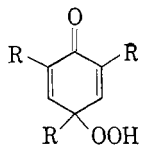
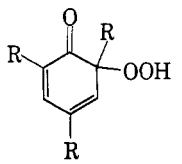
to loss of isobutene and water from the intermediate hydroperoxide XI. It is clear that, under the conditions of our experiment, the peroxide VIII cannot be the precursor of quinone V. If the formation of peroxide VIII is viewed as the addition of oxygen to the phenoxy radical which is followed by reaction with another phenoxy radical, it may be assumed that hydrogen donors present in the solution can compete effectively with phenoxy radicals in the second step. The decomposition of hydroperoxides XI and XII generated in this manner can then give rise to quinones V and VI, respectively.



XI



XII

Experimental

All the solvents used were of C.P. grade. The melting points reported are corrected, and boiling points are uncorrected. Ultraviolet spectra were determined in cyclohexane with a Beckman Model DK-2 spectrophotometer, and infrared spectra were measured in KBr disks with a Baird Model 4-55 recording infrared spectrometer. Gas chromatographic analyses were carried out with a Perkin-Elmer vapor fractometer, Model 154, and an F and M Model 500 linear programmed temperature gas chromatograph. Microanalyses were performed by Schwarzkopf Microanalytical Laboratory, Woodside 77, N. Y.

Purification of Cycloheptatriene.—Cycloheptatriene (500 g., 91% pure, Shell Chemical Co.) was distilled through a Heligrid-packed Podbielniak column. Fractions containing 99.8% cycloheptatriene and 0.2% toluene (analyzed by gas chromatography) amounted to 87 g. and had b.p. 115–116° at 760 mm., $n^{18}D$ 1.5254 (lit.[9a] b.p. 114° at 760 mm., $n^{25}D$ 1.5215).

2,4,6-Tri *t*-Butylphenoxy Radical.[11,19]—A solution of 2,4,6-tri-*t*-butylphenol (26.0 g., 0.099 mole) in 1.2 l. of benzene was stirred with a suspension of potassium ferricyanide (130.0 g., 0.51 mole) in 650 ml. of a 2 *N* potassium hydroxide solution for 2.5 hr. Precautions taken to exclude air from the radical solution during its preparation and during its reaction with cycloheptatriene included operating under an atmosphere of higher purity nitrogen, and deaerating the solvents before use. Titration of 10-ml. aliquots of the dark blue organic layer with standard sodium thiosulfate solution indicated a 91.9% yield of 2,4,6-tri-*t*-butylphenoxy radical. The radical solution was dried over freshly fused potassium carbonate before use.

Reaction with Cycloheptatriene.—Cycloheptatriene (8.37 g., 0.090 mole, 99.8% pure) was added under nitrogen to 1.0 l. of the phenoxy radical solution (19.76 g., 0.076 mole) and the resulting solution was stirred at room temperature for 24 hr. During this time the color changed from dark blue to light green. Comparison of the gas chromatogram of this solution with that of the initial mixture indicated that 0.032 mole of cycloheptatriene had been consumed. No further change occurred on the addition of another 1.0 g. of cycloheptatriene and stirring for an additional 12 hr. Analysis of an aliquot showed that 97% of the phenoxy radical had reacted. The solvent was evaporated, leaving a green liquid. Chromatography of this material on 625 g. of Merck acid-washed alumina afforded seven major fractions.

(1) A colorless crystalline solid was eluted with pentane, weighed 18.07 g., and had m.p. 129.5–131°. It was identified as 2,4,6-tri-*t*-butylphenol by comparison of its infrared spectrum with that of an authentic sample.

(2) A colorless crystalline solid, 0.66 g., m.p. 56–58, was obtained by vacuum sublimation of fraction 1 at room temperature. This material was identified as ditropyl (lit.[9a] m.p. 61°) by its infrared spectrum.[20]

(3) Light yellow needles, 1.35 g., m.p. 146–147°, were eluted with pentane–benzene (1:1) and proved to be bis(1,3,5-tri-*t*-butyl-2,5-cyclohexadien-4-one) 1-peroxide (lit.[19] m.p. 147–148°) by infrared analysis.[21]

(4) Orange plates, eluted with pentane–benzene (1:1), weighed 0.48 g. and had m.p. 63.5–67° after vacuum sublimation. The ultraviolet spectrum of this compound has $\lambda_{max}^{C_6H_{12}}$ 254.5 mμ (log ε 4.38) and a shoulder at 261.5 mμ (log ε 4.30).

Anal. Calcd. for $C_{14}H_{20}O_2$: C, 76.4; H, 9.1; mol. wt., 220. Found: C, 76.5; H, 9.4; mol. wt., 250.

Authentic 2,6-di-*t*-butyl-1,4-benzoquinone, prepared according to the method of Yoke, *et al.*,[22] had m.p. 65–67° and ultraviolet and infrared spectra identical with those of the product.

(5) Colorless needles, which were eluted with benzene, weighed 0.37 g. and had m.p. 125.5–127.5° after recrystallization from aqueous alcohol. The infrared spectrum of this compound shows prominent maxima at 2.85, 3.40, 6.02, 6.15, 7.40, 10.00, 10.40, 11.00, and 11.35 μ. The ultraviolet spectrum has $\lambda_{max}^{C_6H_{12}}$ 276.5 mμ (log ε 4.15) and 242.5 mμ (log ε 4.08).

Anal. Calcd. for $C_{18}H_{30}O_2$: C, 77.7; H, 10.8; mol. wt., 278. Found: C, 78.3; H, 11.0; mol. wt., 276.

(6) Crimson crystals were eluted with ether, weighed 0.14 g., and had m.p. 110.5–111.5 after vacuum sublimation and crystallization from pentane. The ultraviolet spectrum shows $\lambda_{max}^{C_6H_{12}}$ 385 mμ (log ε 3.45). The infrared spectrum of this compound is identical with that of 3,5-di-*t*-butyl-1,2-benzoquinone.[23]

Anal. Calcd. for $C_{14}H_{20}O_2$: C, 76.4; H, 9.1. Found: C, 76.3; H, 9.2.

(7) A rapidly darkening oil, also eluted with ether, weighed 1.66 g. The infrared spectrum[24] identified it as almost pure tropone.

(19) E. Müller and K. Ley, *Chem. Ber.*, **87**, 922 (1954).

(20) An authentic sample of ditropyl was prepared according to ref. 9a.

(21) A sample of this peroxide was prepared according to the method of ref. 19.

(22) G. R. Yoke, J. E. Dunbar, R. L. Pedrotti, F. M. Scheidt, F. G. H. Lee, and E. C. Smith, *J. Org. Chem.*, **21**, 1289 (1956).

(23) A sample of 3,5-di-*t*-butyl-1,2-benzoquinone was kindly supplied by Dr. J. J. Conradi, Shell Oil Co., Wood River, Ill.

(24) H. J. Dauben, Jr., and H. J. Ringold, *J. Am. Chem. Soc.*, **73**, 876 (1951); W. von E. Doering and F. L. Detert, *ibid.*, **73**, 876 (1951).

Preparation of Steroidal 3-Haloandrosta-1,3,5-trienes and 1-Halo-4-methylestra-1,3,5(10)-trienes

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3-Haloandrosta-1,3,5-trienes and 1-halo-4-methylestra-1,3,5(10)-trienes were prepared by the reaction of androsta-1,4-dien-3-ones with oxalyl halides. The 3-haloandrostatrienes were easily isomerized to the aromatic 1-halo-4-methylestratrienes. The mechanisms of this isomerization and of the dienone–phenol rearrangement are discussed.

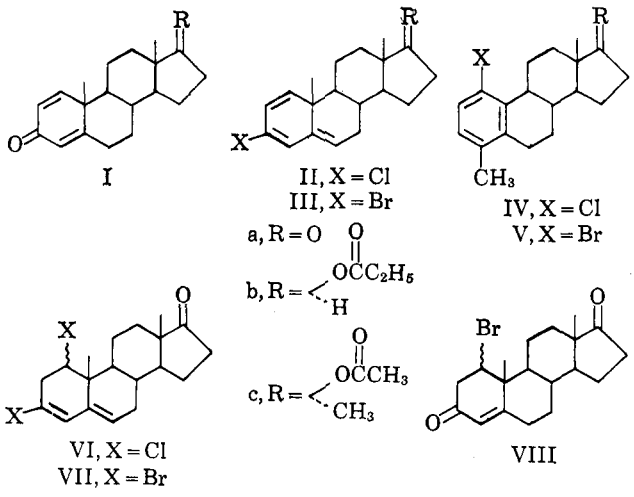
The reaction of oxalyl chloride and of oxalyl bromide with 3-ketoandrosta-1,4-dienes (I) has led to the preparation of 3-haloandrosta-1,3,5-trienes (II and III). These halotrienes were found to be quite labile, being readily isomerized with acid to 1-halo-4-methylestra-1,3,5(10)-trienes (IV and V). Under suitable condi-

tions, these aromatic products could be obtained directly from the 3-keto-1,4-dienes (I).

The 3-chloroandrosta-1,3,5-trienes (II) were best prepared by allowing the corresponding androsta-1,4-dien-3-one (I) and oxalyl chloride to react for a short time at room temperature in benzene solution. Extended reaction times, the addition of oxalic acid, or the use of chloroform as a solvent led instead to the isomeric 1-chloro-4-methylestra-1,3,5(10)-trienes (IV). The 3-chloroandrosta-1,3,5-trienes (II) were themselves readily isomerized to these same aromatic products (IV) in the presence of an oxalic acid–oxalyl chloride mixture in benzene or in a sulfuric acid–acetic acid mixture. In some cases, oxalyl chloride alone in benzene sufficed.

The course of the reaction was readily followed by ultraviolet spectroscopy. The original dienone absorption at 244 mμ decreased as the reaction proceeded with concurrent appearance of a wide peak centered at 311 mμ due to the 3-chloroandrosta-1,3,5-triene. The 311-mμ peak gradually diminished in intensity as the reaction progressed further, giving finally a spectrum nearly identical with that of a 1-chloro-4-methylestra-1,3,5(10)-triene. In this manner the effect of solvent on the rate of the reaction was studied. A chloroform solution of 17β-hydroxyandrosta-1,4-dien-3-one 17-propionate (Ib) was almost completely converted to the 1-chloro-4-methylestra-1,3,5(10)-triene (IVb) in less than 1 hr., whereas in cyclohexane solution, a major portion of the intermediate 3-chloroandrosta-1,3,5-triene (IIb) remained unchanged after 4 days. The rate of the isomerization was also affected by substitution at C-17. Whereas, androsta-1,4-diene-3,17-dione (Ia) yielded 3-chloroandrosta-1,3,5-trien-17-one (IIa) as the only isolable product after 24 hr., 17β-hydroxy-17α-methylandrosta-1,4-dien-3-one 17-acetate (Ic) under the same conditions afforded a good yield of 3-chloro-17α-methylandrosta-1,3,5-trien-17β-ol acetate (IIc) in 2 hr., but gave 1-chloro-4,17α-dimethylestra-1,3,5(10)-trien-17β-ol acetate (IVc) in 70% yield after 20 hr.

The reaction of androsta-1,4-diene-3,17-dione (Ia) with oxalyl bromide and oxalic acid in benzene gave a mixture of 1-bromo-4-methylestra-1,3,5(10)-trien-17-one (Va) and a dibromoandrostadiene (VII). The ultraviolet spectrum of VII was consistent with a 3,5-diene. This dibromoandrostadiene was assigned the 1,3-dibromo structure since it was easily dehydrobrominated to give 3-bromoandrosta-1,3,5-trien-17-one (IIIa) and since treatment of the androstadienone (Ia) with hydrogen bromide and subsequently with oxalyl bromide and oxalic acid in benzene afforded this same dibromodiene (VII) in higher yield. Like the analogous 3-chloroandrosta-1,3,5-trienes (II), the bromoandrostatriene (IIIa) was readily isomerized by treatment with acid, giving 1-bromo-4-methylestra-1,3,5(10)-trien-17-one (Va). The possible formation of a small amount of 1,3-dichloroandrosta-3,5-dien-17-one (VIa) in the reaction of oxalyl chloride with Ia was indicated by weak absorption at 242 and 250 mμ in the ultraviolet spectrum of the crude reaction product. This dichlorodiene was prepared by bubbling hydrogen chloride through a benzene solution of 3-chloroandrosta-1,3,5-trien-17-one (IIa). The formation of the dihalodienes in the oxalyl halide reactions probably occurs by addition of the hydrogen halide to either the starting androsta-1,4-dien-3-one or the 3-haloandrosta-1,3,5-triene.



Spectral data established the structures of II and III as haloandrostatrienes. The ultraviolet spectra (absorption maxima at 316 and 306 mμ[1]) and the nuclear magnetic resonance spectra (four vinyl protons) were consistent with a conjugated triene structure. The infrared spectra exhibited a single peak in the 1610–1616-cm.$^{-1}$ region due to C=C stretching. Solutions of the chloroandrostatrienes (II) in commercial chloroform exposed to the atmosphere slowly hydrolyzed to the original androsta-1,4-dien-3-ones (I). This facile hydrolysis can be accommodated only by the 3-chloroandrosta-1,3,5-triene structure.

The structures of the 1-halo-4-methylestra-1,3,5(10)-trienes (IV and V) were also assigned with the help of spectral data. The ultraviolet spectra [λ_{max} 271 mμ (ϵ *ca.* 275)] were consistent with a benzenoid structure, and the infrared (strong sharp absorbance in the 801–816-cm.$^{-1}$ region) and the n.m.r. spectra (an aromatic proton quartet centered near 7 p.p.m. which integrated for two protons, J = 7 c.p.s.) indicated a 1,2,3,4-tetrasubstituted benzene nucleus. The carbon skeleton was established by catalytic dehalogenation of 1-chloro-4-methylestra-1,3,5(10)-trien-17-one (IVa), which afforded the known 4-methylestra-1,3,5(10)-trien-17-one.[2] The attachment of the halogen atom at C-1 was shown by the identity of the bromoestratriene (Va) with a sample of 1-bromo-4-methylestra-1,3,5(10)-trien-17-one prepared independently by Morrow and Butler.[3]

The structural similarity of the 1-chloro-4-methylestratrienes to the 1-hydroxy-4-methylestratrienes obtained in the well-known dienone–phenol rearrangement[4] suggests that these compounds may be formed by similar mechanisms (Scheme I). When androsta-1,4-diene-3,17-dione was rearranged with zinc chloride in acetic anhydride, however, no absorption could be de-

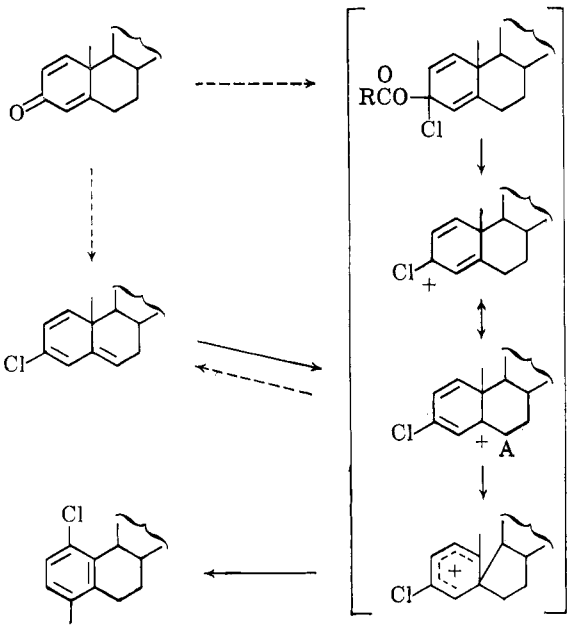
(1) The wave length calculated for the parent androsta-1,3,5-triene system by Woodward's rules is 303 mμ. According to Dannenberg (L. Fieser and M. Fieser, "Natural Products Related to Phenanthrene," Reinhold Publishing Corp., New York, N. Y., 1949, p. 188) a bathochromic correction of 4 mμ should be added for the halogen atom. However, in the case of the 3-chloroandrosta-3,5-dienes (242 mμ) [G. W. Moersch and W. A. Neuklis, *Can. J. Chem.*, **41**, 1627 (1963)] a bathochromic shift of 8 mμ was observed relative to the parent androsta-3,5-dienes (234 mμ). Thus, the calculated wave length for the 3-haloandrosta-1,3,5-trienes is in the range 307–311 mμ.

(2) E. Caspi, P. K. Grover, N. Grover, E. J. Lynde, and T. H. Nussbaumer, *J. Chem. Soc.*, 1710 (1962).

(3) D. F. Morrow and M. E. Butler, *J. Org. Chem.*, **29**, 1893 (1964).

(4) L. Fieser and M. Fieser, "Steroids," Reinhold Publishing Corp., New York, N. Y., 1959, p. 327.

SCHEME I



tected corresponding to a 1,3,5-triene system (beyond 300 mμ) during which time the dienone absorption at 244 mμ disappeared. On the other hand, Dannenberg has observed weak ultraviolet absorption maxima attributable to the triene system in the dienol–benzene rearrangement.[5] These results may indicate that the halo-1,3,5-trienes are intermediates through which the cation A (Scheme I) is formed en route to the aromatic product. It is alternatively possible that the halogen-substituted cases allow much greater accumulation of the 1,3,5-trienes by an equilibration with the intermediate cation A than do the 3-oxygenated analogs.

It is interesting to consider that Elks, *et al.*,[6] were unable to isolate 3-ethoxyandrosta-1,3,5-trienes in reacting $\Delta^{1,4}$-3-ketones with ethyl orthoformate under acidic conditions. The aromatic rearrangement products were obtained instead. Weinstock[7] attempted to prepare 3-alkoxypregna-1,3,5-trienes *via* the $\Delta^{1,4}$-3-ketones and was successful only when a 6-substituent (halogen or methyl) was present. His preparations of these compounds from pregna-1,5-dien-3-ones were acid catalyzed, but no mention of the aromatization products appears in his published patent.

These reports suggest that 3-ethoxy-1,3,5-trienes may be reasonably stable to acid conditions such as aromatize the 1,4-dien-3-ones. It is unfortunately difficult to draw conclusions concerning the relationship of these reactions from such data without a better understanding of the influence of the 3-substituent as well as of further substitution of the steroid nucleus upon the stability of the 1,3,5-triene system.

The reaction of oxalyl halides with androsta-1,4-dien-3-ones is thus a method for the replacement of the phenolic hydroxyl by halogen in a dienone–phenol rearrangement product.[8] The earlier experiments of Auwers and Julicher[9] and of Newman[9] using cyclohexadienone systems achieve replacement of the dienone carbonyl oxygen by chlorine with attendant alkyl migration and in this sense may also be a related reaction.

(5) H. Dannenberg and H. G. Neumann, *Ann.*, **646**, 148 (1961).
(6) J. Elks, J. F. Oughton, and L. Stephenson, *J. Chem. Soc.*, 4531 (1961).
(7) L. M. Weinstock, U. S. Patent 3,068,253 (1962).

Experimental

Melting points are determined in capillary tubes unless otherwise indicated and are uncorrected. The infrared spectra were recorded with a Beckman IR-7 in potassium bromide disks unless otherwise noted. The n.m.r. spectra were recorded in deuteriochloroform solution with a Varian A-60 instrument; resonances are reported as parts per million downfield from tetramethylsilane, used as an internal reference. The ultraviolet spectra were run in methanol solution. The rotations were determined in a 1-dm. tube in chloroform solution unless otherwise stated.

3-Chloroandrosta-1,3,5-trien-17-one (IIa).—A solution of 1.0 g. of androsta-1,4-diene-3,17-dione in 100 ml. of dry benzene was cooled and treated with 3 ml. of oxalyl chloride. The mixture was allowed to stand at 25° for 24 hr. and was then evaporated to give a solid which was triturated with saturated aqueous sodium bicarbonate. The product was removed by filtration and washed with water to yield 1.12 g. of yellow solid. Crystallization from methanol gave 0.66 g. of yellow crystals, m.p. 171–173°; λ_{max} 316 mμ (ε 5810) and 306 mμ (ε 5600); $[\alpha]^{23}D$ −248° (initial) → +114° (*c* 0.34, final, 19 hr.); ν_{max} 1740 and 1614 cm.$^{-1}$.

Anal. Calcd. for $C_{19}H_{23}ClO$ (302.8): C, 75.36; H, 7.66; Cl, 11.70. Found: C, 75.20; H, 7.53; Cl, 12.00.

The material recovered by evaporation of the optical rotation sample exhibited λ_{max} 243 mμ and had an infrared spectrum identical in all essential respects with that of androsta-1,4-diene-3,17-dione, $[\alpha]^{25}D$ +119°.[10]

3-Chloro-17α-methylandrosta-1,3,5-trien-17β-ol Acetate (IIc).—To a solution of 1.0 g. of 17β-hydroxy-17α-methylandrosta-1,4-dien-3-one 17-acetate in 25 ml. of dry benzene was added 6 ml. of oxalyl chloride with cooling. The soution was allowed to stand at 25° for 2 hr. and then evaporated under reduced pressure to give a yellow solid. The solid was slurried with saturated aqueous sodium bicarbonate solution and the product was separated by filtration, washed with water, and dried. Crystallization from acetone–ethanol gave 0.55 g. of pale yellow crystals, m.p. 172–174°; λ_{max} 316 mμ (ε 5810) and 306 mμ (ε 5560); $\lambda_{max}^{cyclohexane}$ 317 mμ (ε 6150) and 306 mμ (ε 5900); $[\alpha]^{23}D$ −330° (initial) → +16° (*c* 0.50, final, 2 hr.) (a rotation of $[\alpha]^{23}D$ +17° was observed for our sample of 17β-hyroxy-17α-methylandrosta-1,4-dien-3-one 17-acetate); ν_{max} 1723 and 1613 cm.$^{-1}$; $\nu_{max}^{CHCl_3}$ 1728 and 1615 cm.$^{-1}$; the n.m.r. spectrum had resonances at δ = 0.85 (18-Me), 1.10 (19-Me), 1.36 (17-Me), 1.86 (CH_3CO), and a complex multiplet at 5.3–6.1 p.p.m. which integrated for four protons (at positions 1, 2, 4, and 6).

Anal. Calcd. for $C_{22}H_{29}ClO_2$ (360.9): C, 73.21; H, 8.10; Cl, 9.82. Found: C, 73.06; H, 8.01; Cl, 9.86.

1-Chloro-4-methylestra-1,3,5(10)-trien-17β-ol Propionate (IVb).—A solution of 7.0 g. of 17β-hydroxyandrosta-1,4-dien-3-one 17-propionate in 250 ml. of dry benzene was cooled and treated with 20 ml. of oxalyl chloride and allowed to stand for 24 hr. at room temperature. The solution was then evaporated under reduced pressure to a yellow oil, which was dissolved in benzene and washed with sodium bicarbonate solution and with water. The benzene solution was dried and evaporated to a yellow oil which was dissolved in hexane and passed through 12 g. of Florisil. The oil obtained from evaporation of the hexane eluates was crystallized from methanol to yield 4.25 g. of white crystals, m.p. 75–76°, λ_{max} 271 mμ (ε 260); ν_{max} 1737 and 808 cm.$^{-1}$; $\nu_{max}^{CHCl_3}$ 1729 and 812 cm.$^{-1}$.

Anal. Calcd. for $C_{22}H_{29}ClO_2$ (360.9): C, 73.21; H, 8.10; Cl, 9.82. Found: C, 73.03; H, 8.17; Cl, 10.01.

(8) Since this article was submitted, one of the authors (G. W. M.) has heard Professor Andre Dreiding of the University of Zurich describe, at the Anniversary Meeting of the Chemical Society (London), Birmingham, April 9, 1964, his work on the aromatization of 1,4-dienones with acetyl chloride and with acetyl bromide to produce similar halogen-containing steroids. Professor Dreiding, whose contributions to the field of 1,4-dienone rearrangements began some years ago, has informed us of his intention to publish his results.

(9) K. Auwers and W. Julicher, *Ber.*, **55**, 2167, 2180 (1922); M. S. Newman and L. L. Wood, Jr., *J. Am. Chem. Soc.*, **81**, 6450 (1959); *J. Org. Chem.*, **23**, 1236 (1958); M. S. Newman, J. Eberwein, and L. L. Wood, Jr., *J. Am. Chem. Soc.*, **81**, 6454 (1959); M. S. Newman, D. Pawellek, and S. Ramachandran, *ibid.*, **84**, 995 (1962).

(10) J. P. Mathieu and A. Petit, "Pouvoir Rotatoire Naturel I. Steroides," Masson and Cie, Paris, 1956, p. 13.

1-Chloro-4-methylestra-1,3,5(10)-trien-17β-ol.—A solution of IVb (2.5 g.) in 90 ml. of 5% ethanolic potassium hydroxide was refluxed under nitrogen for 1 hr. The reaction was cooled in ice and the product precipitated by dilution with water. The solid was separated by filtration, dissolved in benzene, washed with water, and dried over magnesium sulfate. Evaporation of the benzene solution under reduced pressure gave a colorless gum which crystallized from aqueous methanol to yield 1.72 g. of white crystals, m.p. 70° with bubbling; $[\alpha]^{24}D$ +221° (*c* 0.52); the n.m.r. spectrum showed resonances at δ = 0.80 (18-Me), 2.13 (4-Me), 6.70, 6.84, 6.96, and 7.10 p.p.m. (2,3-H).

Anal. Calcd. for $C_{19}H_{25}ClO$ (304.9): C, 74.85; H, 8.26; Cl, 11.63. Found: C, 74.59; H, 8.54; Cl, 11.61.

1-Chloro-4-methylestra-1,3,5(10)-trien-17-one (IVa). A. From Androsta-1,4-diene-3,17-dione (Ia).—A solution of 0.65 g. of Ia in 30 ml. of benzene was treated with 4.5 ml. of oxalyl chloride and 0.30 g. of powdered oxalic acid dihydrate. The mixture was stirred at room temperature overnight and then evaporated under reduced pressure to give a light yellow oil. Crystallization was effected by trituration with cold dry ether. Separation of the solid by filtration yielded 0.50 g. of white crystals, m.p. 153–154°. Concentration of the ether filtrate to dryness and recrystallization of the residue from methanol afforded an additional 0.10 g. of product, m.p. 153–154°. The first crop had λ_{max} 271 mμ (ε 282); $[\alpha]^{24}D$ +314° (*c* 0.55); ν_{max} 1740 and 819 cm.$^{-1}$; $\nu_{max}^{CHCl_3}$ 1738 and 816 cm.$^{-1}$.

Anal. Calcd. for $C_{19}H_{23}ClO$ (302.8): C, 75.36; H, 7.66; Cl, 11.70. Found: C, 75.06; H, 7.47; Cl, 11.47.

B. From 3-Chloroandrosta-1,3,5-trien-17-one (IIa).—A solution of 0.65 g. of IIa in 25 ml. of dry benzene was cooled while 3 ml. of oxalyl chloride and 0.20 g. of oxalic acid dihydrate were added. The cooling bath (ice–water) was removed and the reaction was stirred at 25° for 16 hr. The mixture was filtered and then evaporated at reduced pressure. The orange residue was triturated with 2 ml. of warm methanol, cooled, and filtered to give 0.35 g. of almost white crystals, m.p. 152.5–154.5°.

C. From 1-Chloro-4-methylestra-1,3,5(10)-trien-17β-ol.— A solution of 0.7 g. of 1-chloro-4-methylestra-1,3,5(10)-trien-17β-ol in 75 ml. of acetic acid was treated with 3 ml. of chromic acid solution (Jones reagent[11]) with cooling in ice and was then allowed to stand at room temperature for 1 hr. The mixture was poured into ice–water, and the solid product was separated by filtration and washed with water. The crude product was crystallized from methanol to give colorless crystals, m.p. 147–149°. Recrystallization from acetone–methanol gave 0.2 g. of colorless needles, m.p. 151°.

1-Chloro-4,17α-dimethylestra-1,3,5(10)-trien-17β-ol Acetate (IVc). A. From 17β-Hydroxy-17α-methylandrosta-1,4-dien-3-one 17-Acetate (Ic).—A solution of 4.0 g. of Ic in 100 ml. of dry benzene was cooled and treated with 14 ml. of oxalyl chloride. The solution was allowed to stand for 20 hr. at room temperature and was then evaporated at 50–60° to an amber gum. The product was allowed to stand for 20 min. in warm saturated aqueous sodium bicarbonate solution, and the solid was collected by filtration, washed with water, and dried under reduced pressure at 50°. The crude product obtained, 4.2 g., m.p. 151–156°, was recrystallized from methanol to give 2.85 g. of colorless needles, m.p. 162–164°; λ_{max} 271 mμ (ε 253); $[\alpha]^{24}D$ +189° (*c* 0.50); ν_{max} 1723 and 801 cm.$^{-1}$; the n.m.r. spectrum showed resonances at δ = 0.94 (18-Me), 1.52 (17-Me), 1.97 (CH_3CO), 2.14 (4-Me), 6.84, 6.96, 7.08, and 7.20 p.p.m. (2,3-H).

Anal. Calcd. for $C_{22}H_{29}ClO_2$ (360.9): C, 73.21; H, 8.10; Cl, 9.82. Found: C, 73.05; H, 7.83; Cl, 9.93.

B. From 3-Chloro-17α-methylandrosta-1,3,5-trien-17β-ol Acetate (IIc).—A solution of 0.60 g. of IIc in 25 ml. of dry benzene was treated with 3 ml. of oxalyl chloride and allowed to stand overnight at 25° while protected by a drying tube. The reaction mixture was evaporated at 50–60° under reduced pressure to a light orange glass. This was warmed with aqueous sodium bicarbonate and cooled in ice. The solid product was separated by filtration, washed with water, and dried in air. The crude product weighed 0.57 g., m.p. 148–157°. Crystallization from methanol gave 0.33 g. of pale yellow crystals, m.p. 164.5–166°, λ_{max} 271 mμ (ε 268).

1-Chloro-4,17α-dimethylestra-1,3,5(10)-trien-17β-ol.—A solution of 1.5 g. of 1-chloro-4,17α-dimethylestra-1,3,5(10)-trien-17β-ol acetate in 100 ml. of ethanol was treated with 5 ml. of 24% aqueous potassium hydroxide, and the solution was refluxed 2.5 hr. on a steam bath. The mixture was cooled and diluted with water. The product was separated by filtration, washed with water, and dried under reduced pressure at 50°. The crude product, 1.23 g., m.p. 149–153°, was crystallized from methanol to give 0.88 g. of crystals, m.p. 153–154°. Recrystallization from hexane gave 0.61 g. of colorless needles, m.p. 156–158°; $[\alpha]^{24}D$ +190° (*c* 0.51); ν_{max} 3450, 3340, and 800 cm.$^{-1}$.

Anal. Calcd. for $C_{20}H_{27}ClO$ (318.9): C, 75.32; H, 8.53; Cl, 11.12. Found: C, 75.53; H, 8.52; Cl, 10.92.

1,3-Dichloroandrosta-3,5-dien-17-one (VI).—A solution of 1.25 g. of androsta-1,4-diene-3,17-dione in 25 ml. of dry benzene was cooled and treated with 6 ml. of oxalyl chloride. After 3 hr. at room temperature, the reaction was treated with a stream of hydrogen chloride. The reaction was cooled initially and allowed to warm to room temperature during 45 min. At the end of this time the solution had changed from amber to yellow and hydrogen chloride introduction was stopped. The reaction was allowed to stand for 30 min. longer and was evaporated to a yellow gum under reduced pressure. The gum was warmed with dilute sodium bicarbonate solution and cooled in ice until it solidified. The product was collected on a filter, washed with water, and dried to give 1.34 g. of pale yellow solid. Crystallization of 0.5 g. from methanol gave 0.15 g. of crystals, m.p. 211–214°; λ_{max} 251 mμ (ε 16,300), 242 (23,700), 235 (21,000); $\nu_{max}^{CHCl_3}$ 1738 and 1624 cm.$^{-1}$ (unchanged after 2 hr.).

Anal. Calcd. for $C_{19}H_{24}Cl_2O$ (339.3): C, 67.25; H, 7.14; Cl, 20.90. Found: C, 67.11; H, 7.12; Cl, 20.71.

1,3-Dibromoandrosta-3,5-dien-17-one (VII).—A solution of 2.0 g. of androsta-1,4-diene-3,17-dione in 155 ml. of anhydrous ether was cooled in ice, and a stream of hydrogen bromide was bubbled through the solution for 15 min. The solution was allowed to stand at 0–5° for 10 min. and was then evaporated under reduced pressure. The yellow residue was treated with 0.6 g. of oxalic acid dihydrate and 6 ml. of oxalyl bromide in 175 ml. of dry benzene. The mixture was stirred at 25° for 3.5 hr. and filtered, and the filtrate was evaporated under reduced pressure. The residue was dissolved in ether and the solution was washed with saturated aqueous sodium bicarbonate and with water, and dried over anhydrous magnesium sulfate. Evaporation of the ether solution left a yellow residue which was crystallized from methanol to give 1.3 g. of pale yellow needles, m.p. 205–207°. A second crop, 0.6 g., m.p. 203–206°, was obtained from the mother liquors. The first crop had λ_{max} 253 mμ (ε 13,200), 245 (20,000), and 237 (19,800); ν_{max} 1737 and 1620 cm.$^{-1}$.

Anal. Calcd. for $C_{19}H_{24}Br_2O$ (428.2): C, 53.29; H, 5.65; Br, 37.32. Found: C, 53.06; H, 5.82; Br, 37.07.

3-Bromoandrosta-1,3,5-trien-17-one (IIIa).—A solution of 1.0 g. of 1,3-dibromoandrosta-3,5-dien-17-one in 40 ml. of 2% methanolic potassium hydroxide was refluxed under an atmosphere of nitrogen for 5 min. The solution was cooled in ice and the crystals were collected by filtration, washed with water, and dried under reduced pressure. The pale yellow crystals, 0.63 g., had m.p. 164–165°; λ_{max} 318 mμ (ε 6150) and 307 mμ (ε 5840); ν_{max} 1729 and 1610 cm.$^{-1}$.

Anal. Calcd. for $C_{19}H_{23}BrO$ (347.3): C, 65.71; H, 6.68; Br, 23.01. Found: C, 65.96; H, 6.58; Br, 22.80.

1-Bromo-4-methylestra-1,3,5-trien-17-one (Va). A. From Androsta-1,4-diene-3,17-dione (Ia).—A solution of 1.0 g. of Ia in 55 ml. of benzene was treated with 3 ml. of oxalyl bromide and 0.5 g. of oxalic acid dihydrate. The mixture was allowed to stand for 16 hr. at 25° and then evaporated under reduced pressure. The residual gum was triturated with warm saturated aqueous sodium bicarbonate, and the resulting solid was removed by filtration. After washing with water, the crude product was dried and crystallized from methanol to give 0.18 g. of crystals, m.p. 202–203°, which on recrystallization from methanol gave 0.06 g. of 1,3-dibromoandrosta-3,5-dien-17-one as off-white needles, m.p. 204–206°. Concentration of the mother liquors afforded crystals of 1-bromo-4-methylestra-1,3,5(10)-trien-17-one, 0.10 g., m.p. 171–173°. This sample was identical with a sample of 1-bromo-4-methylestra-1,3,5(10)-trien-17-one prepared by an independent synthesis.[3]

B. From 3-Bromoandrosta-1,3,5-trien-17-one (IIIa).—To a solution of 40 mg. of IIIa in 2 ml. of acetic acid was added 1 drop of concentrated sulfuric acid. The solution was allowed to stand at 25° for 5 min. and was then poured into a mixture of ice and saturated sodium bicarbonate solution. The precipitated product was removed by filtration, washed with water, and crystallized from methanol to give needles, m.p. 167–168°. The in-

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frared spectrum of this compound was identical with that of the sample prepared above from androstadienedione (Ia).

4-Methylestra-1,3,5(10)-trien-17-one.—To a solution of 177 mg. of 1-chloro-4-methylestra-1,3,5(10)-trien-17-one (IVa) and 50 mg. of sodium acetate in 50 ml. of 95% ethanol was added 50 mg. of 20% palladium on carbon, and the resulting mixture was hydrogenated at room temperature and atmospheric pressure. One equivalent of hydrogen was absorbed in 15 min. The mixture was filtered and concentrated to dryness under reduced pressure. The residue was extracted with ether, the extracts were concentrated to dryness, and the residue was recrystallized from methanol, giving 129 mg. of colorless crystals, m.p. 191–192°. A mixture of this compound and a sample of 4-methylestra-1,3,5(10)-trien-17-one prepared by an independent synthesis (m.p. 189–191°)[2] melted at 190–192°. The infrared spectra of the two samples were identical when run in both potassium bromide disks and in chloroform solution.

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Silicon Heterocyclic Compounds. II. Synthesis of 3-Sila-1-heterocycloheptanes[1]

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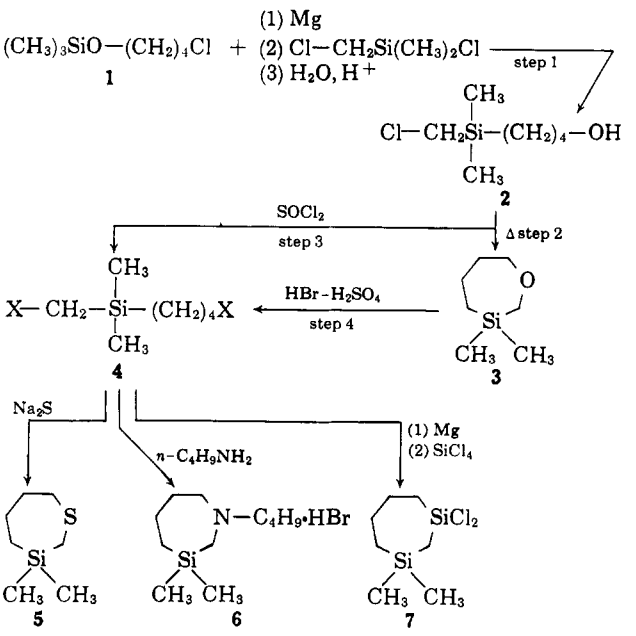
A series of 1-sila-3-heterocycloheptanes of the general formula, $(CH_3)_2\overline{SiCH_2ZCH_2CH_2CH_2CH_2}$, where Z is O (**3**), S (**5**), $NC_4H_9\cdot HBr$ (**6**), and $SiCl_2$ (**7**), have been prepared. Reaction of $(CH_3)_3SiO(CH_2)_4MgCl$ with $(ClCH_2)SiCl(CH_3)_2$ gave $HO(CH_2)_4Si(CH_3)_2CH_2Cl$ (**2**) after water work-up. Atmospheric distillation of **2** yielded **3**. Reaction of **2** with $SOCl_2$ yielded $X(CH_2)_4Si(CH_3)_2CH_2X$ (**4**, X = Cl), and cleavage of **3** with HBr and H_2SO_4 yielded **4** (X = Br). Preparation of the di-Grignard reagent of **4** (X = Br) and reaction with $SiCl_4$ gave **7**. Reaction of **4** (X = Cl) with Na_2S gave **5** and with *n*-butylamine yielded **6**.

In a previous study[2] we described the synthesis of a new class of stable silicon heterocyclic compounds, the 3-sila-1-heterocyclohexanes. This report is concerned with the extension of the synthetic method to the 3-sila-1-heterocycloheptanes.

The reports of silaheterocycloheptanes are sparse[3]; the parent silacycloheptane and a few of its derivatives have been reported and studied.[4]

The key step in the synthesis of the silaheterocyclohexanes was a silicon hydride addition to a silyl-blocked allyl alcohol. This study differs in that the key intermediate, δ-hydroxybutyl(chloromethyl)dimethylsilane (**2**), was obtained by means of a Grignard reaction (Scheme I). The preparation of 4-(trimethylsiloxy)-1-chlorobutane (**1**), and the chemistry of the corresponding Grignard reagent have been studied by Speier.[5] The reaction of this Grignard reagent with (chloromethyl)dimethylchlorosilane (step 1) was smooth, and the yield of the desired alcohol (**2**) was high (77%). In step 1 the blocking trimethylsilyl group was removed by the acid work-up so that **2** could be isolated directly from the reaction. In contrast to the isolation of γ-hydroxyalkyl(chloromethyl)dimethylsilanes, used for the synthesis of the 3-sila-1-oxacyclohexanes,[2] no difficulty was encountered in the isolation of **2**.

SCHEME I



The ring closure (step 2) leading to 3,3-dimethyl-3-sila-1-oxacycloheptane (**3**) was carried out using a slow atmospheric distillation. As would be expected,[6] the yields in this ring-closure step were low (35–38%). No attempt was made to characterize the residue.

The other 3-sila-1-heterocycloheptanes were obtained using the dihalogen intermediate **4**. δ-Chlorobutyl(chloromethyl)dimethylsilane (**4**, X = Cl) was obtained in a 61% yield by reaction of **2** with thionyl chloride. δ-Bromobutyl(bromomethyl)dimethylsilane (**4**, X = Br) was obtained by the ring cleavage of **3** with hydrobromic acid and sulfuric acid using the proce-

(1) This work was supported by a grant (GP-315) from the National Science Foundation.

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