tions. The mixture was then stirred at room temperature for 20 hr and poured into 250 ml of ice and water, yielding either an oil or white precipitate. This material was extracted from the aqueous phase with three 50-ml portions of chloroform, and the $CHCl_3$ extracts were dried and evaporated. The resulting oil or solid was dissolved in 2-propanol and the solution was cooled in an ice bath while 2.1 ml (0.021 mole) of 37% aqueous HCl was added. Ether was added to precipitate all of the hydrochloride salt, which was filtered and crystallized from 2-propanol. The yields of once recrystallized products were the following: **3c**, 33%; **3d**, 7.3%; and **3e**, 34%. Further crystallization from 2-propanol afforded analytical samples.

Method B.—A quantity of 5.0 g (19 mmoles) of **3a** was dissolved in a minimum amount of boiling dry benzene, 4.55 g (38 mmoles) of $SOCl_2$ (distilled from quinoline then redistilled from linseed oil) was added dropwise over a period of 10 min from a pressure-equalizing separatory funnel, and the mixture refluxed on a steam bath for 1 hr. The excess $SOCl_2$ was removed as an azeotrope with benzene, 2 l. of benzene being distilled. The reaction mixture was cooled in an ice bath and 19 mmoles of dialkylaminoalkanol was added dropwise over a period of 20 min. The mixture was stirred in an ice bath for 1 hr, then at room temperature for 1 hr; the solvent was removed by a stream of air. The resulting oil was dissolved in a small amount of 1-propanol and dry HCl was added, yielding a white solid, which was filtered and recrystallized from 2-propanol. The yields of **3c** and **3d** obtained by this method were 33 and 17%, respectively.

β-Chloroethyl 1-Oxo-2a,3,4,5-tetrahydroacenaphthene-2a-carboxylate (3f).—A mixture of 2.16 g (0.01 mole) of **3a**, 1.6 g (0.02 mole) of ethylene chlorohydrin, 30 ml of benzene, and 5 drops of concentrated H_2SO_4 was refluxed under a Dean-Stark water trap for 20 hr. The solvent was evaporated, the resulting oil was dissolved in $CHCl_3$, and the $CHCl_3$ solution was washed with three 25-ml portions of 5% aqueous Na_2CO_3, dried, and evaporated, yielding an oil which solidified upon standing. Recrystallization first from 95% ethanol, then from ethyl acetate–hexane, afforded 0.18 g of long colorless needles, mp 53–55°. Condensation of the filtrate afforded an additional 0.75 g of material melting at 49–52°; over-all yield 0.93 g (33%). An additional recrystallization from ethyl acetate–hexane yielded an analytical sample melting at 56–57°, λ_{max}^{KBr} 5.9 μ (CO_2R and CO).

2a-Carboxamido-2a,3,4,5-tetrahydroacenaphthen-1-one (3g).—A mixture of 1.0 g of **3b** and 10 ml of concentrated H_2SO_4 was stirred at room temperature for 6 hr and then poured into 100 ml of ice water, yielding 0.92 g (85%) of a white precipitate, mp 206–208°. Two recrystallizations from 95% ethanol afforded colorless prisms: mp 208–209°; λ_{max}^{KBr} 2.94 and 3.2 (NH), 3.44 (CH), and 5.86–6.1 μ (CO and $CONH_2$).

2a-Carboxy-2a,3,4,5-tetrahydroacenaphthen-1-ol (4a).—A solution of 1 g of the keto acid **3a** in 10 ml of 2 *N* NaOH was stirred during the dropwise addition of 0.2 g of $NaBH_4$ in 10 ml of 2 *N* NaOH. The resulting solution was stirred for 5 hr and acidified with 20% H_2SO_4. Cooling caused the precipitation of 0.76 g (75%) of white crystals, mp 166–167°. Recrystallization from water gave white crystals of **4a**: λ_{max}^{KBr} 3.0 (OH), 3.75–3.9 (COOH), 5.9 μ (COOH). Thin layer chromatography using benzene–methanol (6:1) produced two spots to give evidence for the presence of two isomers.

2a-Cyano-2a,3,4,5-tetrahydroacenaphthen-1-ol (4b).—A solution of 1 g of ketonitrile **3b** in 10 ml of methanol was stirred during the dropwise addition of 0.1 g of $NaBH_4$ dissolved in 5 ml of 1% NaOH. The solution was stirred at room temperature for 2 hr and then acidified with dilute H_2SO_4. The aqueous layer was extracted with chloroform. The chloroform extracts were dried ($MgSO_4$) and evaporated *in vacuo*. Recrystallization of the residue from aqueous ethanol yielded 1.02 g (100%) of **4b**, mp 57–60°. Further recrystallization gave an analytical sample: λ_{max}^{KBr} 2.81, 2.95, and 3.15 (OH), 4.5 μ (CN).

β-Diethylaminoethyl 1-Hydroxy-2a,3,4,5-tetrahydroacenaphthene-2a-carboxylate Hydrochloride (4c).[14]—The method employed is similar to that of Campaigne and Bourgeois[15] for preparing hydroxy esters. To a solution of 1.7 g of β-chloroethyldiethylamine in 17 ml of anhydrous isopropyl alcohol was added 2.78 g of **4a** in 17 ml of anhydrous isopropyl alcohol, and the mixture refluxed for 10 hr. The solvent was condensed under aspirator vacuum, and the resulting white solid crystallized from ethanol and then 2-propanol, yielding 1.8 g (40.3%) of colorless crystals: λ_{max}^{KBr} 3.00 (OH), 3.34 (CH), 3.80 and 4.02 (NH^+), and 5.88 μ (CO_2R).

(14) We are indebted to Sister M. M. Christine, of Clarke College, Dubuque, Iowa, National Science Foundation Research Participant, summer 1963, for the preparation of this compound.

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The Synthesis of Some 2,3-Epithio-5α-pregnanes

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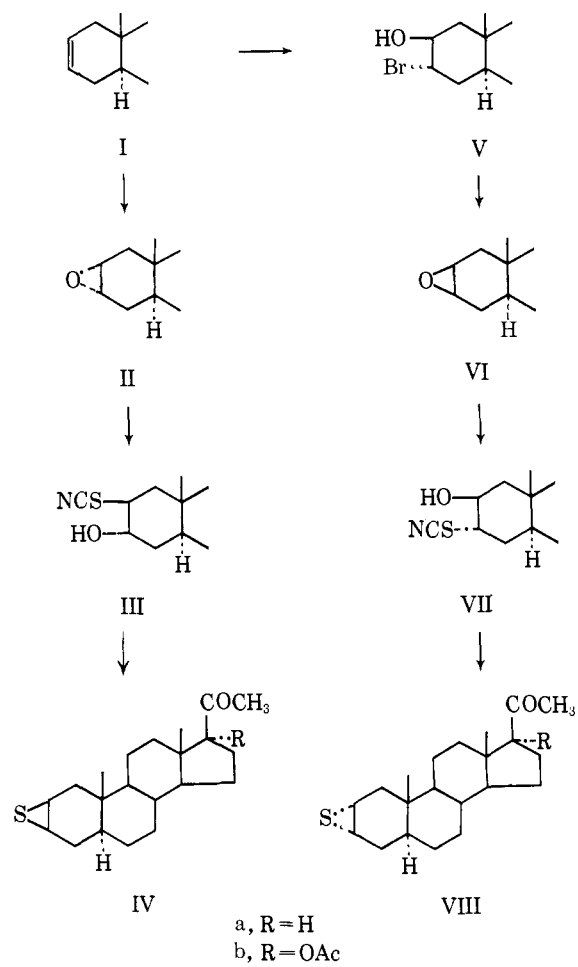
The recent observation of the potent anabolic activity of some 2,3-epithioandrostane derivatives[1] prompted the synthesis of some similar compounds in the 5α-pregnane series.

The episulfide derivatives (Table I) were prepared by a procedure similar to that reported earlier[2] for episulfides in the cholestane series. When the 2,3-dehydro analogs (I)[3,4] were treated with perbenzoic acid, the 2,3α-epoxides II were obtained (Chart I). Subsequent

CHART I



treatment with thiocyanic acid afforded the thiocyanohydrins III. Treatment with an alcoholic solu-

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TABLE I
THIOCYANOHYDRINS AND EPISULFIDES

Compd	Recrystn media	Mp, °C	$[\alpha]^{25}D$, deg	Yield, %	Formula	Calcd, % C	Calcd, % H	Found, % C	Found, % H
IIIa	MeOH	158–161	+95	84.2	$C_{22}H_{33}NO_2S$	70.36	8.86	70.67	8.63
IIIb[a]			+10	90.2	$C_{24}H_{35}NO_3S$	66.48	8.14	66.74	8.37
VIIa	EtOH	234–236.5	+113	84.3	$C_{22}H_{33}NO_2S$	70.36	8.86	70.47	8.96
VIIb	MeOH	221–222.5	+28.5	80	$C_{24}H_{35}NO_4S$	66.48	8.14	66.81	8.16
IVa	Me_2CO	168–170	+116	67.5	$C_{21}H_{32}OS$	75.85	9.70	75.95	9.66
IVb	MeOH	189–192	+17	72	$C_{23}H_{34}O_3S$	70.73	8.78	70.32	8.75
VIIIa	Me_2CO–H_2O	165–166	+113.5	68	$C_{21}H_{32}OS$	75.85	9.70	75.98	9.58
VIIIb	Me_2CO–H_2O	167–170	+20	82.6	$C_{23}H_{34}O_3S$	70.73	8.78	70.58	8.91

[a] An oil which resisted crystallization from a variety of solvents.

tion of potassium hydroxide gave the 2,3β-episulfides IV in good yield.

When the 2,3-olefins I were treated with hypobromous acid, the corresponding bromohydrins V were obtained. Treatment of V with sodium carbonate solution afforded the β-epoxides VI. Reaction with thiocyanic acid followed by base as described above gave the 2,3α-episulfides VIII.

The intermediate epoxides II and VI and thiocyanohydrins III and VII as well as the episulfides IV and VIII were evaluated[5] for progestational activity in the McPhail assay[6] and found inactive by injection at a screening dose of 1 mg/day/rat.

Experimental Section[7]

2,3α-Epoxy-5α-pregnan-20-one (IIa).—To a solution of Ia (12.0 g) in benzene (100 ml) was added with stirring and cooling *m*-chloroperbenzoic acid (8.0 g, 85% pure) in benzene (125 ml). The reaction mixture was allowed to stand for 1 hr at 3° and then 0.5 hr at room temperature. The solution was washed repeatedly with 5% $NaHCO_3$ solution followed by H_2O alone, and dried (Na_2SO_4). Solvent removal *in vacuo* and recrystallization from methanol afforded pure IIa (9.6 g, 76%), mp 148–150°, 158–160°, $[\alpha]D$ 110.5°.

Anal. Calcd for $C_{21}H_{32}O_2$: C, 79.70; H, 10.19. Found: C, 79.88; H, 10.09.

2,3α-Epoxy-5α-pregnan-17α-ol-20-one acetate (IIb) was prepared from Ib as described above, mp 212–214°, $[\alpha]D$ +12°, in 87.6% yield.

Anal. Calcd for $C_{23}H_{34}O_4$: C, 73.76; H, 9.15. Found: C, 74.00; H, 9.06.

3α-Bromo-5α-pregnan-2β-ol-20-one (Va).—To a solution of Ia[3,4] (20.0 g) in cold H_2O was added with stirring a mixture of N-bromosuccinimide (13 g), $HClO_4$ (11.3 g, 60%), and H_2O (125 ml) over 15 min. The reaction was stirred for 2.5 hr and poured into ice and H_2O. The precipitate was collected, washed with H_2O, dissolved in chloroform, and dried (Na_2SO_4 containing Darco). Removal of the solvent *in vacuo* left a solid which was recrystallized from methanol to give Va (15.45 g, 56.4%), mp 206–208°. Further recrystallization from ethanol gave pure Va (12.3 g), mp 210.5–212°, $[\alpha]D$ +126°.

Anal. Calcd for $C_{21}H_{33}BrO_2$: C, 63.49; H, 8.37. Found: C, 63.47; H, 8.31.

3α-Bromo-17α-hydroxy-5α-pregnan-2β-ol-20-one (Vb) was prepared from Ib[3] as described above, mp 220–223.5°, $[\alpha]D$ +126° in 76.5% yield.

Anal. Calcd for $C_{23}H_{35}BrO_4$: C, 60.65; H, 7.75. Found: C, 60.43; H, 7.62.

2,3β-Epoxy-5α-pregnan-20-one (VIa).—To a solution of Va in tetrahydrofuran (250 ml) was added Na_2CO_3 (1.5 g) in H_2O (175 ml). The reaction mixture was allowed to stand at room temperature for 2.5 days. Dilution with H_2O gave a precipitate which was collected, washed with H_2O, and air dried. Recrystallization from methanol gave pure VIa (4.1 g, 80%), mp 174–175.5°, $[\alpha]D$ +119°.

Anal. Calcd for $C_{21}H_{32}O$: C, 79.70; H, 10.19. Found: C, 79.92; H, 10.16.

2,3β-Epoxy-5α-pregnan-17α-ol-20-one acetate (VIb) was prepared from Vb as described above, mp 184–185°, $[\alpha]D$ +29°, in 82% yield.

Anal. Calcd for $C_{23}H_{34}O_4$: C, 73.76; H, 9.15. Found: C, 73.85; H, 9.10.

2β-Thiocyano-5α-pregnan-3α-ol-20-one (IIIa). General Method.—To a mixture of potassium thiocyanate (88 g) in H_2O (43 ml) and ether (300 ml) containing a few ice chips was added H_3PO_4 (132.8 g) in small portions with continuous agitation. The solution washed with two 25-ml portions of cold H_2O and dried briefly (Na_2SO_4). To a solution of IIa (8.0 g) in ether (60 ml) was added the freshly prepared ethereal thiocyanic acid. The reaction was allowed to stand for 2 days at room temperature. The solution was washed with 5% Na_2CO_3 until neutral. After washing with H_2O and drying (Na_2SO_4 containing Darco), solvent removal left a white solid. Recrystallization from methanol gave pure IIIa (6.2 g, 84.2%), mp 158–161°.

2,3β-Epithio-5α-pregnan-20-one (IVa). General Method.—To a warm solution of IIIa (1.0 g) in methanol (25 ml) was added KOH (0.5 g) in methanol (5 ml) with stirring. The reaction was allowed to stand at room temperature for 2 hr. A needlelike precipitate gradually formed as the reaction progressed. Water was added to the mixture and the product was collected, washed with H_2O, and air dried. Recrystallization from acetone gave pure IVa (0.6 g, 67.5%), mp 168–170°.

(5) The author thanks Drs. R. L. Elton and E. F. Nutting for furnishing this biological information.

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(7) The elemental analysis and optical rotations in chloroform at ambient temperatures were furnished by Mr. E. Zielinski and Mr. J. Damascus of our analytical department under the supervision of Dr. R. T. Dillon. The melting points were obtained on a Fisher-Johns apparatus and are corrected.

Totally Synthetic Steroid Hormones. X.[1] Some (±)-13β-Ethyl-7α-methylgonane Derivatives

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The interesting steroid hormonal activity reported for a number of 7α-methyltestosterone[2] and 7α-methyl-19-nortestosterone[3] derivatives has induced us to extend our studies on the structure–biological activity relationships of 13β-ethyl- and higher alkylgonane derivatives[4] to various (±)-13β-ethyl-7α-methylgon-4-en-3-ones. Here we report the synthesis of the ketones II (R = H; R^1 = H, C_2H_5, and C≡CH; R^2 = CH_3) and compare their anabolic, androgenic, and progesta-

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