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Summary

Syntheses of UDP-β-glucose and 5-Bromo-UDPG was attempted to investigate the stereospecificity of coenzyme UDPG. UMP-amidate and monobrucinium β-D-glucose 1-phosphate were reacted in pyridine, and UDP-β-glucose was obtained as its lithium salt by the aid of ion exchange chromatography. The structure of (Ⅶ) thus obtained was ascertained by acid hydrolysis.

5-Bromo-UMP was converted to the phosphoramidate and reacted with α-D-glucose 1-phosphate. 5-Bromo-UDPG was detected on paper chromatogram and ion exchange chromatogram, but the yield was low and 5-Bromo-UMP and another by-product were detected.

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82. Ken'ichi Takeda and Taichiro Komeno : Bile Acids and Steroids. XII.*2 Thiosteroids (1). The Fission of Epoxide in the C-Ring of Steroids by Thiocyanic Acid.

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There have been a few attempts[1] to introduce a sulfur atom into steroids, but no evidence that a sulfur atom has been introduced into the C-ring. These methods mostly consisted of substitution reactions, in which halides or tosylates are converted to thiocyanates or thiols by treatment with thiocyanato or mercapto ion, respectively. In the study of alkene episulfide, van Tamelen[2] found that cyclohexene and cyclopentene epoxides could be converted into the corresponding thiocyanatohydrins on being treated with thiocyanic acid in ether. Thus, this method was applied to steroidal epoxides and succeeded in introducing thiocyanato groups into the C-ring. The present paper is concerned with the fission of steroidal epoxides by thiocyanic acid.

When methyl 3α-acetoxy-11α,12α-epoxycholanate[3] (Ⅱ) was treated with thiocyanic acid in ether at room temperature for 60~70 hours, the compound (Ⅲ), m.p. 169~171°, which showed peaks at 3390 cm^{-1} (OH) and 2151 cm^{-1} (SCN) in its infrared spectrum, was

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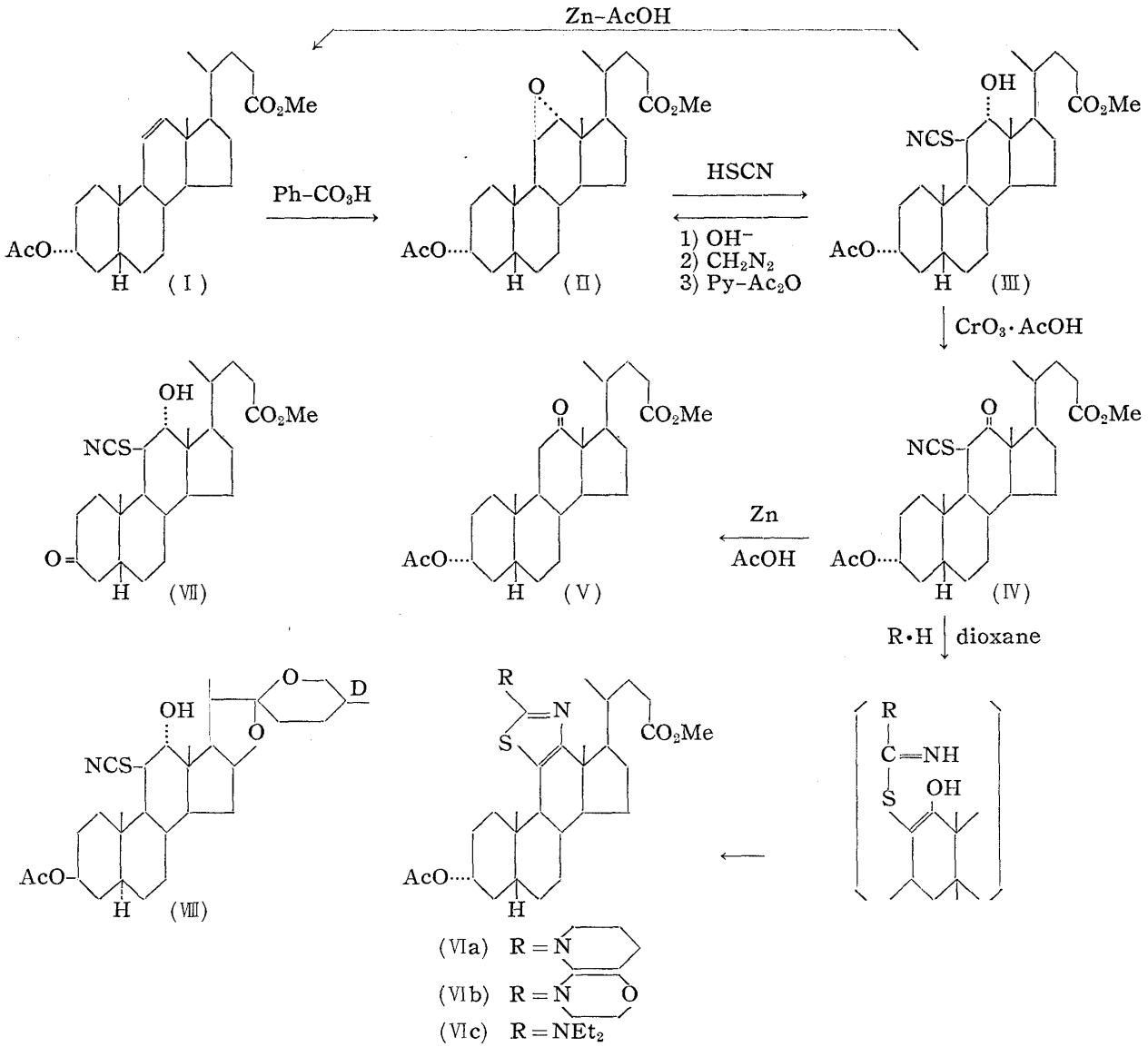
*2 Part XI. K. Takeda, K. Igarashi : J. Biochem. (Japan), **46**, 1313(1959).

1) (3β-SH) H. R. Rosenberg, S. G. Turnball : U. S. Pat., 2,375,873, 2,375,874 (C. A., **39**, 5049(1954)); L. King, R. M. Dodson, L. A. Subluskey : J. Am. Chem. Soc., **70**, 1176(1948); S. Bernstein, K. J. Sax : J. Org. Chem., **16**, 685(1951). (3-Thione) L. Jirousek : Chem. Listy, **47**, 726(1953). (7-SCN and 7-SH) S. Frederikson, Sr. Liiberg : Chem. Ber., **88**, 684(1955). (21-SH) C. Djerassi, A. L. Nussbaum : J. Am. Chem. Soc., **75**, 3700(1953). (1α- and 7α-SH) R. M. Dodson, R. C. Tweit: *Ibid.*, **81**, 1224(1959).

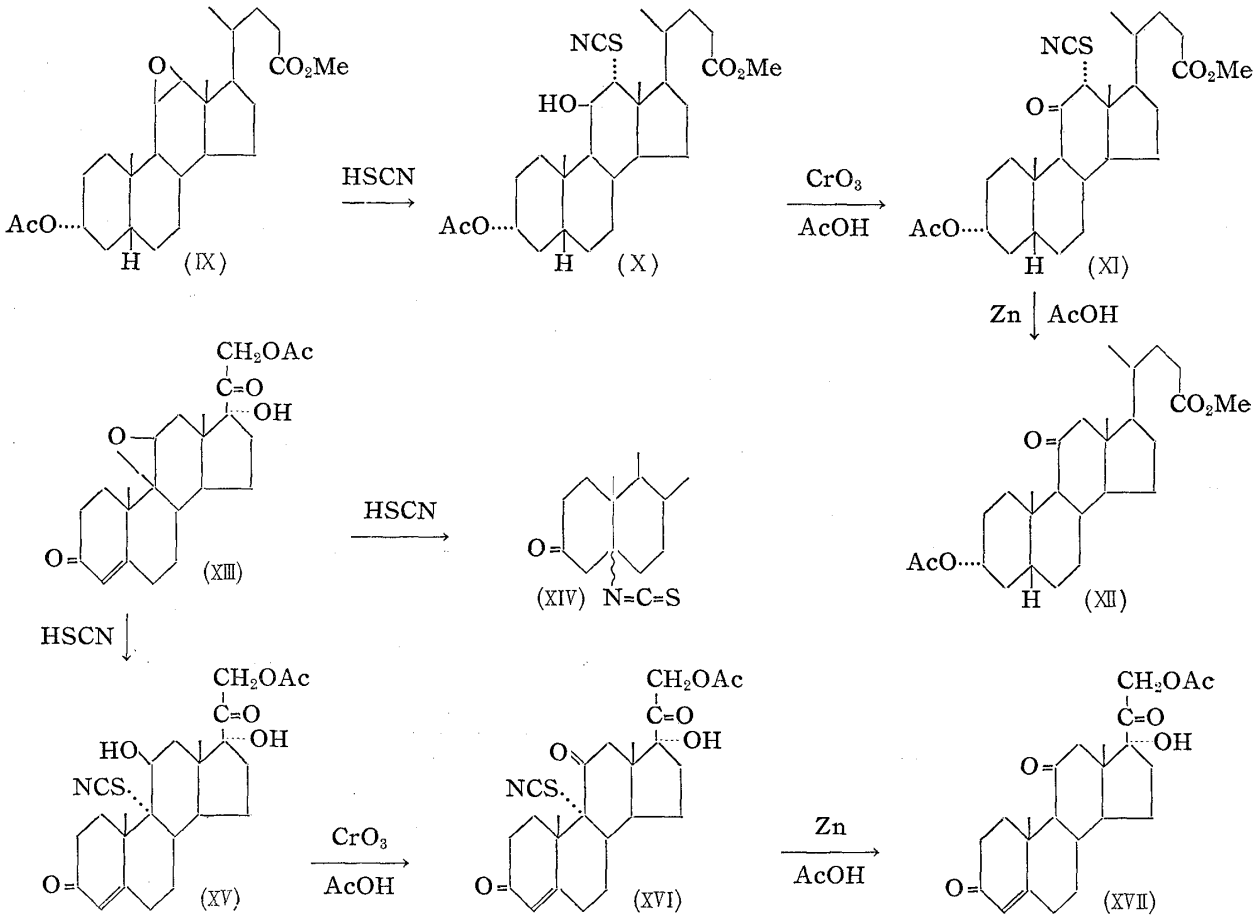
2) E. E. van Tamelen : J. Am. Chem. Soc., **73**, 3444(1951).

3) J. Press, T. Reichstein : Helv. Chim. Acta, **25**, 878(1942); G. H. Ott, T. Reichstein : *Ibid.*, **26**, 1799(1943).

obtained in 78% yield. The structure of this compound (Ⅲ) was assumed from the following procedures. The compound (Ⅲ) was regenerated to the parent epoxide (Ⅱ) with methanolic alkali, liquid ammonia, or even sodium borohydride–methanol, while the reduction of the compound (Ⅲ) with zinc–acetic acid gave methyl 3α-acetoxy-11-cholenate (I). The compound (Ⅲ) was oxidized by chromium trioxide into a thiocyanato-ketone (Ⅳ), m.p. 192~194°, which was converted to the known methyl 3α-acetoxy-12-oxocholanate (V) by treatment with zinc–acetic acid. The compound (Ⅳ) has weak absorption maxima at 250 and 308 mμ in its ultraviolet spectrum. It seems that the bathochromic shift in the ultraviolet spectrum and the normal frequency of C=O stretching vibration (1689 cm^{-1}) in the infrared spectrum are in agreement with those of α-axial haloketones.[4] According to Barton's generalization,[5] the C–OH bond and the newly formed C-added bond produced by the ring-opening of the steroidal epoxide are both axial and *trans* to each other. From these data, the fission product (Ⅲ) must be methyl 3α-acetoxy-11β-thiocyanato-12α-hydroxycholanate.



4) R. N. Jones : J. Am. Chem. Soc., **74**, 2828(1952); E. J. Corey : *Ibid.*, **76**, 175(1954); R. C. Cookson: J. Chem. Soc., **1954**, 282; K. Takeda, K. Igarashi, T. Komeno : This Bulletin, **2**, 348(1954).
5) D. H. R. Barton : J. Chem. Soc., **1953**, 1027.



When the thiocyanato-ketone (IV) was treated with a catalytic amount of piperidine in order to obtain an 11α-epimer of (IV), a small amount of a product (VIa), m.p. 110~112°, was obtained besides the starting material. This compound was obtained in a good yield when the thiocyanato-ketone was treated with a sufficient amount of piperidine. Elemental analysis of the compound (VIa) agreed well with $C_{33}H_{50}O_4N_2S$. The compound (VIa) has a strong absorption maximum at 280 mμ (ε 9,700) in its ultraviolet spectrum and a peak at 1515 cm^{-1} in its infrared spectrum caused by vibration of the aromatic ring. Erlenmeyer[6] reported that 2-amino-4,5-tetramethylenethiazole has an absorption maximum at 275 mμ (ε 7,900) in its ultraviolet spectrum. It was also reported[7] that the thiocyanato-ketones were converted to 2-mercapto-, 2-amino-, and 2-hydroxythiazole by treatment with hydrogen sulfide, ammonium chloride, and hydrochloric acid, respectively. From these facts, it should be assumed that the compound (VIa) may be methyl 3α-acetoxy-2'-piperidinothiazolo[5,'4'-11,12]chol-11-enate, formed by the ring closure of the condensation product of piperidine and (IV). Similarly, treatment of this thiocyanato-ketone (IV) with morpholine or diethylamine gave a 2-morpholinothiazolo compound (VIb), m.p. 116~118°, λ_{max}^{EtOH} 277 mμ (ε 10,880), or a 2'-diethylaminothiazolo compound (VIc), m.p. 123~125°, λ_{max}^{EtOH} 282 mμ (ε 10,470), respectively.

In the same manner, methyl 3-oxo-11α,12α-epoxycholanate[8] produced methyl 3-oxo-11β-thiocyanato-12α-hydroxycholanate (VII), m.p. 154~156°, and 3β-acetoxy-11α,12α-epoxy-25D,5α-spirostane[9] gave 3β-acetoxy-11β-thiocyanato-12α-hydroxy-25D,5α-spiro-

6) H. Erlenmeyer : Helv. Chim. Acta, **24**, 172(1941).
7) J. T. Gregory : J. Am. Chem. Soc., **74**, 1719(1952).
8) G. H. Ott, T. Reichstein : Helv. Chim. Acta, **26**, 1799(1943).
9) J. Elks, G. H. Phillips, D. A. H. Taylor, L. A. Wyman : J. Chem. Soc., **1954**, 1739.

stane (Ⅷ), m.p. 229~230° (decomp.), by treatment with an ether solution of thiocyanic acid.

When methyl 3α-acetoxy-11β,12β-epoxycholanate[10] (Ⅸ) was treated with an ether solution of thiocyanic acid, a product (Ⅹ) of m.p. 105°/163~165°, was obtained in 82% yield. It showed the peaks at 3534 (OH) and 2169 cm^{-1} (SCN) in its infrared spectrum. Its structure was assumed to be methyl 3α-acetoxy-11β-hydroxy-12α-thiocyanatocholanate from the following experiments. It was oxidized by chromium trioxide to a thiocyanato-ketone (Ⅺ), m.p. 107~109°, which shows no shift of C=O stretching vibration, and this (Ⅺ) gave a ketone (Ⅻ), m.p. 130~132°, with zinc-acetic acid. The ketone (Ⅻ) agreed well in respect to the melting point, crystal form, and specific optical rotation with methyl 3α-acetoxy-11-oxocholanate reported by Fürst.[10]

On the other hand, 9β,11β-epoxy-17α-hydroxy-21-acetoxy-4-pregnene-3,20-dione[11] was not soluble in ether solution of thiocyanic acid and the starting material was recovered. Bück[12] recommended the reaction of powdered potassium hydrogensulfate and potassium thiocyanate for the prepapation of pure thiocyanic acid. Therefore, a solution of thiocyanic acid was prepared by shaking powdered potassium hydrogensulfate and potassium thiocyanate in chloroform or methylene dichloride and, after filtration, the concentration of thiocyanic acid was determined by titration with alkali. When the epoxide (ⅩⅢ) was treated with this solution of thiocyanic acid, two products, (ⅩⅣ), m.p. 180~182° (decomp.), and (ⅩⅤ), m.p. 154~156° (decomp.), were isolated by fractional recrystallization. The former compound (ⅩⅣ) shows no absorption of α,β-unsaturated ketone but a strong peak of isothiocyanato group in its infrared spectrum. The structure of the compound (ⅩⅣ) is probably 3-oxo-5ξ-isothiocyanate formed by addition of isothiocyanic acid to 4-en-3-one, and this reaction will be discussed in the next paper. The other compound (ⅩⅤ) shows absorption maxima at 3509 and 3300 cm^{-1} (OH), and at 2151 cm^{-1} (SCN) in its infrared spectrum. It was assumed by the following reaction that the compound (ⅩⅤ) was 9α-thiocyanatohydrocortisone acetate. It was oxidized by chromium trioxide to 9α-thiocyanatocortisone acetate (ⅩⅥ), m.p. 217~219°, followed by reduction with zinc-acetic acid to cortisone acetate (ⅩⅦ). The ultraviolet spectra of 9α-thiocyanato-hydrocortisone acetate and -cortisone acetate are summarized in Table I together with those of 9α-halo-hydrocortisone acetate and -cortisone acetate reported by Fried, *et al.*[11] 9α-Thiocyanatohydrocortisone acetate (ⅩⅤ) showed no corticoid-hormone activity.

Table I. Ultraviolet Spectra

λ_{max}^{EtOH} mμ (ε)

X	9α-X-Hydrocortisone acetate	9α-X-Cortisone acetate
F[11]	238 (16, 800)	234 (17, 000)
Cl[11]	241 (15, 800)	236 (16, 600)
Br[11]	243 (14, 500)	237 (16, 100)
I[11]	243 (11, 000)	
SCN	243 (15, 680)	238 (16, 120)

Experimental*3

Preparation of HSCN-Ether Solution—In a 300-cc. dropping funnel 40 g. of KSCN was dissolved in a small amount of H_2O and shaved ice, and 150 cc. of Et_2O was added. The mixture was shaken

*3 All m.p.s are uncorrected. Infrared spectra were measured with a Perkin-Elmer Single-beam Infrared spectrophotometer, Model 12C, and ultraviolet spectra were taken with a Beckman Model DU spectrophotomer.

10) A. Fürst, R. Scotoni, Jr.: Helv. Chim. Acta, **36**, 1410(1953).
11) J. Fried, E. F. Sabo: J. Am. Chem. Soc., **79**, 1130(1957).
12) U. Bück, H. Steinmetz: Z. anorg. Chem., **77**, 51(1912).

and 60 g. of H_3PO_4 was added in small portions. The Et_2O layer was washed with a small amount of H_2O, dried over Na_2SO_4, and used for the following experiment.

Methyl 3α-Acetoxy-11β-thiocyanato-12α-hydroxycholanate (III)—To the above solution of HSCN, 5.1 g. of methyl 3α-acetoxy-11α,12α-epoxycholanate (m.p. 145~147°) was added, the mixture was shaken for some time, and set aside for 66 hr. at room temperature. The reaction mixture was washed with Na_2CO_3 solution and H_2O, dried over Na_2SO_4, and evaporated to dryness. The residue was recrystallized from MeOH to 4.5 g. of needles (III), m.p. 169~170°, $[\alpha]_D^{23}$ +80°±2° (c=1.077, $CHCl_3$). *Anal.* Calcd. for $C_{28}H_{43}O_5NS$: C, 66.50; H, 8.57; N, 2.77; S, 6.34. Found: C, 66.75; H, 8.67; N, 2.73; S, 6.45. IR ν_{max}^{Nujol} cm^{-1}: 3390 (OH), 2151 (SCN), 1724, 1718 (C=O), 1247 (C-O).

Methyl 3α-Acetoxy-11α,12α-epoxycholanate (II) from (III)—a) With $NaBH_4$: To a solution of 220 mg. of (III) in 20 cc. of MeOH, 50 mg. of $NaBH_4$ was added. The reaction mixture was allowed to stand overnight at room temperature, evaporated *in vacuo*, and H_2O was added. The precipitate formed was collected by filtration, dried (m.p. 80~100°), and recrystallized twice from MeOH to give 50 mg. of (II), m.p. 144~145°. The mother liquor was acetylated with pyridine and Ac_2O overnight at room temperature. The product was recrystallized from MeOH to give 110 mg. of (II), m.p. 142~144°.
b) With KOH-MeOH: To a solution of 400 mg. of KOH in 6 cc. of MeOH, 300 mg. of (III) was added. The reaction mixture was shaken for some time, until dissolved clearly, and set aside overnight at room temperature. It was added to H_2O, acidified with HCl, and extracted with Et_2O. The extract was esterified with CH_2N_2 and then acetylated with pyridine and Ac_2O overnight at room temperature. The product was recrystallized from MeOH to 280 mg. of (II), m.p. 143~145°.
c) With liq. NH_3: In a sealed tube, 310 mg. of (III) was shaken with 6 cc. of liq. NH_3 at room temperature, by which it dissolved solwly to become clear. After 3 hr., a precipitate appeared and the mixture was treated in the usual manner. The product was recrystallized from MeOH to 250 mg. of (II), m.p. 144~145°. Identification was confirmed in each case by mixed m.p. and infrared spectrum.

Methyl 3α-Acetoxy-11-cholenate (I) from (III)—To a solution of 220 mg. of (III) in 10 cc. of AcOH, 2.2 g. of Zn dust was added, the mixture was refluxed for 4 hr., poured into H_2O, and extracted with Et_2O. The Et_2O solution was washed with Na_2CO_3 solution and H_2O, dried over Na_2SO_4, and evaporated to dryness. The residue was chromatographed over 6 g. of Al_2O_3. The eluate with petr. ether and benzene (3:1, 2:1) gave 100 mg. of (I), m.p. 118~120° (from MeOH), which was identified by mixed m.p. and infrared spectrum.

Methyl 3α-Acetoxy-11β-thiocyanato-12-oxocholanate (IV)—To a solution of 700 mg. of (III) in 23 cc. of AcOH, 1 cc. of 20% CrO_3 solution was added under cooling with ice. The mixture was set aside overnight at room temperature, MeOH and then H_2O were added, and extracted with benzene. The extract was recrystallized from MeOH to 580 mg. of cubic crystals (IV), m.p. 192~194°, $[\alpha]_D^{31}$ +90.6°±4° (c=0.658, $CHCl_3$). *Anal.* Calcd. for $C_{28}H_{41}O_5NS$: C, 66.77; H, 8.20; S, 6.37. Found: C, 66.71; H, 8.31; S, 6.18. UV λ_{max}^{EtOH} mμ (ε): 250 (107), 308 (112). IR ν_{max}^{Nujol} cm^{-1}: 2151 (SCN), 1742, 1235 (OAc), 1698 (C=O).

Methyl 3α-Acetoxy-12-oxocholanate (V) from (IV)—To a solution of 200 mg. of (IV) in 10 cc. of AcOH, 2 g. of Zn dust was added, the mixture was heated under reflux for 5 hr., and filtered. The filtrate was added to H_2O and gave 170 mg. of a precipitate, m.p. 135~145°. It was recrystallized from MeOH to 140 mg. of (V), m.p. 152~154°, which showed no depression on admixture with an authentic sample. Its infrared spectrum was also in full agreement with that of the authentic sample.

Methyl 3α-Acetoxy-2′-piperidinothiazolo[5′,4′-11,12]chol-11-enate (VIa)—To a solution of 400 mg. of (IV) in 6 cc. of dioxane, 0.20 cc. of piperidine was added, the reaction mixture was warmed on a steam bath for 18 hr. avoiding moisture, H_2O was added, and extracted with Et_2O. The Et_2O residue was recrystallized from MeOH to 300 mg. of silky needles (VI), m.p. 110~112°. *Anal.* Calcd. for $C_{33}H_{50}O_4N_2S$: C, 69.43; H, 8.83; N, 4.91; S, 5.62. Found: C, 69.71; H, 9.15; N, 5.01; S, 5.26. UV λ_{max}^{EtOH} 280 mμ (ε 9,700). IR ν_{max}^{Nujol} cm^{-1}: 1742 (C=O), 1515 (aromatic).

Methyl 3α-Acetoxy-2′-morpholinothiazolo[5′,4′-11,12]chol-11-enate (VIb)—To a solution of 500 mg. of (IV) in 6 cc. of dioxane, 500 mg. of morpholine was added, the mixture was warmed on a steam bath for 16 hr., H_2O was added, and extracted with ether. The ethereal residue was chromatographed over 12 g. of Al_2O_3 and the eluate with petr. ether-benzene was crystallized from MeOH to give 350 mg. of prisms, m.p. 113~116°, which was further recrystallized twice from MeOH to give prisms (VIb), m.p. 116~118°. *Anal.* Calcd. for $C_{32}H_{48}O_5N_2S$: C, 67.10; H, 8.45; N, 4.89; S, 5.60. Found: C, 67.11; H, 8.41; N, 4.98; S, 5.53. UV λ_{max}^{EtOH} 277 mμ (ε 10,880). IR ν_{max}^{Nujol} cm^{-1}: 1740, 1235, 1217, 1166, 1515.

Methyl 3α-Acetoxy-2′-diethylaminothiazolo[5′,4′-11,12]chol-11-enate (VIc)—In a sealed tube, a solution of 590 mg. of (IV) in 6 cc. of dioxane and 390 mg. of diethylamine was warmed on a steam bath for 16 hr. To the reaction mixture H_2O was added and extracted with Et_2O. The Et_2O residue was chromatographed over 19 g. of Al_2O_3 and the eluate with petr. ether-benzene was recrystallized

from MeOH to 250 mg. of needles (VIc), m.p. 123~125°. *Anal.* Calcd. for $C_{32}H_{50}O_4N_2S$: C, 68.78; H, 9.02; N, 5.01; S, 5.74. Found : C, 69.09; H, 9.10; N, 4.85; S, 5.61. UV λ_{max}^{EtOH} 282 mμ (ε 10,470). IR ν_{max}^{Nujol} cm^{-1} : 1742, 1237, 1167, 1642 (w), 1547 (st), 1537 (sh), 1520 (m).

Methyl 3-Oxo-11β-thiocyanato-12α-hydroxycholanate (VII)—To HSCN-Et_2O solution, 1.4 g. of methyl 3-oxo-11α,12α-epoxycholanate (impure, m.p. 110~118°) was added. The reaction mixture was set aside for 45 hr. at room temperature and treatment as above gave a resinous residue. By chromatography over 30 g. of neutral Al_2O_3, 390 mg. of methyl 3-oxo-11-cholenate, m.p. 120~125°, was obtained from the eluate with petr. ether-benzene (2:1). The eluate with the same solvent (1:1, 1:2) gave 300 mg. of methyl 3-oxo-11α,12α-epoxycholanate, m.p. 115~118°, and the eluate with benzene, benzene-ether (9:1, 4:1, 3:2), and ether gave 320 mg. of needles (VII), m.p. 154~156°, by recrystallization from MeOH. $[\alpha]_D^{31}$ +43.1°±4° (c=0.682, $CHCl_3$). *Anal.* Calcd. for $C_{26}H_{39}O_4NS$: C, 67.64; H, 8.52; N, 3.03; S, 6.95. Found : C, 67.33; H, 8.60; N, 3.28; S, 7.03. IR ν_{max}^{Nujol} cm^{-1} : 3521 (OH), 2146 (SCN), 1736, 1698 (C=O).

3β-Acetoxy-11β-thiocyanato-12α-hydroxy-25D,5α-spirostane (VIII)—To HSCN-Et_2O solution, 180 mg. of 11α,12α-epoxytigogenin acetate (m.p. 210~215°) was added, the mixture was allowed to stand for 2 days at room temperature, and treatment as above gave a resinous residue. By chromatography over neutral Al_2O_3, 100 mg. of epoxide was recovered from the eluate with petr. ether-benzene (1:1) and benzene. The eluate with benzene-Et_2O and Et_2O gave 50 mg. of silky needles (VIII), m.p. 229~230° (decomp.), by recrystallization from MeOH. *Anal.* Calcd. for $C_{30}H_{45}O_5NS$: C, 67.76; H, 8.53; S, 6.03. Found : C, 67.33; H, 8.60; S, 5.56. IR ν_{max}^{Nujol} cm^{-1} : 3448 (OH), 2179 (SCN), 1733 (O-Ac).

Methyl 3α-Acetoxy-11β-hydroxy-12α-thiocyanatocholanate (X)—To HSCN-Et_2O solution, 650 mg. of methyl 3α-acetoxy-11β,12β-epoxycholanate (IX) (m.p. 153~155°) was added, the mixture was allowed to stand for 45 hr. at room temperature, and treatment as above gave 600 mg. of needles (X), m.p. 105°/163~165°, by recrystallization from Et_2O-petr. ether. $[\alpha]_D^{21.5}$ +108°±2° (c=0.633, $CHCl_3$). *Anal.* Calcd. for $C_{28}H_{43}O_5NS$: C, 66.50; H, 8.57; N, 2.77; S, 6.34. Found : C, 66.90; H, 8.92; N, 3.01; S, 6.04. IR ν_{max}^{Nujol} cm^{-1} : 3534 (OH), 2169 (SCN), 1739, 1248 (O-Ac).

Methyl 3α-Acetoxy-12α-thiocyanato-11-oxocholanate (XI)—To a solution of 200 mg. of (X) in 4 cc. of AcOH, 0.265 cc. of 20% CrO_3-AcOH was added. The mixture was allowed to stand overnight at room temperature, H_2O was added, and extracted with Et_2O. The extract was chromatographed over 6 g. of Al_2O_3. The eluate with petr. ether-benzene and benzene gave 150 mg. of a residue, which gave 100 mg. of (XI), m.p. 107~109°, by recrystallization from petr. ether-Et_2O. $[\alpha]_D^{21.5}$ +37°±2° (c=0.717, $CHCl_3$). *Anal.* Calcd. for $C_{28}H_{41}O_5NS$: C, 66,77; H, 8.20; S, 6.37. Found : C, 67.23; H, 8.33; S, 6.49. IR ν_{max}^{Nujol} cm^{-1} : 2169 (SCN), 1736, 1235 (C-Ac), 1706 (C=O).

Methyl 3α-Acetoxy-11-oxocholanate (XII)—To a solution of 100 mg. of crude (XI) in 6 cc. of AcOH, 2 g. of Zn dust was added. The mixture was warmed on a steam bath for 2 hr. with occasional shaking, H_2O was added, and extracted with Et_2O. The extract gave 70 mg. of crystals, m.p. 120~125°, from Et_2O-petr. ether, which were recrystallized twice from MeOH to flat needles (XII), m.p. 130~132°; $[\alpha]_D^{23.5}$ 70°±2° (c=0.606, $CHCl_3$) (reported[10] m.p. 133°, $[\alpha]_D$ +76.4° (c=0.748, $CHCl_3$)). *Anal.* Calcd. for $C_{27}H_{42}O_5$: C, 72.61; H, 9.48. Found : C, 72.77; H, 9.56. IR ν_{max}^{Nujol} cm^{-1} : 1733, 1258 (O-Ac), 1706 (C=O).

HSCN-Fission of 9β,11β-Epoxy-17α-hydroxy-21-acetoxy-4-pregnene-3,20-dione (XIII)—HSCN-$CHCl_3$ solution was prepared by shaking 17 g. of powdered $KHSO_4$ and 10 g. of KSCN in 35 cc. of $CHCl_3$ and filtered.

a) To HSCN-$CHCl_3$ solution, 1.5 g. of (XIII) (m.p. 209~211°) was added, the mixture was stored in a refrigerator overnight, and filtered. The filtrate was washed with Na_2CO_3 solution and H_2O, dried over Na_2SO_4, and evaporated to dryness. The residue was crystallized from AcOEt to give 1.10 g. of crystals, m.p. 142~145° (decomp.). This was separated into less-soluble crystals (XIV) of m.p. 180~182° (decomp.), and more-soluble crystals (XV) of m.p. 145~147° (decomp.) from acetone.

Less-soluble substance (XIV), m.p. 180~182° (decomp.). *Anal.* Calcd. for $C_{24}H_{31}O_6NS$: C, 62.45; H, 6.77. Found : C, 62.48; H, 6.88. IR ν_{max}^{Nujol} cm^{-1} : 3484 (w), 2077 (-N=C=S), 1715 (C=O).

The more-soluble crystals were recrystallized twice from acetone-hexane to crystals (XV) of m.p. 154~156° (decomp.); $[\alpha]_D^{29}$ +188.6°±4° (c=0.421, $CHCl_3$). *Anal.* Calcd. for $C_{24}H_{31}O_6NS$: C, 62.45; H, 6.77; N, 3.03; S, 6.95. Found : C, 62.33; H, 6.79; N, 3.40; S, 6.52. UV λ_{max}^{EtOH} 243 mμ (ε 15,680). IR ν_{max}^{Nujol} cm^{-1} : 3509, 3300 (OH), 2151 (SCN), 1733, 1639 (C=O).

b) To a suspension of 1.10 g. of (XII) in 6 cc. of AcOH, 6.5 cc. of HSCN-CH_2Cl_2 solution (100 mg. HSCN/cc.) was added, the mixture was allowed to stand overnight at room temperature, and treated as above. The residue was crystallized from AcOEt to 500 mg. of impure (XV), m.p. 130~135° (decomp.), which was further recrystallized from acetone-hexane to pure (XV), m.p. 154~156° (decomp.).

9α-Thiocyanatocortisone Acetate (XVI)—To a solution of 100 mg. of (XV) in 4 cc. of AcOH, 0.15 cc. of 20% CrO_3-AcOH was added, the mixture was allowed to stand for 1 hr. at room temperature, H_2O was added, and extracted with $CHCl_3$. The extract was recrystallized twice from Me_2CO-MeOH to

80 mg. of needles (XVI), m.p. 217~219°; $[\alpha]_D^{29}$ +339.2°±2° (c=0.995, $CHCl_3$). *Anal.* Calcd. for $C_{24}H_{29}O_6NS$: C, 62.72; H, 6.36; N, 3.05; S, 6.98. Found : C, 62.59; H, 6.53; N, 2.88; S, 6.68. UV λ_{max}^{EtOH} 238 mμ (ε 16,120). IR ν_{max}^{Nujol} cm^{-1} : 3322 (OH), 2165 (SCN), 1736, 1709, 1667, 1621 (C=O).

Cortisone Acetate (XVII) from (XVI)—To a solution of 50 mg. of (XV) in 2 cc. of AcOH, 200 mg. of Zn dust was added, the mixture was heated on a steam bath for 1 hr., H_2O was added, and extracted with $CHCl_3$. The extract was recrystallized twice from Me_2CO to crystals (XVII) of m.p. 235~239°, which showed no depression on admixture with an authentic sample and its infrared spectrum was in full agreement with the authentic sample. IR ν_{max}^{Nujol} cm^{-1} : 3401 (OH), 1751, 1721, 1704, 1650, 1613 (C=O).

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Summary

When steroidal 11α,12α-, 11β,12β-, and 9β,11β-epoxides were each treated with thiocyanic acid, the corresponding thiocyanatohydrins were obtained. The thiocyanato and hydroxyl groups of these ring-fission products were assumed to be *trans* and diaxial to each other by Barton's generalization, and from infrared and ultraviolet data. This was also confirmed by chemical methods.

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