Steroidal Allylic and Homoallylic Rearrangements during Halogenation with Triphenylphosphine and Carbon Tetrachloride

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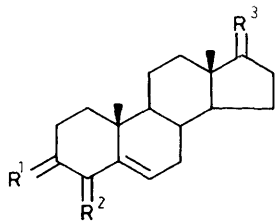
Treatment of 3β-hydroxyandrost-5-en-17-one with triphenylphosphine and carbon tetrachloride under various conditions affords 3α- and 3β-chloroandrost-5-en-17-one, 3α,5-cycloandrost-6-en-17-one, and minor amounts of 17-dichloromethylene derivatives. In contrast, 4β-acetoxy-3β-hydroxyandrost-5-en-17-one affords 4β-acetoxy-3α-chloro- and 3β-acetoxy-4α-chloro-androst-5-en-17-ones. 3β-Acetoxy-4β-hydroxyandrost-5-en-17-one affords 3β-acetoxyandrost-4,6-dien-17-one and minor amounts of the 3β-acetoxy-4α-chloro-5-ene and 3β-acetoxy-6α-chloro-4-ene.

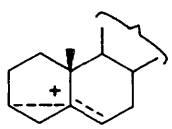
The activation of alcohols with triphenylphosphine in carbon tetrachloride affords a mild, widely used method for their conversion to alkyl chlorides.[1] The reaction normally proceeds with inversion of configuration[2] and is reported[3] to proceed without the rearrangement of neighbouring double bonds. However in connection with the partial synthesis of gibberellin plant hormones, we used this reagent and found[4] that the reaction was accompanied by allylic rearrangements. In this paper we describe the products of the reaction with dehydroisoandrosterone (**1**) and some 4β-substituted relatives with triphenylphosphine–carbon tetrachloride which reveal a number of aspects of alkene neighbouring-group participation in this system.

In the steroids the homoallylic participation by a Δ^5-double bond substantially modifies the course of reactions of the equatorial 3β-substituents, both increasing their rate of solvolysis and affording products possibly arising from a delocalized i-steroid carbocation (**12**).[5] Thus substitution occurs either with retention of configuration at C-3β or at C-6β with the formation of a 3α,5-cyclosteroid. Only in the reaction with a powerful nucleophile does inversion of configuration predominate at C-3.[6]

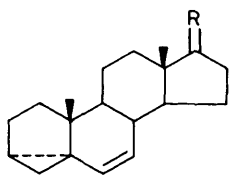
Cholesterol, on treatment with triphenylphosphine–carbon tetrachloride was reported[7] to give 3α-chlorocholest-5-ene, 3β-chlorocholest-5-ene, cholesta-3,5-diene and 3α,5-cyclocholest-6-ene together with a phosphorus-containing product. In our hands, dehydroisoandrosterone (**1**) afforded 3α,5-cycloandrost-6-en-17-one (**13**),[8] and 3α- and 3β-chloroandrost-5-en-17-one (**2**) and (**3**),[9] although in different proportions from the cholesterol series. The products were readily identified by their ^{1}H n.m.r. spectra. 6β-Chloro-3α,5-cyclocholestane is reported[10] to be unstable, readily affording 3β-chlorocholest-5-ene possibly *via* an ion-pair intermediate. It is possible that the variable amounts of 3β-chloroandrost-5-en-17-one which were obtained, could arise in a similar manner. In connection with other work we required a facile preparation of 3α,5-cycloandrost-6-en-17-one (**13**). By introducing a base into the system, we hoped to favour the elimination of a 6β-chlorine and the formation of the 6-ene. Indeed, although 3β-chloroandrost-5-en-17-one (**3**) did not appear to react readily with triphenylphosphine–carbon tetrachloride–pyridine, treatment of 6β-hydroxy-3α,5-cycloandrostan-17-one (**15**) with this reagent gave 3α,5-cycloandrost-6-en-17-one (**13**). Dehydroisoandrosterone (**1**) itself gave 3α,5-cycloandrost-6-en-17-one (**13**), 3α-chloroandrost-5-en-17-one (**2**) and small amounts of the Wittig products (**4**), (**5**), and (**14**). The latter were identified by their ^{13}C n.m.r. (δ_C 149 and 110; no C=O signal). Similar products have been observed with other ketones.[11,12]



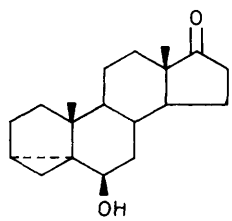
(**1**) R^1 = α-H, β-OH; R^2 = H_2; R^3 = O
(**2**) R^1 = α-Cl, β-H; R^2 = H_2; R^3 = O
(**3**) R^1 = α-H, β-Cl; R^2 = H_2; R^3 = O
(**4**) R^1 = α-Cl, β-H; R^2 = H_2; R^3 = Cl_2C=
(**5**) R^1 = α-H, β-Cl; R^2 = H_2; R^3 = Cl_2C=
(**6**) R^1 = α-H, β-OTs; R^2 = α-H, β-OAc; R^3 = O
(**7**) R^1 = α-H, β-OTs; R^2 = H_2; R^3 = O
(**8**) R^1 = α-H, β-OH; R^2 = α-H, β-OAc; R^3 = O
(**9**) R^1 = α-Cl, β-H; R^2 = α-H, β-OAc; R^3 = O
(**10**) R^1 = α-H, β-OAc; R^2 = α-Cl, β-H; R^3 = O
(**11**) R^1 = α-H, β-OAc; R^2 = α-H, β-OH; R^3 = O



(**12**)



(**13**) R = O
(**14**) R = Cl_2C=



(**15**)

The use of hexachloroacetone in place of carbon tetrachloride has been recommended[13] to give cleaner products but in this case the products, (**3**) and (**13**) were difficult to separate from the excess hexachloroacetone. The rate of reaction of the triphenylphosphine–carbon tetrachloride system is very sensitive to solvent. The reaction is reported to be particularly fast in acetonitrile.[1] The system triphenylphosphine–carbon tetrachloride–imidazole in acetonitrile has been reported[14] to be an efficient method for chlorinating carbohydrates. In the case of dehydroisoandrosterone (**1**) it

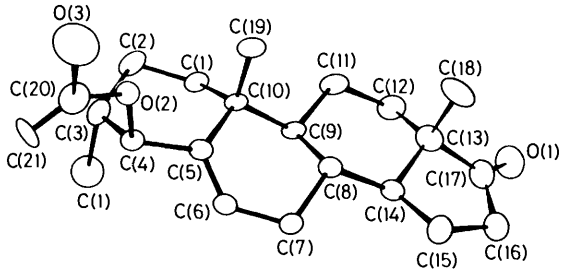


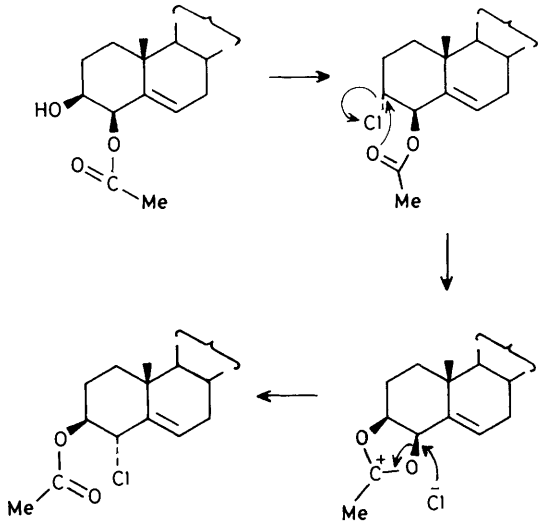
Figure 1. Crystal stucture of compound (**9**)

provided a clean method of producing 3α,5-cycloandrost-6-en-17-one and 3β-chloroandrost-5-en-17-one which were separated chromatographically.

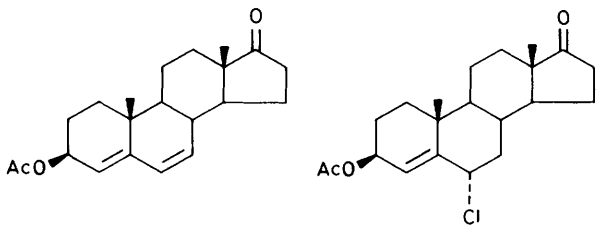
In previous work we have shown[15] that the presence of a 4β-acetoxy group significantly slows down the rate of unimolecular acetolysis of a Δ^5-3-toluene-*p*-sulphonate. Indeed 4β-acetoxy-3β-toluene-*p*-sulphonyloxyandrost-5-en-17-one (**16**) was recovered substantially unchanged from the i-steroid reaction (treatment with sodium acetate in refluxing aqueous acetone) after 80 h whilst the corresponding unsubstituted 3β-toluene-*p*-sulphonate (**7**) afforded the cyclosteroid (**15**) in high yield.

Treatment of 4β-acetoxy-3β-hydroxyandrost-5-en-17-one (**8**)[16] with triphenylphosphine–carbon tetrachloride–pyridine gave a complex mixture. On one occasion 4β-acetoxy-3α-chloroandrost-5-en-17-one (**9**) was the only isolable product. Since the ^{1}H n.m.r spectrum of this compound, in which 4-H appeared as a singlet, δ 5.27, was potentially ambiguous, the structure was confirmed by an *X*-ray analysis (see Figure 1). A further product was 3β-acetoxy-4α-chloroandrost-5-en-17-one (**10**), the structure of which was established on the basis of its ^{1}H n.m.r. spectrum. Spin decoupling experiments showed that the alkene proton resonance (6-H) (δ 6.17) contained an allylic coupling (2 Hz) to the CHCl (4-H) signal (δ 4.64) and was also coupled to two resonances within the methylene envelope (δ 2.31, *J* 5.5 Hz; δ 1.76, *J* 2.2 Hz) (7-H). The CHCl resonance was coupled (*J* 11 Hz) to a triplet (*J* 11 Hz) of doublets (*J* 5 Hz) at δ 4.72 (3-H). Decoupling experiments also showed that apart from the allylic coupling (2 Hz) to the alkene signal there was also long-range couplings (2 Hz) to the signals at δ 1.76 and 2.31. Thus in contrast to the 4-desacetoxy compound, the substitution reaction has proceeded with inversion of configuration at C-3 and without any evidence of participation of the Δ^5-double bond. Indeed the formation of the 3α- and 4α-chloro compounds may be accounted for by the intervention of a 3β,4β-acetoxylinium ion (see the Scheme). The intervention of such an ion has been established in other situations.[17]

When the isomeric 3β-acetoxy-4β-hydroxyandrost-5-en-17-one (**11**)[18] was treated with triphenylphosphine–carbon tetrachloride–imidazole, the major product was 3β-acetoxyandrosta-4,6-dien-17-one (**16**) [δ 5.43 (4-H); δ 5.7, dd, *J* 1 and 10 Hz, 6-H; δ 6.0, dd, *J* 3 and 10 Hz, (7-H)]. 3β-Acetoxy-4α-chloroandrost-5-en-17-one (**10**) and the isomeric 3β-acetoxy-6α-chloroandrost-4-en-17-one (**17**) were minor products. The structure and stereochemistry of the latter followed from ^{1}H n.m.r. studies. Irradiation of the alkene proton (4-H) resonance at δ 5.90 removed 2 Hz couplings from the signals at δ 4.61 (6-H) and 5.31 (3-H). Analysis of the signal at δ 5.31 (3-H) revealed a 10 Hz (axial–axial) and a 6 Hz (axial–equatorial) coupling together with the vicinal 2 Hz coupling to 4-H and a further long-range coupling (2 Hz) to 6-H. Irradiation of the δ 5.31 signal confirmed the 2 Hz couplings and affected multiplets at δ 1.6 and 2.1 within the methylene envelope. Analysis of the signal at δ 4.61 (6-H) showed that it comprised a 13 Hz (axial–axial) and 4.5 Hz (axial–equatorial) coupling as well as two



Scheme.



(16) **(17)**

smaller 2 Hz couplings to 3-H and 4-H. This resonance showed a nuclear Overhauser enhancement of 10% on irradiation of the C-10β methyl resonance (δ 1.12) and hence the C-6 chlorine atom must be an 'α' substituent. The formation of this 6α-chloro compound contrasts with the reaction with thionyl chloride which, in the cholestane series, affords[19] the 6β-chloride possibly through a cyclic process. In the case of the triphenylphosphine–carbon tetrachloride reaction, it is possible that inversion occurs first to afford the 4α-chloro-5-ene and this then undergoes rearrangement.

In conclusion we have shown that the reaction of steroidal alcohols with triphenylphosphine–carbon tetrachloride may be accompanied by neighbouring group participation of acetoxy, allylic, and homoallylic double bonds indicative of a substantial ionic character in the halogenation reaction.

Experimental

Light petroleum refers to the fraction, b.p. 60—80 °C, silica for chromatography was Merck 9385. Extracts were dried over sodium sulphate. ^{1}H n.m.r. spectra were determined on a Bruker WH 360 spectrometer for solutions in $CDCl_3$; i.r. spectra were recorded as Nujol mulls.

Reaction of Triphenylphosphine–Carbon Tetrachloride and Dehydroisoandrosterone.—(*a*) A solution of dehydroisoandrosterone (5 g) and triphenylphosphine (10 g; freshly recrystallized from light petroleum) in dry pyridine (5 ml) and carbon tetrachloride (100 ml) was heated under reflux for 5 h. The solution was cooled and decanted from a brown residue. The latter was taken up in chloroform and both solutions were then combined and washed with dilute hydrochloric acid, aqueous sodium hydrogen carbonate, and water, and then dried. The solvent was evaporated to give a brown residue which was

Table 1. Fractional atomic co-ordinates ($\times 10^4$) with estimated standard deviations in parentheses

	x	*y*	*z*
Cl	7 536(4)	89(2)	4 040(1)
O(1)	8 081(11)	5 255(5)	7 387(3)
O(2)	6 987(7)	−1 486(4)	5 701(2)
O(3)	6 571(15)	−3 128(6)	6 083(5)
C(1)	5 264(11)	1 016(6)	5 253(4)
C(2)	4 757(11)	−2(6)	4 913(4)
C(3)	6 386(13)	−585(6)	4 696(4)
C(4)	7 768(11)	−720(6)	5 254(4)
C(5)	8 056(10)	241(5)	5 660(4)
C(6)	9 735(10)	483(6)	5 791(3)
C(7)	10 308(11)	1 368(6)	6 182(4)
C(8)	8 727(10)	1 847(5)	6 548(4)
C(9)	7 161(10)	1 944(5)	6 068(4)
C(10)	6 475(10)	890(5)	5 865(4)
C(11)	5 659(11)	2 618(6)	6 358(5)
C(12)	6 262(12)	3 644(6)	6 618(5)
C(13)	7 719(13)	3 497(6)	7 119(4)
C(14)	9 277(12)	2 935(6)	6 797(4)
C(15)	10 801(13)	3 029(7)	7 286(4)
C(16)	10 550(16)	4 113(8)	7 533(4)
C(17)	8 723(13)	4 392(7)	7 358(4)
C(18)	7 030(16)	2 954(7)	7 769(5)
C(19)	5 487(11)	368(6)	6 424(4)
C(20)	7 400(15)	−2 442(5)	5 556(5)
C(21)	8 077(13)	−2 705(5)	5 047(4)

chromatographed on silica. Elution with 3% ethyl acetate–light petroleum gave 3α,5-cycloandrost-6-en-17-one (**13**) (1.6 g) which was recrystallized from acetone as plates, m.p. 138—140 °C (lit.,[8] 136—137 °C), δ 0.48 (1 H, m, 4-H), 0.95 (6 H, s, 18-H_3 and 19-H_3), 5.25 (1 H, dd, *J* 2 and 10 Hz, 7-H), and 5.62 (1 H, dd, *J* 1 and 10 Hz, 6-H). Further elution gave *3α-chloroandrost-5-en-17-one* (**2**) (2.5 g) which was recrystallized from acetone as plates, m.p. 161—164 °C, $[\alpha]_D^{20}$ − 6° (c, 0.3 in $CHCl_3$) (Found: C, 74.4; H, 8.9. $C_{19}H_{27}ClO$ requires C, 74.4; H, 8.9%); $\nu_{max.}$ 1 740 cm^{-1}; δ 0.90 (3 H, s, 18-H_3), 1.05 (3 H, s, 19-H_3), 4.45 (1 H, t, *J* 3.0 Hz, 3-H), and 5.42 (1 H, m, 6-H). Further elution gave 3α,5-cyclo-20,20-dichloroandrost-6-ene as a gum, *m/z* 336 ($C_{20}H_{26}{}^{35}Cl_2$, M^+), 321 ($M^+ - 15$), and 301 ($M^+ - 35$); $\nu_{max.}$ 1 640 and 725 cm^{-1}; δ (90 MHz) 0.45 (1 H, m, 4-H), 0.9 (3 H, s, 18-H_3), 1.07 (3 H, s, 19-H_3), 5.17 (1 H, dd, *J* 2 and 10 Hz, 7-H), and 5.49 (1 H, dd, *J* 1 and 10 Hz, 6-H). 3β-20,20-*Trichloroandrost-5-ene* (**5**) (230 mg) crystallized from acetone as needles, m.p. 167—170 °C (Found: C, 64.6; H, 7.4. $C_{20}H_{27}Cl_3$ requires C, 64.3; H, 7.3%); *m/z* 372 ($C_{20}H_{27}{}^{35}Cl_3$); $\nu_{max.}$ 1 630 and 885 cm^{-1}; δ 0.94 (3 H, s, 18-H_3), 1.03 (3 H, s, 19-H), 3.76 (1 H, t of dd, J_t 9.5, J_d, 4.8 Hz, 3-H), and 5.37 (1 H, ddd, *J* 2.0, 2.0 and 5.3 Hz, (6-H). 3α,20,20-*Trichloroandrost-5-ene* (**4**) (115 mg) crystallized from acetone as needles, m.p. 155—158 °C (Found: C, 64.8; H, 7.2. $C_{20}H_{27}{}^{35}Cl_3$ requires C, 64.3; H, 7.2%); *m/z* 372 ($C_{20}H_{27}{}^{35}Cl_3$); $\nu_{max.}$ 1 625 and 875 cm^{-1}; δ 0.97 (3 H, s, 18-H_3), 1.0 (3 H, s, 19-H_3), 4.54 (1 H, quintet, *J* 3.0 Hz, 3-H), 5.43 (1 H, ddd, *J* 2.0, 2.5 and 5.3 Hz, 6-H). In the absence of pyridine the dichloromethylene derivatives were not detected, but on occasions, 3β-chloroandrost-5-en-17-one (**3**), m.p. 155—157 °C (lit.,[9] 155—157 °C), identified from its n.m.r. spectrum, was obtained in variable amounts.

(*b*) Dehydroisoandrosterone (3 g) in hexachloroacetone (15 ml) and triphenylphosphine (3.5 g) was stirred at room temperature for 4 h, (t.l.c. monitoring). The solution was diluted with water and the steroid was recovered in ethyl acetate. The extract was washed consecutively with aqueous sodium hydroxide, dilute hydrochloric acid, aqueous sodium hydrogen carbonate, and water, and then dried. The solvent was evaporated and the residue was chromatographed on silica to give 3α,5-cycloandrost-6-en-17-one (**13**) (500 mg) and 3β-chloroandrost-5-en-17-one (2 g) (**3**) which crystallized from ethyl acetate–light petroleum as flakes, m.p. 149—154 °C (lit.,[9] 155—157 °C), δ (90 MHz) 0.92 (3 H, s, 18-H_3), 1.10 (3 H, s, 19-H_3), 3.72 (1 H, m, *w*/2 20 Hz, 3-H), and 5.44 (1 H, d, *J* 6 Hz, 6-H).

(*c*) Dehydroisoandrosterone (2 g) in carbon tetrachloride (10 ml) and acetonitrile (10 ml) was treated with triphenylphosphine (3 g) and imidazole (2 g) and warmed to 50 °C for 4.5 h. The solution was cooled, diluted with water, and the steroids were recovered in dichloromethane. The extract was washed with dilute hydrochloric acid, aqueous sodium hydrogen carbonate, and water and then dried. The solvent was evaporated and the residue was chromatographed on silica to give 3α,5-cycloandrost-6-en-17-one (**13**) (250 mg) and 3β-chloroandrost-5-en-17-one (**3**) (610 mg), identified from their n.m.r. and i.r. spectra.

Reaction of 6β-*Hydroxy*-3α,5-*cycloandrostan*-17-*one*.—The steroid (500 mg) in carbon tetrachloride (10 ml) was heated with triphenylphosphine (1 g) and pyridine (0.5 ml) under reflux for 30 h. The mixture was cooled, diluted with chloroform, and the extract was washed with dilute hydrochloric acid, aqueous sodium hydrogen carbonate, and water, and then dried. The solvent was evaporated to give a gum which

Table 2. Intramolecular distances (Å) and angles (°) with estimated standard deviations in parentheses

(*a*) Bonds

Cl–C(3)	1.812(7)	O(1)–C(7)	1.239(8)
O(2)–C(4)	1.474(6)	O(2)–C(20)	1.333(7)
O(3)–C(20)	1.527(9)	C(1)–C(2)	1.556(8)
C(1)–C(10)	1.540(8)	C(2)–C(3)	1.513(9)
C(3)–C(4)	1.542(8)	C(4)–C(5)	1.524(8)
C(5)–C(6)	1.332(8)	C(5)–C(10)	1.524(8)
C(6)–C(7)	1.473(8)	C(7)–C(8)	1.537(8)
C(8)–C(9)	1.530(8)	C(8)–C(14)	1.576(8)
C(9)–C(10)	1.540(7)	C(9)–C(11)	1.554(8)
C(10)–C(19)	1.514(8)	C(11)–C(12)	1.521(9)
C(12)–C(13)	1.503(10)	C(13)–C(14)	1.533(9)
C(13)–C(17)	1.484(10)	C(13)–C(18)	1.579(9)
C(14)–C(15)	1.516(9)	C(15)–C(16)	1.528(10)
C(16)–C(17)	1.468(11)	C(20)–C(21)	1.194(9)

(*b*) Angles

C(4)–O(2)–C(20)	115.1(5)	C(2)–C(1)–C(10)	113.8(5)
C(1)–C(2)–C(3)	111.5(5)	Cl–C(3)–C(2)	110.4(4)
Cl–C(3)–C(4)	105.2(4)	C(2)–C(3)–C(4)	113.4(5)
O(2)–C(4)–C(3)	104.6(5)	O(2)–C(4)–C(5)	107.6(4)
C(3)–C(4)–C(5)	113.0(5)	C(4)–C(5)–C(6)	116.2(5)
C(4)–C(5)–C(10)	120.0(5)	C(6)–C(5)–C(10)	123.7(5)
C(5)–C(6)–C(7)	125.1(5)	C(6)–C(7)–C(8)	110.7(5)
C(7)–C(8)–C(9)	109.3(4)	C(7)–C(8)–C(14)	108.8(4)
C(9)–C(8)–C(14)	109.1(4)	C(8)–C(9)–C(10)	110.5(4)
C(8)–C(9)–C(11)	111.9(5)	C(10)–C(9)–C(11)	111.8(5)
C(1)–C(10)–C(5)	108.0(5)	C(1)–C(10)–C(9)	108.2(4)
C(1)–C(10)–C(19)	110.5(5)	C(5)–C(10)–C(9)	108.5(5)
C(5)–C(10)–C(19)	109.2(4)	C(9)–C(10)–C(19)	112.4(5)
C(9)–C(11)–C(12)	114.9(5)	C(11)–C(12)–C(13)	109.5(6)
C(12)–C(13)–C(14)	109.9(5)	C(12)–C(13)–C(17)	119.1(6)
C(12)–C(13)–C(18)	111.9(6)	C(14)–C(13)–C(17)	97.6(6)
C(14)–C(13)–C(18)	112.5(6)	C(17)–C(13)–C(18)	105.1(6)
C(8)–C(14)–C(13)	111.9(5)	C(8)–C(14)–C(15)	118.7(5)
C(13)–C(14)–C(15)	105.5(5)	C(14)–C(15)–C(16)	101.2(6)
C(15)–C(16)–C(17)	105.9(7)	O(1)–C(17)–C(13)	123.3(8)
O(1)–C(17)–C(16)	125.8(8)	C(13)–C(17)–C(16)	110.9(7)
O(2)–C(20)–O(3)	108.4(7)	O(2)–C(20)–C(21)	124.2(7)
O(3)–C(20)–C(21)	126.6(6)		

was chromatographed on silica to afford a 3α,5-cycloandrost-6-en-17-one (**13**) (330 mg) and 3β-chloroandrost-5-en-17-one (**3**) (100 mg), identified from their ^{1}H n.m.r. spectra.

Reaction of 3β-*Acetoxy*-4β-*hydroxyandrost*-5-*en*-17-*one*.—The steroid (600 mg) in carbon tetrachloride (3 ml) and acetonitrile (3 ml) containing triphenylphosphine (900 mg) and imidazole (600 mg) was stirred at 45—50 °C for 4 h. The mixture was cooled and diluted with water and the products were recovered in dichloromethane. The extract was washed with dilute hydrochloric acid, aqueous sodium hydrogen carbonate, and water, and then dried (Na_2SO_4). The solvent was evaporated to give a brown solid which was chromatographed on silica. Elution with 10% ethyl acetate–light petroleum gave 3β-*acetoxyandrosta*-4,6-*dien*-17-*one* (**16**) (220 mg) which crystallized from methanol as needles, m.p. 149—152 °C (Found: C, 76.7; H, 8.8. $C_{21}H_{28}O_3$ requires C, 76.8; H, 8.5%); $\nu_{max.}$ 1 740 and 1 725 cm^{-1}; δ 0.94 (3 H, s, 18-H), 1.03 (3 H, s, 19-H_3), 2.03 (3 H, s, OAc), 5.43 (2 H, m, 3-H and 4-H), 5.71 (1 H, dd, *J* 1.6 and 9.8 Hz, 6-H), and 6.0 (1 H, dd, *J* 2.7 and 9.8 Hz, 7-H). Further elution gave 3β-*acetoxy*-4α-*chloroandrost*-5-*en*-17-*one* (**10**) (75 mg) which was recrystallized from ethyl acetate–light petroleum as needles, m.p. 146—151 °C (Found: C, 68.4; H, 8.15. $C_{21}H_{29}ClO_3$ requires C, 69.1; H, 8.0%); $\nu_{max.}$ 1 740 cm^{-1}; δ 0.89 (3 H, s, 18-H_3), 1.08 (3 H, s, 19-H_3), 2.11 (3 H, s, OAc), 4.64 (1 H, ddd, *J* 10.8, 2.0, and 2.0, 4-H), 4.71 (1 H, td, *J* 10.8 Hz, J_d 4.9 Hz, 3-H), and 6.17 (1 H, ddt, J_t 2.0 Hz, J_d 2.2, 5.5 Hz, 6-H). Elution with 15% ethyl acetate–light petroleum gave 3β-*acetoxy*-6α-*chloroandrost*-4-*en*-17-*one* (**17**) (75 mg), m.p. 118—121 °C (Found: C, 68.5; H, 8.15. $C_{21}H_{29}ClO_3$ requires C, 69.1; H, 8.0%); $\nu_{max.}$ 1 735 cm^{-1}; δ 0.89 (3 H, s, 18-H_3), 1.12 (3 H, s, 19-H_3), 2.07 (3 H, s, OAc), 4.61 (1 H, ddt, J_d 13.0 and 4.5 Hz, J_t 2.2 Hz, 6-H), 5.31 (1 H, d, *J* 9.9 Hz, d, *J* 5.9 Hz, dd, *J* 2.2 Hz, 3-H), and 5.90 (1 H, dd, *J* 2.2 Hz, 4-H).

Reaction of 4β-*Acetoxy*-3β-*hydroxyandrost*-5-*en*-17-*one*.—A solution of the steroid (600 mg) in carbon tetrachloride (20 ml) containing triphenyl phosphine (1 g) was heated under reflux for 5 h. The solution was cooled, the solvent was evaporated, and the residue was chromatographed on silica. The first fractions to be eluted were intractable mixtures. Elution with 5% ethyl acetate–light petroleum gave 3β-acetoxy-4α-chloroandrost-5-en-17-one (**10**) (120 mg) which crystallized from ethyl acetate as needles, m.p. 147—151 °C, identified from its ^{1}H n.m.r. spectrum. On one occasion the steroid (1 g) and triphenylphosphine (2 g) in carbon tetrachloride (20 ml) and pyridine (1 ml) (3h reflux) gave, after extensive chromatography, 4β-*acetoxy*-3α-*chloroandrost*-5-*en*-17-*one* (**9**) (210 mg) which crystallized from acetone as prisms, m.p. 154—156 °C, $[\alpha]_D^{20}$ −99 ° (*c* 0.3, $CHCl_3$) (Found: C, 69.1; H, 8.1. $C_{21}H_{29}ClO_3$ requires C, 69.1; H, 8.0%); $\nu_{max.}$ 1 745 cm^{-1}; δ 0.89 (3 H, s, 18-H_3), 1.15 (3 H, s, 19-H_3), 2.05 (3 H, s, OAc), 4.23 (1 H, q, *J* 2.5 Hz, 3-H), 5.27 (1 H, s, 4-H), and 5.88 (1 H, dd, *J* 2.2 and 2.5 Hz, 6-H).

Crystal Structure Determination.—*Crystal data*. $C_{21}H_{29}ClO_3$, *M* = 364.9, orthorhombic, *a* = 7.539(2), *b* = 13.203(2), *c* = 20.096(5) Å, *U* = 2 000.3 Å^3 *Z* = 4, D_c = 1.21 g cm^{-3}, space group $P2_12_12_1$, monochromated Mo-K_α radiation λ = 0.710 69 Å, μ 2.1 cm^{-1}.

Data were measured on an Enraf–Nonius CAD4 diffractometer using a crystal of size *ca.* 0.2 × 0.2 × 0.2 mm. Intensities for *h*,*k*,*l* reflections with $2 < \theta < 23°$ were measured with a θ/2θ scan with a maximum scan time of 120 s. Data were corrected for Lp effects but not for absorption and 932 reflections with $|F^2| > \sigma(F^2)$ were used in the structure refinement, where $\sigma(F^2) = [\sigma^2(I) + (0.02\ I)]^{\frac{1}{2}}/\mathrm{Lp}$. The structure was solved using MULTAN. Refinement of non-hydrogen atoms with anisotropic temperature factors was by full matrix least squares. Hydrogen atoms except for those on C(21) were included at calculated positions (C–H 1.08 Å) and held fixed with a common temperature factor of $B = 6.0$ Å^2. Refinement converged at $R = 0.058$, $R' = 0.065$ when the maximum shift/error was 0.01 and the weighting scheme was $\omega = 1/\sigma^2(F)$. A final difference map was everywhere featureless. All calculations were done on a PDP11/34 computer using the Enraf–Nonius structure determination package. Final atomic co-ordinates, intramolecular distances, and angles are given in Tables 1 and 2. Torsion angles, anisotropic temperature factors, and hydrogen atom co-ordinates are available on request from the Cambridge Crystallographic Data Centre.*

* For details of the data deposition scheme, see Instructions for Authors (1988), *J. Chem. Soc. Perkin Trans. 1*, 1988, issue 1, paragraph 5.6.3.

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