[CONTRIBUTION FROM THE SQUIBB INSTITUTE FOR MEDICAL RESEARCH]

Selenium Derivatives of $\Delta^{1,4}$-3-Ketosteroids[1]

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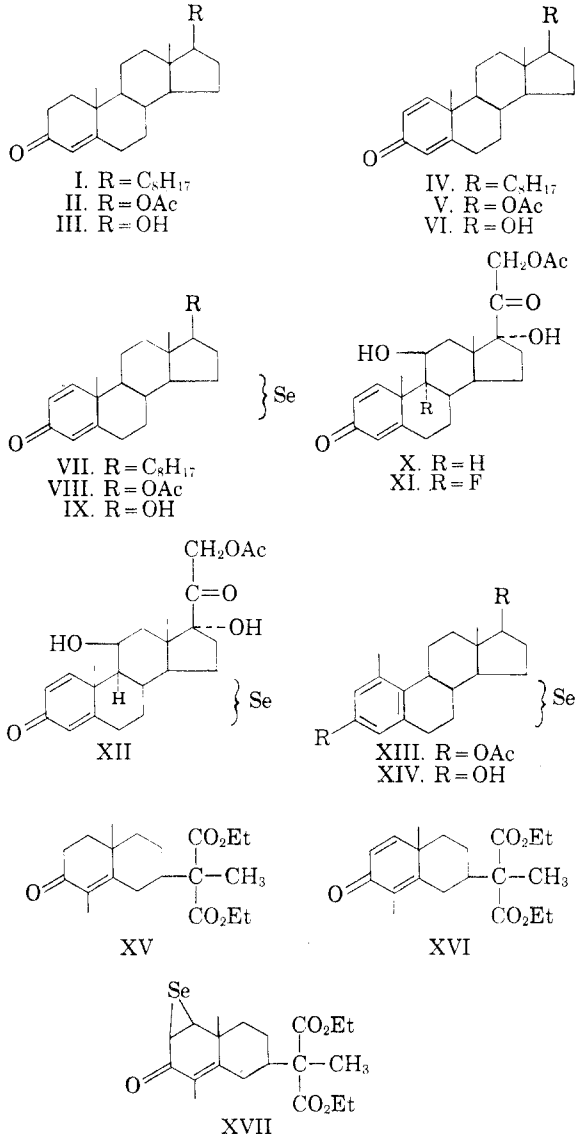
In reacting Δ^4-3-ketosteroids with selenium dioxide the corresponding $\Delta^{1,4}$-3-ketosteroids and/or their monoselenium derivatives were isolated. Transformation products of the selenium compounds are described.



The action of selenium dioxide on Δ^4-3-ketosteroids was first studied by Stiller and Rosenheim.[2] These investigators observed that Δ^4-cholesten-3-one reacted readily with selenium dioxide in glacial acetic acid at 100°C., but not in alcohol. The nature of the reaction products was not reported. The current interest in 1-dehydrosteroids such as 1-dehydrocortisone, 1-dehydrohydrocortisone[3] and 1-dehydrofluorohydrocortisone[4] made it desirable to reinvestigate this reaction as a possible method to introduce the 1,2 double bond.

When Δ^4-cholesten-3-one(I) was reacted with an excess of selenium dioxide in refluxing acetic acid for 1 hr., the corresponding 1-dehydro compound (IV) was not detected in the reaction mixture after chromatographic purification. Instead a crystalline reaction product (VII) was obtained in about 17% yield, the analytical figures of which fitted a compound of the formula $C_{27}H_{40}OSe$.[5] Since three bands of the infrared spectrum at 6.08 μ, 6.16 μ, and 6.26 μ were characteristic for $\Delta^{1,4}$-3-keto compounds, VII has been provisionally named seleno-$\Delta^{1,4}$-cholestadiene-3-one.

An analogous selenium compound of the composition $C_{21}H_{26}O_3Se$ was obtained by reacting testosterone acetate (II) with an excess of selenium dioxide in refluxing acetic acid or dioxane for 1 hr. In this case the crystalline seleno-1-dehydrotestosterone acetate (VIII) crystallized directly from the reaction mixture. No 1-dehydrotestosterone acetate was detected after chromatographic purification of the mother liquors. By refluxing VIII in alcoholic potassium carbonate or potassium hydroxide crystalline seleno-1-dehydrotestosterone (IX) was obtained which could be reacetylated to VIII.

In a recent note Ringold, Rosenkranz, and Sond-

(1) Presented at the First Regional Meeting of the Delaware Valley Section of the AMERICAN CHEMICAL SOCIETY, Philadelphia, on Feb. 16, 1956.

(2) E. T. Stiller and O. Rosenheim, *J. Chem. Soc.*, 353 (1938).

(3) H. L. Herzog, C. C. Payne, M. A. Jevnik, D. Gould, E. L. Shapiro, E. P. Oliveto, and E. B. Hershberg, *J. Am. Chem. Soc.*, **77**, 4781 (1955).

(4) R. F. Hirshmann, R. Miller, R. E. Beyler, L. H. Sarett, and M. Tishler, *J. Am. Chem. Soc.*, **77**, 3166 (1955); J. Fried, K. Florey, E. F. Sabo, J. E. Herz, A. R. Restivo, A. Borman, and F. M. Singer, *J. Am. Chem. Soc.*, **77**, 4181 (1955). J. A. Hogg, F. H. Lincoln, A. H. Nathan, A. R. Hanze, W. P. Schneider, P. F. Beal, and J. Korman, *J. Am. Chem. Soc.*, **77**, 4438 (1955).

(5) After completion of this manuscript Ch. Meystre, H. Frey, W. Voser, and A. Wettstein [*Helv. Chim. Acta*, **39**, 734 (1955)] and S. A. Szpilfogel, T. A. P. Posthumus, M. S. de Winter, and D. A. van Dorp, *Rec. trav. chim.*, **75**, 475 (1956) reported on the preparation of $\Delta^{1,4}$-3-ketosteroids by selenium dioxide dehydrogenation in tertiary alcohols as solvents. Meystre, *et al.* characterized a monoselenium derivative of methyl-1-dehydrotestosterone which appears to be an analogue of the selenium compounds described in this paper.

heimer[6] reported that by reacting testosterone (III) with selenium dioxide and a small amount of water in refluxing benzene for 64 hr., 1-dehydrotestosterone (VI) was obtained after chromatographic purification. By following this procedure we were able to isolate from the chromatogram 1-dehydrotestosterone (VI) in about 12% yield, as described by Ringold, and in addition seleno-1-dehydrotestosterone (IX) in about 6% yield. We further found that with testosterone acetate (II) the Ringold procedure gave seleno-1-dehydrotestosterone acetate (VIII) in the same yield (35%) as the acetic acid procedure. Chromatographic purification of the mother liquors failed to show any evidence for the formation of 1-dehydrotestosterone acetate (V). $\Delta^{1,4}$-3-ones do not appear to be intermediates in the formation of these selenium compounds, since chromatographic fractionation of the reaction product of 1-dehydrotestosterone acetate (V) with selenium dioxide did not reveal the presence of seleno-1-dehydrotestosterone acetate (VIII), but yielded mainly unchanged V.

Hydrocortisone acetate reacted with selenium dioxide in acetic acid to give 1-dehydrohydrocortisone acetate (X) in 6–8% yield. Chromatographic purification afforded very small amounts of the corresponding selenium compound (XII). 9α-Fluorohydrocortisone acetate under the same conditions yielded small amounts of 1-dehydro-9α-fluoro-hydrocortisone acetate (XI) after chromatographic purification but no crystalline selenium compound was isolated.

Seleno-1-dehydrotestosterone acetate (VIII) appears to undergo the dienone-phenol rearrangement, characteristic for $\Delta^{1,4}$-3-ketosteroids, when heated in acetic anhydride in the presence of *p*-toluenesulfonic acid. A yellow crystalline compound (XIII) was isolated, exhibiting an infrared band at 5.67 μ, indicative of a phenol acetate. The analysis of XIII agreed with a formula of $C_{23}H_{28}O_4Se$.[7] XIII was saponified to the corresponding crystalline alcohol XIV of the composition $C_{19}H_{24}O_2Se$. The infrared spectrum showed low intensity bands at 6.35 μ and 6.41 μ, typical of benzenoid systems. The ultraviolet spectra of the selenium compounds (see experimental part) are more complex than would be expected of simple $\Delta^{1,4}$-3-keto and phenolic systems and undoubtedly reflect the presence of selenium as part of the chromophoric system. The stability of these compounds to treatment with acid (VIII was recovered unchanged after refluxing with dilute sulfuric acid in ethanol for 1 hr.) and alkali make it likely that selenium is incorporated in the molecule in an ether-like linkage.

Seleno-1-dehydrotestosterone acetate (VIII) was not reduced by palladium or platinum catalysts in ethyl acetate. Treatment of seleno-$\Delta^{1,4}$-cholestadiene-3-one (VII) with Raney nickel gave a selenium free resinous product which after chromatographic fractionation yielded small amounts of $\Delta^{1,4}$-cholestadiene-3-one (IV). The presence of Δ^4-cholesten-3-one, cholestan-3-one, and/or coprostan-3-one in some of the less polar chromatographic fractions was indicated by spectroscopic evidence (see experimental part).

When VII was heated to 370°C. *in vacuo*, metallic selenium separated and chromatography of the reaction mixture yielded selenium free crystalline fractions which could not be purified to a well defined entity. Ultraviolet and infrared absorption data indicate that they might be mixtures of Δ^4-cholesten-3-one, $\Delta^{1,4}$-cholestadien-3-one, and $\Delta^{4,6}$-cholestadien-3-one.[8]

Treatment of VIII with hydrogen peroxide in acetic acid at room temperature gave a crystalline alkali-soluble, rather unstable substance (XVIII) exhibiting the characteristic infrared dienone bands. On treatment with aqueous sodium bisulfite XVIII easily reverted to VIII. Analytical data of XVIII best fitted a formula $C_{21}H_{28}O_5Se$, which can be interpreted as representing the hydrated form of a selenoxide. The formation of such a compound by the action of hydrogen peroxide on 4-acetamidodiphenyl selenide has been reported.[9]

An interesting parallel to our work is provided in the related field of santonin chemistry by Japanese investigators who used selenium dioxide oxidations to prepare intermediates in the total synthesis of santonin. On reacting ethyl 11-carbethoxy-3-oxo-eusanton-4-enate (XV) with SeO_2 Abe and collaborators[10] obtained ethyl 11-carbethoxy-3-oxo-eusantona-1,4-dienate (XVI) in 30% yield, and Miki[11] isolated a monoselenium compound $C_{20}H_{26}O_5Se$ (XVII), which on pyrolysis yielded the dienone XVI in 30 to 40% yield. The selenium compound XVII exhibited ultraviolet maxima at 242 mμ (log ϵ 3.58) and 260 mμ (log ϵ 3.85) and an infrared maximum in the 6.0–6.5 μ region. From these data Miki postulated a C_1–C_2 selenium bridge as shown in formula XVII. If, as is likely, the attachment of selenium to the rest of the molecule in Miki's compound is analogous to that of the steroidal selenium compounds, it would be difficult to reconcile the presence of the three infrared bands at 6 μ of the steroidal selenium com-

(6) H. J. Ringold, G. Rosenkranz, and F. Sondheimer, *J. Org. Chem.*, **21**, 239 (1956).

(7) In the formulas of XIII and XIV the rearrangement is represented with migration of the methyl group from position 10 to position 1, but it is also possible that the rearrangement proceeds with opening of the 9–10 bond, rotation of ring A about the 5–6 bond and reattachment of carbon 4 to carbon 10. [*Cf.* R. B. Woodward, H. H. Inhoffen, H. O. Larson, and K. H. Menzel, *Ber.*, **86**, 594 (1953).]

(8) Molecular compounds of $\Delta^{1,4}$- and $\Delta^{4,6}$-cholestadiene-3-ones have been described by A. L. Wilds and C. Djerassi, *J. Am. Chem. Soc.*, **68**, 1712 (1946).

(9) W. R. Gaythwaite, J. Kenyon, and H. Phillips, *J. Chem. Soc.*, 2287 (1928).

(10) Y. Abe, T. Harukawa, H. Ishikawa, T. Miki, M. Sumi, and T. Toga, *Proc. Jap. Acad.*, **30**, 116 (1954); *J. Am. Chem. Soc.*, **78**, 1422 (1956).

(11) T. Miki, *J. Pharm. Soc. Japan*, **75**, 403 (1955).

pounds, so characteristic for $\Delta^{1,4}$-3-ketones, and the results of the dienone-phenol rearrangement of VIII with Miki's $C_1 = C_2$ bridge hypothesis. Further work is in progress for a clarification of this question.

EXPERIMENTAL[12]

Seleno-$\Delta^{1,4}$-cholestadiene-3-one (VII) *from Δ^4-cholesten-3-one* (I). A mixture of 2.0 grams of I and 2.0 grams of selenium dioxide in 40 ml. of acetic acid was refluxed for 1 hr., cooled to room temperature and filtered from selenium. The filtrate was diluted with 100 ml. of chloroform and washed with water and sodium bicarbonate solution. The solvent was evaporated. The resulting residue (2.0 grams) was dissolved in hexane and chromatographed on 100 grams of acid washed alumina (Merck). With hexane–benzene (1:4) 344 mg. of crystalline material, m.p. 165–187°, was recovered which upon recrystallization from ether-methanol yielded 310 mg. of VII, m.p. 187–188°. Repeated recrystallization did not raise the melting point. $[\alpha]_D^{25}$ + 251° (c 0.87 in chloroform; α + 2.19°): λ_{max}^{alc} 244 mμ (ϵ 10,200); 258 mμ (ϵ 10,300); 305 mμ (ϵ 1280): λ_{max}^{Nujol} 6.08 μ; 6.16 μ; 6.26 μ; ($\Delta^{1,4}$-3-keto).

Anal. Calcd. for $C_{27}H_{40}OSe$: C, 70.56; H, 8.77; Se, 17.18. Found: C, 70.76; H, 8.92; Se, 17.63.

Seleno-1-dehydrotestosterone acetate (seleno-$\Delta^{1,4}$-androstadiene-17β-ol-3-one 17-acetate) (VIII) *from testosterone acetate (Δ^4-androstene-17β-ol-3-one 17-acetate) (II).* A. *In refluxing acetic acid.* A mixture of 2.0 grams of II and 2.0 grams of selenium dioxide in 40 ml. of acetic acid was refluxed for 1 hr. and worked up as above. Crystallization of the residue from acetone-hexane yielded 700 mg. of VIII. By repeated recrystallizations the melting point was raised to 154–157°. Chromatography of the mother liquor on 50 grams of alumina (acid washed, Merck) yielded another 95 mg. of VIII, m.p. 148–154°, from benzene-ether (19:1) mixtures but no other crystalline product. $[\alpha]_D^{25}$ + 125° (c 0.62 in chloroform) λ_{max}^{alc} 244 mμ [ϵ 7930); 257 mμ (ϵ 7800); 306 mμ (ϵ 889): λ_{max}^{Nujol} 5.76 μ (acetyl); 6.10 μ; 6.17 μ; 6.27 μ; ($\Delta^{1,4}$-3-keto).

Anal. Calcd. for $C_{21}H_{26}O_3Se$: C, 62.22; H, 6.47; Se, 19.49; Mol. wt., 405. Found: C, 63.06; H, 7.07; Se, 17.85; Mol. wt. (Rast), 422.

B. *In refluxing benzene.*[6] A mixture of 300 mg. of II and 300 mg. of selenium dioxide in 10 ml. of benzene and 1.6 ml. of water was refluxed for 68 hr. and worked up as above. From acetone 54 mg. of VIII, m.p. 153–154°, were isolated. Chromatography of the mother liquor on 13 grams of alumina (acid washed, Merck) yielded another 47 mg. of VIII, m.p. 148–150°, from benzene-ether mixtures (9:1). More polar fractions failed to give 1-dehydro-testosterone acetate (V).

C. *In refluxing dioxane.* A mixture of 1.1 grams of II and 1.0 gram of selenium dioxide in 10 ml. of redistilled dioxane was refluxed for 90 min. After the usual workup 320 mg. of VIII, m.p. 147–150°, crystallized from acetone.

Seleno-1-dehydrotestosterone (seleno-$\Delta^{1,4}$-androstadiene-17β-ol-3-one) (IX). A. *By saponification of seleno-1-dehydro-testosterone acetate* (VIII). To 107 mg. of VIII in 10 ml. of ethanol was added 50 mg. of potassium carbonate in 0.5 ml. of water. The mixture was refluxed for 2 hr., taken up in 50 ml. of chloroform, washed free of alkali with H_2O, and concentrated to dryness *in vacuo*. The semisolid residue upon crystallization from acetone-ether yielded 47 mg. of IX, m.p. 250–255°. By repeated recrystallizations from acetone and methanol the melting point was raised to 273–275°. $[\alpha]_D^{25}$ −46° (c 0.54 in chloroform; α −0.25°) λ_{max}^{alc} 245 mμ (ϵ 10,800); 257 mμ (ϵ 10,700); 307 mμ (ϵ 1170): λ_{max}^{Nujol} 2.87 μ; (17-OH); 6.12 μ; 6.20 μ; 6.28 μ. ($\Delta^{1,4}$-3-keto).

Anal. Calcd. for $C_{19}H_{24}O_2Se$: C, 62.80; H, 6.66; Se, 21.73. Found: C, 62.58; H, 6.76; Se, 22.12.

(12) The melting points were determined with the Fisher-Johns melting point apparatus and are uncorrected.

B. *As by-product in the preparation of 1-dehydro-testosterone* (VI).[6] A mixture of 750 mg. of III and 750 mg. of selenium dioxide in 0.37 ml. of water and 23 ml. of benzene was refluxed for 55 hr. and worked up as before. The resinous residue was dissolved in benzene and chromatographed on 35 g. of alumina (acid washed, Merck). With benzene-ether mixtures (1:1) there was eluted 227 mg. of crystalline material which upon recrystallization yielded 151 mg. of VI, m.p. 173–174°; $[\alpha]_D^{25}$ + 26.8° (c 0.76 in chloroform; α + 0.203°; λ_{max}^{alc} 244 mμ (ϵ 15,400).

Anal. Calcd. for $C_{19}H_{26}O_2$: C, 79.68; H, 9.15. Found: C, 79.76; H, 8.97.

With ether-ethyl acetate mixtures (1:1) there was eluted 122 mg. of a second crystalline fraction which upon repeated recrystallization from acetone-hexane and methanol–ether yielded 40 mg. of IX, m.p. 273–275°. This material proved to be identical as to melting point, rotation, microanalysis, and infrared spectrum to IX, obtained by Method A.

Reacetylation of seleno-1-dehydrotestosterone (IX) *to seleno-1-dehydrotestosterone acetate* (VIII). To 42 mg. of IX in 1.0 ml. of pyridine was added 0.5 ml. of acetic anhydride. The mixture was kept at room temperature overnight. Dilution with water yielded 40 mg. of crystals, m.p. 148–150°, which upon recrystallization gave 35 mg. of VIII, m.p. 155–158°, identical with authentic material as to rotation and infrared spectrum.

1-Dehydrohydrocortisone acetate ($\Delta^{1,4}$-pregnadiene-11β,17α,-21-triol-3,20-dione 21-acetate) (X) *and seleno-1-dehydro-hydrocortisone acetate (seleno-$\Delta^{1,4}$-pregnadiene-11β,17α,21-triol-3,20-dione 21-acetate)* (XII) *from hydrocortisone acetate (Δ^4-pregnene-11β,17α,21-triol-3,20-dione 21-acetate).* A mixture of 2.0 grams of hydrocortisone acetate and 1.0 gram of selenium dioxide in 40 ml. of acetic acid was refluxed for 1 hr. and worked up as before. The resulting resin, upon recrystallization from ethyl acetate, yielded 160 mg. of X, m.p. 232–235°. Upon recrystallization from ethanol the melting point is raised to 237°–239°C. $[\alpha]_D^{25}$ + 112° (dioxane) λ_{max}^{alc} 242 mμ (ϵ 15,100): λ_{max}^{Nujol} 2.94 μ, 3.05 μ (OH); 5.73 μ (acetyl); 5.81 μ (20-keto); 6.06 μ, 6.24 μ, 6.29 μ ($\Delta^{1,4}$-3-keto).

Anal. Calcd. for $C_{23}H_{30}O_6$. C, 68.62; H, 7.51. Found: C, 69.11; H, 7.44.

The mother liquors were chromatographed on 50 grams of alumina (Merck, acid washed). With chloroform-benzene (9:1) another 60 mg. of X, m.p. 235–237° was eluted and immediately thereafter with the same solvent mixture, 111 mg. of XII, m.p. 291–293°. By recrystallization from acetone-hexane the melting point was raised to 298–300°. $[\alpha]_D^{25}$ − 204.6° (c 0.71 in dioxane; α − 1.45°) λ_{max}^{alc} 244 mμ (ϵ 10,400); 258 mμ (ϵ 9760); 303 mμ (ϵ 1360): λ_{max}^{Nujol} 5.74 μ (acetyl); 5.80 μ (20-carbonyl); 6.12 μ, 6.18 μ, 6.20 μ ($\Delta^{1,4}$-3-keto).

Anal. Calcd. for $C_{23}H_{29}O_6Se$: C, 57.62; H, 5.89; Se, 16.48. Found: C, 58.39; H, 6.32; Se, 15.93.

1-Dehydro-9α-fluorohydrocortisone acetate (XI) *from 9α-fluorohydrocortisone acetate.* A mixture of 2.0 grams of 9α-fluorohydrocortisone acetate and 1.0 gram of selenium dioxide in 40 ml. of acetic acid was refluxed for 30 min. and worked up as usual. The dark residue was chromatographed on 50 grams of alumina (acid washed, Merck). With benzene-chloroform (1:4) 170 mg. of crystals were eluted, identical to starting material, as to melting point and infrared spectrum. With benzene-chloroform (1:9) 6.5 mg. of XI were obtained, identical with authentic XI as to melting point and infrared spectrum.

Dienone-phenol rearrangement of seleno-1-dehydro-testosterone acetate (XIII *from* VIII). A mixture of 300 mg. of VIII and 100 mg. of *p*-toluenesulfonic acid in 17 ml. of acetic anhydride was heated to 100°C. for 4 hr. The reaction mixture was cooled to room temperature and diluted with water. After decomposition of the acetic anhydride, 50 ml. of chloroform was added. The chloroform layer was washed acid free with sodium bicarbonate solution and water and concentrated to dryness *in vacuo*. Upon crystallization of the

residue from acetone 215 mg. of XIII, m.p. 245–247°, were obtained, $[\alpha]_D^{25}$ + 130° (c 0.75 in chloroform; α + 0.98°) λ_{max}^{ether} 243 mμ (ϵ 10,700); λ_{max}^{Nujol} 5.67 μ, 5.78 μ.

Anal. Calcd. for $C_{28}H_{28}O_4Se$: C, 61.74; H, 6.31. Found: C, 62.00; H, 6.53.

Deacetylation of XIII *to* XIV. A total of 200 mg. of XIII was refluxed in 30 ml. of 2% methanolic potassium hydroxide for 75 min. The reaction mixture was neutralized with 1 ml. of acetic acid, diluted with chloroform, washed with water, and concentrated to dryness *in vacuo*. From acetone 81 mg. of yellow crystals of XIV, m.p. 209–211°, were obtained. By repeated recrystallization from acetone the melting point was raised to 213–214°C. $[\alpha]_D^{23}$ + 638° (c 0.58 in chloroform; α + 3.68°) λ_{max}^{alc} 258 mμ (ϵ 5200); 292 mμ (ϵ 3500); 325 mμ (shoulder) (ϵ 2700) λ_{max} (ethanolic KOH): 314 mμ (ϵ 6950); λ_{max}^{Nujol} 2.96 μ (hydroxyl) 6.35 μ, 6.41 μ.

Anal. Calcd. for $C_{19}H_{24}O_2Se$: C, 62.80; H, 6.66; Se, 21.73. Found: C, 62.58; H, 7.25; Se, 21.28.

$\Delta^{1,4}$-Cholestadiene-3-one (IV) *from seleno-$\Delta^{1,4}$-cholestadiene-3-one (VII).* To 200 mg. of VII in 15 ml. of benzene there was added 3 g. of Raney nickel in 6 ml. of ethanol. The mixture was refluxed for 5 hr., filtered from nickel, washed with water, and concentrated to dryness *in vacuo*. The colorless residue (178 mg.) was chromatographed on alumina. Fractions obtained with hexane-benzene solvent mixtures in order of elution were: (a) crystalline mixtures, m.p. range 40–55°C., of Δ^4-cholesten-3-one, cholestan-3-one, and/or coprostan-3-one. These mixtures exhibited ultraviolet maxima at 240 mμ (ϵ 3000) and an infrared band at 5.82 μ (3-keto). They were not further purified; (b) several crystalline fractions, m.p. range 88–95°, which upon recrystallization from methanol yielded 25 mg. of IV, m.p. 108–110°, $[\alpha]_D^{28}$ + 29.3° (c 0.82 in chloroform), λ_{max}^{EtOH} 244 mμ, (ϵ 12,500), λ_{max}^{Nujol} 6.01 μ, 6.15 μ, 6.24 μ ($\Delta^{1,4}$-3-keto).

Anal. Calcd. for $C_{27}H_{42}O$: C, 84.75; H, 11.07. Found: C, 84.62; H, 10.92.

Pyrolysis of seleno-$\Delta^{1,4}$-cholestadiene-3-one (VII). A total of 500 mg. of VII was heated to 350–370°C. at 1 mm. pressure for 30 min. The odor of H_2Se was detected. The reaction mixture was diluted with chloroform, filtered from 65 mg. of metallic selenium (77% of theory), washed with water, and concentrated to dryness *in vacuo*. The residue was chromatographed on alumina. With hexane-benzene solvent mixtures several crystalline fractions, totalling 150 mg., m.p. range 65–75°C., were eluted. All fractions exhibited ultraviolet maxima at 240 mμ and 280 mμ (in ethanol) of varying intensity. In the earlier fractions the 240 mμ maximum, in the later fractions the 284 mμ maximum, was the stronger. Repeated recrystallizations of various fractions did not yield material exhibiting one or the other maximum exclusively.

Hydrogen peroxide oxidation of seleno-1-dehydro-testosterone acetate (VIII) *to selenoxide* XVIII *at room temperature.* To 100 mg. of VIII in 1 ml. of acetic acid was added 0.15 ml. of 50% hydrogen peroxide. The solution was kept at room temperature for 20 min. and then diluted with water until precipitation occurred. The precipitate was collected and upon crystallization from acetone yielded 43 mg. of crystalline XVIII, m.p. 150–155°. By recrystallization from acetone the melting point was raised to 155–157° (with some dec.); $[\alpha]_D^{23}$ − 44° (c 0.51 in chloroform; α − 0.22°) λ_{max}^{alc} 248 mμ (ϵ 11,500); λ_{max}^{Nujol} 5.76 μ; 6.02 μ, 6.14 μ, 6.23 μ.

Anal. Calcd. for $C_{21}H_{28}O_5Se$: C, 57.40; H, 6.42; Se, 17.97. Found: C, 57.72; H, 6.50; Se, 21.91.

A solution of 40 mg. of XVIII in 10 ml. of ethyl acetate was shaken with a 10% aqueous solution of sodium bisulfite. Upon evaporation of the solvent 32 mg. of VIII, m.p. 148–152°, were isolated.

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[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT, THE UNIVERSITY, ABERDEEN]

Flavothebaone. Part II. Exhaustive Methylation of Flavothebaone Trimethyl Ether[1,2]

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Flavothebaone trimethyl ether methine ($C_{28}H_{31}O_5N$), on heating with alcoholic potassium hydroxide suffers molecular rearrangement to a *pseudo*methine ($C_{27}H_{33}O_5N$), acetolysis, and further Hofmann degradation of which affords derivatives of 1,2,7,10-tetramethoxychrysofluorene. On the basis of these results and of spectral data a complete structure is allotted to the *pseudo*methine.

In part I of this investigation,[3] flavothebaone trimethyl ether methine was shown to contain an aromatization-blocking group, presumably the quinol dimethyl ether nucleus at C_{14} of the phenanthrene skeleton, and the part-structure (I) was allotted to flavothebaone. Further confirmation of the presence of the substituent at C_{14} is provided by the fact that the 7,8-double bond in the trimethyl ether methine does not migrate into conjugation with that at position 9,10- when the methine is heated with alcoholic potash (contrast the behavior of α-codeimethine [II][4] and $\Delta^{7,9}$-thebainone methine [III][5]. Under these conditions

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(2) K. W. Bentley, J. Dominguez, and J. P. Ringe, *Chemistry and Industry*, 1353 (1956).

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