Calcd. for $C_{20}H_{32}OS$: C, 74.94; H, 10.06; S, 10.00. Found: C, 75.06; H, 10.21; S, 9.41. IR ν_{max} cm^{-1}: 3268 (OH), 1082, 1051, 1028, 1010, 990, 959.

17-Acetate (16c)——(acetone), mp 138—140°. $[\alpha]_D^{23.5}$ 20.2±2° (c=1.074). *Anal.* Calcd. for $C_{22}H_{34}O_2S$: C, 72.88; H, 9.45; S, 8.84. Found: C, 73.18; H, 9.48; S, 8.67. IR ν_{max} cm^{-1}: 1734, 1251, 1238 (OAc), 1046, 1032, 955, 906, 895.

(b) From Thiocyanatohydrin Acetate: A mixture of 10 mmole of thiocyanatohydrin acetate and 100 mmole of KOH was heated in 10 ml of abs. EtOH for 1—2 hr. After working up the following compounds were isolated in a similar manner as described above.

2β-Methyl-17β-hydroxy-5α-androstan-2α,3α-episulfide[21]——69.9% yield from (**15b**, X=Ac) (acetone–hexane), mp 151.5—153.5°. $[\alpha]_D^{27}$ 27.5±2° (c=1.213). *Anal.* Calcd. for $C_{20}H_{32}OS$: C, 74.94; H, 10.06; S, 10.00. Found: C, 75.04; H, 10.29; S, 9.84. IR ν_{max} cm^{-1}: 3322 (OH), 1053, 1038, 959.

17-Acetate (16b)——(aq. acetone), mp 142.5—144.5°. $[\alpha]_D^{26}$ 29.7±2° (c=1.111). *Anal.* Calcd. for $C_{22}H_{34}O_2S$: C, 72.88; H, 9.45; S, 8.84. Found: C, 72.85; H, 9.71; S, 8.50. IR ν_{max} cm^{-1}: 1731, 1254 (OAc), 1049, 1041, 1023, 956.

3α-Methyl-17β-hydroxy-5α-androstan-2β,3β-episulfide[21]——65.3% yield from (**10c**, X=Ac) (acetone–hexane), mp 125—127°. $[\alpha]_D^{24}$ 46.5±2° (c=1.065). *Anal.* Calcd. for $C_{20}H_{32}OS$: C, 74.94; H, 10.06; S, 10.00. Found: C, 75.01; H, 10.25; S, 9.90. IR ν_{max} cm^{-1}: 3330 (OH), 1081, 1062, 1035, 961, 929. When in the reaction 1 mmole of thiocyanatohydrin acetate was used and the products were separated by preparative TLC, yield of episulfide was 81.5% and 2.9% of oxide (**8c**) was recovered.

17-Acetate (11c)——(acetone–hexane), mp 133—135°. $[\alpha]_D^{24}$ 27.2±2° (c=1.056). *Anal.* Calcd. for $C_{22}H_{34}O_2S$: C, 72.88; H, 9.45; S, 8.84. Found: C, 72.81; H, 9.58; S, 8.73. IR ν_{max} cm^{-1}: 1727, 1252 (OAc), 1045, 976, 932, 916.

2α,3α-Dimethyl-17β-acetoxy-5α-androstan-2β,3β-episulfide[21] (**11d**)—The reaction products obtained by treatment of (**10d**, X=Ac) with KOH–EtOH were acetylated with pyridine and acetic anhydride and was effected by preparative TLC to give 45.2% of 2α,3α-oxide (**8d**) and 52.1% of episulfide (**11d**), (acetone), mp 168—170°. $[\alpha]_D^{23}$ 36.0±2° (c=1.054). *Anal.* Calcd. for $C_{23}H_{36}O_2S$: C, 73.35; H, 9.64; S, 8.50. Found: C, 73.02; H, 9.68; S, 8.42. IR ν_{max} cm^{-1}: 1731, 1259, 1247, 1234 (OAc), 1043, 1030, 1019.

2β,3β-Dimethyl-17β-acetoxy-5α-androstan-2α,3α-episulfide[21] (**16d**)——The reaction products obtained by treatment of (**15d**, X=Ac) with KOH–EtOH were acetylated and separated by TLC technique to yield 9.0% of 2β,3β-oxide (**13d**) and 86.7% of episulfide (**16d**), (acetone), mp 147—149°, $[\alpha]_D^{23}$ 18.1±2° (c=1.094). *Anal.* Calcd. for $C_{23}H_{36}O_2S$: C, 73.35; H, 9.64; S, 8.50. Found: C, 73.10; H, 9.63; S, 8.57. IR ν_{max} cm^{-1}: 1739, 1254, 1246, 1236 (OAc), 1045, 1036, 909, 896.