A Mild Method for the Conversion of 1,3-Glycols into Unsaturated Alcohols

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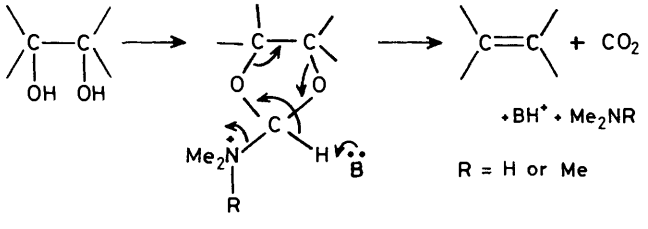
Some transformations of 1,3-glycols utilizing dimethylformamide dimethyl acetal have been examined with the diterpenoids aphidicolin and foliol and some steroids as substrates. Axial alcohols with a suitably disposed *trans* hydrogen atom undergo an elimination reaction to give the formate of an unsaturated alcohol *via* the quaternary salt of the cyclic formamido acetal.

N,N-Dimethylformamide dimethyl acetal (DMFDMA) has proved[1] to be a useful reagent for the activation of alcohols and vicinal glycols through the formation of *N,N*-dimethylformamido acetals. Decomposition of the derivatives obtained from vicinal glycols may afford either epoxides[2] or alkenes,[3] depending upon the conditions and the stereochemistry of the original glycol. For example an alkene is formed when the 1,3-dioxolane obtained by the reaction of a 1,2-diol with DMFDMA is heated with acetic anhydride.[3] A plausible mechanism involves the protonation of the dimethylamino group followed by an elimination to generate the alkene (see Scheme 1) although a carbene alternative has also be considered. In a modification[4] of this reaction sequence, the dimethylamino group of the intermediate acetal (**1**) was quaternized with methyl iodide in toluene and then heated to promote elimination.

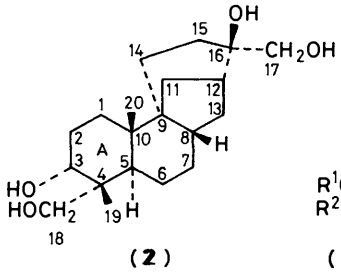


(**1**)

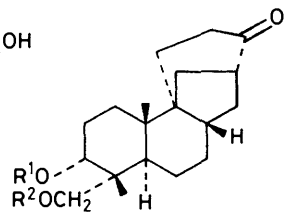
Scheme 1.

Although these reactions have been examined in the context of sugar chemistry,[5] their utility has not been exploited in the case of 1,3-glycols. In this paper we describe some reactions of 1,3-glycols of differing stereochemistry with DMFDMA which lead to a potentially useful elimination reaction.

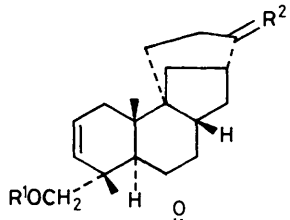
In the course of biosynthetic studies[6] on the diterpenoid inhibitor of DNA polymerase α, aphidicolin (**2**),[7] we required mild routes for the selective removal of the hydroxy groups. This molecule is prone to undergo both rearrangement and cyclic ether formation reactions. Since it possesses both a 1,2- and a 1,3-glycol, it proved to be a useful substrate with which to explore the potential of the dimethylamino acetal system. The reactions of the 1,3-glycol on ring A were examined first. Treatment of 3α,18-dihydroxy-17-noraphidicolan-16-one (**3**)[7] with refluxing DMFDMA for 30 min followed by reaction with acetic anhydride gave 3α-acetoxy-18-formyloxy-17-noraphidicolan-16-one (**4**) together with 18-formyloxy-17-noraphidicol-2-en-16-one (**6**). Addition of sodium acetate to the medium increased the yield of the acetate. Hydrolysis of the latter gave the parent 3α,18-diol (**3**), showing that no inversion had occurred at C-3. The position of the esters in compound (**4**)



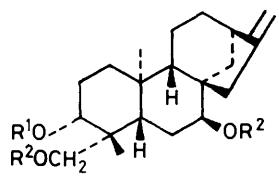
(**2**)



(**3**) $R^1 = R^2 = H$
(**4**) $R^1 = Ac, R^2 = HC(=O)$
(**5**) $R^1 = H, R^2 = HC(=O)$



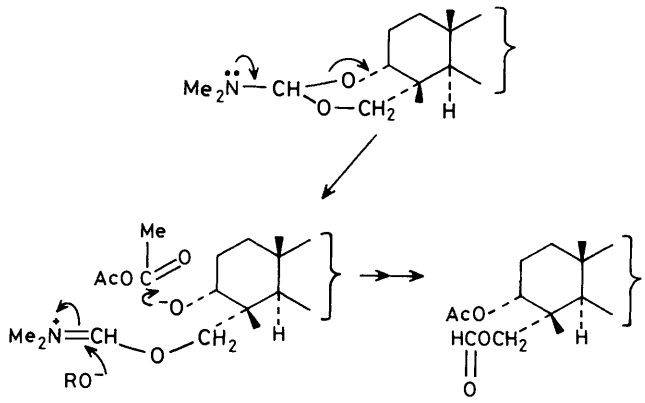
(**6**) $R^1 = HC(=O), R^2 = O$
(**7**) $R^1 = H, R^2 = O$
(**8**) $R^1 = HC(=O), R^2 = CH_2$



(**9**) $R^1 = R^2 = H$
(**10**) $R^1 = H, R^2 = HC(=O)$

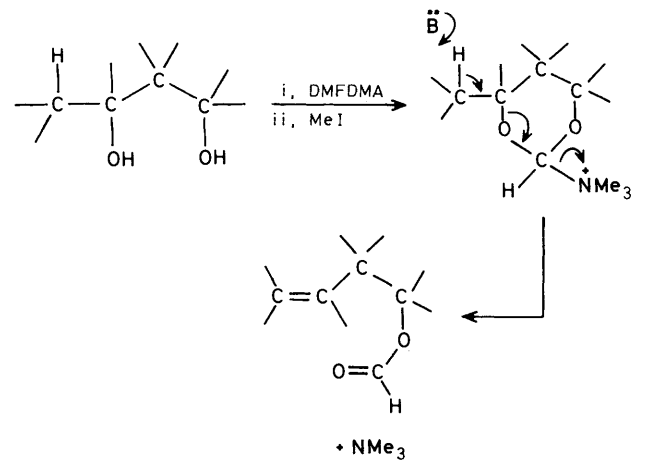
was confirmed by acetylation of the 18-monoformate (**5**). The formation of the 3α-monoacetate (**4**) with retention of configuration is surprising in view of the known propensity of esterification *via* dimethylformamide acetals to proceed with inversion of configuration.[1] A possible explanation, which is in accord with the isolation of the 18-formate, is that the reaction proceeds *via* a cyclic mechanism (see Scheme 2).

In contrast to the effect of sodium acetate, formation of the dimethylaminoacetal from (**3**), followed by quaternization with methyl iodide and decomposition of the salt in refluxing toluene, led to an enhanced yield (60%) of 18-formyloxy-17-noraphidicol-2-en-16-one (**6**). On occasions this was accompanied by the 18-monoformate (δ 3.5, 3-H; 3.92, 18-H; and 8.10, OCHO) (**5**). Hydrolysis of compound (**6**) readily gave the corresponding alcohol (**7**).[6] Aphidicolin (**2**) itself gave an unstable bisdimethylamino acetal [M^+ 448; δ 2.33, 2.36 (each 3 H) and 2.43 (6 H), (2 × NMe_2), 5.42 and 5.52 ()]. Attempts to isolate this in a pure state were unsuccessful.



Scheme 2.

However, quaternization with methyl iodide and heating the methiodide in refluxing toluene gave 18-formyloxyaphidicola-2,16-diene (**8**) [δ 3.92 (2 H, m, CH_2O); 4.48 (2 H, m, 17-H); 5.2 and 5.7 (each 1 H, 2- and 3-H); 8.02 (1 H, s, OCHO)]. Although the yield (24%) was not very high, this provided a mild means of removing three of the four hydroxy groups of aphidicolin in one pot and avoided rearrangements and the generation of double-bond isomers at C-16.

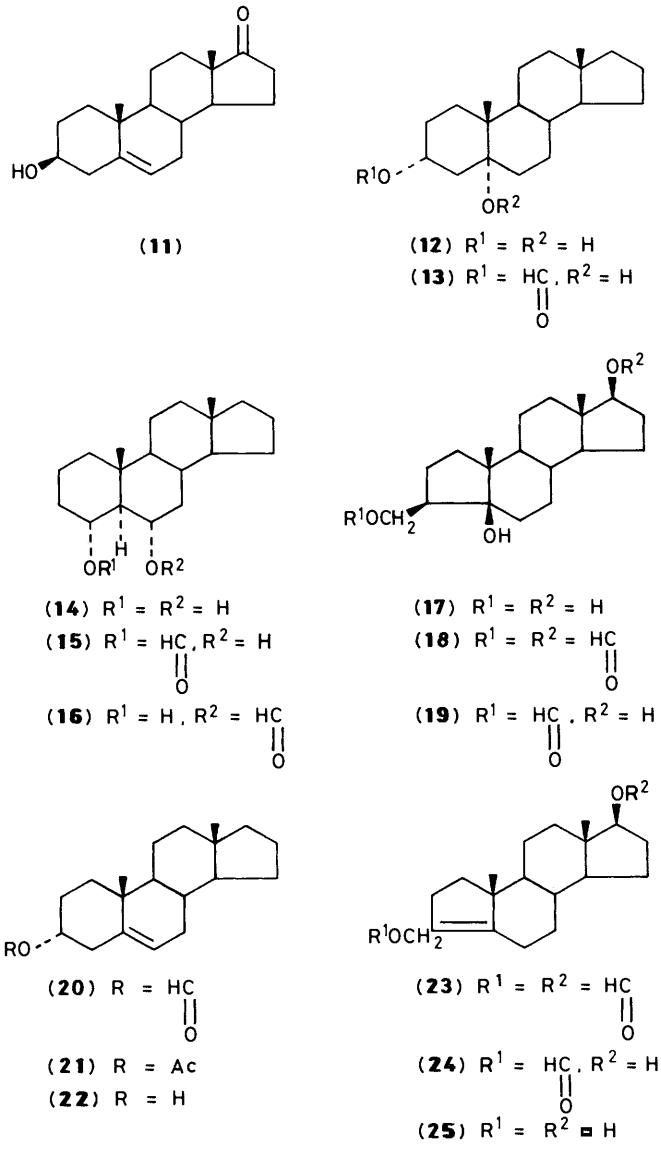


Scheme 3.

This elimination reaction may be formulated (see Scheme 3) as a fragmentation of the intermediate quaternary salt. There are stereochemical implications of this mechanism in terms of the relationship between the hydrogen atom that is eliminated and the cyclic acetal.

Foliol (**9**)[8] resembles aphidicolin in possessing an equatorial C-4 hydroxymethyl substituent. However, the C-3 alcohol is an equatorial rather than an axial substituent on ring A and there is thus no suitably oriented hydrogen atom for elimination. The isolated alcohol at C-7 is axial. Reaction of foliol (**9**) with DMFDMA and then methyl iodide in toluene, and then heating the quaternary salt gave the 7,18-diformate (**10**). There was no detectable elimination product.

The stereochemical requirements for the elimination reaction were examined in more detail in the steroid series. Dehydroisoandrosterone (3β-hydroxyandrost-5-en-17-one) (**11**) was converted into the diaxial 3α,5α-dihydroxyandrostane (**12**),[9] and *via* hydroboration of the 3,5-diene[10] to the diequatorial 4α,6α-dihydroxy-5α-androstane (**14**). Dehydroisoandrosterone (**11**) was also converted *via* the 4β-acetate-3β-toluene-*p*-sulphonate[11] into 5β,17β-dihydroxy-3β-hydroxymethyl-A-norandrostane (**17**). In this compound, although there is a *trans* diaxial relationship between the 5β-hydroxy group and a hydrogen atom at C-3, the 5β-hydroxy group is an equatorial substituent with respect to ring B.



Reaction of the diaxial 3α,5α-dihydroxyandrostane (**12**) with DMFDMA, followed by quaternization with methyl iodide and heating, gave 3α-formyloxyandrost-5-ene (**20**) (62%) and 3α-formyloxy-5α-hydroxyandrostane (**13**) (25%). The ^1H n.m.r. spectrum of compound (**20**) contained a one-proton singlet at δ 8.05 and one-proton resonances at δ 5.34 and 5.17 which were identical in their multiplicity with those of the corresponding acetate (**21**). Hydrolysis of the formate gave the known mono-ol (**22**).[9] The ^1H n.m.r. spectrum of the minor product (**13**) showed a one-proton formyloxy signal at δ 8.06 and a resonance at δ 5.35 assigned to 3-H. An interesting feature of this spectrum was a long-range (1 Hz) coupling between the formate proton and a proton resonance at δ 1.91 (*J* 1, 4, and 16 Hz) which was assigned to 4-H. Coupling across oxygen is relatively rare. Hydrolysis of the monoformate (**13**) with methanolic sodium hydroxide gave the starting diol (**12**).

In contrast the diequatorial diol, 4α,6α-dihydroxy-5α-androstane (**14**), gave an inseparable mixture of the 4α- and 6α-

monoformates (**15**) and (**16**). The 4-H and 6-H n.m.r. signals appeared as two sets of overlapping sextets, δ 3.72 and 3.78 (dt, *J* 5, 10, and 10 Hz) (C*H*OH) and 5.12 and 5.18 (dt, *J* 5, 10, and 10 Hz) (CHOCHO). Hydrolysis with methanolic sodium hydroxide regenerated the 4α,6α-diol (**14**). Hence for elimination to occur, it would appear that at least one of the hydroxy groups must be axial.

The steric relationship of the proton that is eliminated to the departing hydroxy group was examined with 5β,17β-dihydroxy-3β-hydroxymethyl-A-norandrostane (**17**). This gave a mixture of products which were partially separated chromatographically. The least polar product was 17β-formyloxy-3-formyloxymethyl-A-norandrost-3(5)-ene (**23**) (7% yield). Its ^{1}H n.m.r. spectrum contained two OCHO resonances (δ 8.07 and 8.08) and an overlapping CHOCHO and CH_2OCHO signal (δ 4.69), whilst the ^{13}C n.m.r. spectrum contained two quaternary olefinic resonances (δ_C 122 and 125). The product was identical with an authentic sample prepared by formylation of 17β-hydroxy-3-hydroxymethyl-A-norandrost-3(5)-ene (**25**).

A mixture of 3-formyloxy-17β-hydroxy-A-norandrost-3(5)-ene (**24**) (17%) and 17β-formyloxy-3β-formyloxymethyl-5β-hydroxy-A-norandrostane (**18**) (24%) was eluted next. The location of the ester groupings was established by the ^{1}H n.m.r. spectrum of the mixture. Hydrolysis of the mixture gave 17β-hydroxy-3-hydroxymethyl-A-norandrost-3(5)-ene (**25**)[11] and 5β,17β-dihydroxy-3β-hydroxymethyl-A-norandrostane (**17**) which were readily separated. The most polar product was 3β-formyloxymethyl-5β,17β-dihydroxy-A-norandrostane (**19**) (31%). The ^{1}H n.m.r. spectrum showed a single-proton triplet (δ 3.61, *J* 8 Hz) which was assigned to the 17-C*H*(OH) and a two-proton ABX system at δ 4.42 and 4.73 (*J* 7 and 12 Hz) assigned to the methylene protons of the 3β-formyloxymethyl group. The OCHO signal appeared at δ 8.0. The $\Delta^{3(5)}$ olefinic products that were formed in this case reveal the importance of the steric relationship between the hydrogen atom that is eliminated and the carbon–oxygen bond that is broken.

In conclusion we have shown that fragmentation of the quaternary salts of the dimethylformamide acetals of 1,3-glycols can afford a mild method of preparing unsaturated alcohols provided that there is a suitably juxtaposed proton possessing a *trans* diaxial relationship to the departing C–O bond.

Experimental

Dimethylformamide dimethyl acetal (DMFDMA) was carefully redistilled prior to use. Column chromatography was carried out on silica (Merck 9385) under slight positive pressure. Light petroleum refers to the fraction b.p. 60—80 °C. I.r. spectra refer to Nujol mulls, ^{1}H n.m.r. spectra were determined at 360 MHz in deuteriochloroform on a Bruker WH 360 spectrometer, and at 90 MHz on a Perkin-Elmer R32 spectrometer.

Reaction of 3α,18-*Dihydroxy*-17-*noraphidicolan*-16-*one* (**3**) *with DMFDMA*.—(*a*) The ketone (**3**) (120 mg) was heated in DMFDMA (5 ml) under reflux for 30 min under nitrogen. The solvent was evaporated off under reduced pressure and acetic anhydride (5 ml) was added. The mixture was heated under reflux for 3 days under nitrogen, cooled, and diluted with chloroform (10 ml). The solution was then washed successively with dil. hydrochloric acid, saturated aqueous sodium hydrogen carbonate, and water, and was dried (Na_2SO_4). Evaporation of the solvent gave a gum, which was chromatographed on silica. Elution with 15% ethyl acetate–light petroleum gave 18-formyloxy-17-noraphidicol-2-en-16-one (**6**) (10 mg), m.p. 115—120 °C (lit.,[6] 120—123 °C), identified by its n.m.r. spectrum. Further elution with 25% ethyl acetate–light petroleum gave 3α-*acetoxy*-18-*formyloxy*-17-*noraphidicolan*-16-*one* (**4**) (107 mg), which crystallized from ethyl acetate–light petroleum as prisms, m.p. 157—159 °C (Found: C, 69.8; H, 8.45. $C_{22}H_{32}O_5$ requires C, 70.2; H, 8.6%); $\nu_{max.}$ 1 740 and 1 710 cm^{-1}; δ 1.05 (3 H, s, 20-H_3), 1.11 (3 H, s, 19-H_3), 2.00 (3 H, s, OAc), 3.92 (2 H, s, 18-H_2), 5.11 (1 H, m, 3-H), and 8.02 (1 H, s, OCHO); *m*/*z* 376 (M^+, 1%), 330 (5), 316 (3), 288 (7), 270 (35), and 257 (45).

(*b*) Repetition of the experiment by refluxing the ketone (**3**) (1 g) in DMFDMA (15 ml) for 30 min, followed by heating with acetic anhydride (20 ml) containing sodium acetate (250 mg) under reflux for 2 h, gave 3α-acetoxy-18-formyloxy-17-noraphidicolan-16-one (**4**) (900 mg). Hydrolysis of the 3α-acetate 18-formate (100 mg) in methanol (5 ml) containing potassium carbonate (74 mg) in water (2 ml) at room temperature for 2 h and recovery of the products in chloroform gave 3α,18-dihydroxy-17-noraphidicolan-16-one (**3**) (40 mg), m.p. 155—156 °C (lit.,[7] 155—156 °C), identified by its i.r. and n.m.r. spectra.

(*c*) The reaction with DMFDMA followed by treatment with methyl iodide in toluene is given in ref. 6.

Reaction of Aphidicolin (**2**) *with DMFDMA*.—(*a*) Aphidicolin (100 mg) was heated in DMFDMA (5 ml) under reflux for 2 days under nitrogen. Acetic anhydride (8 ml) was added and the mixture was heated under reflux for a further 3 days. The solvents were removed under reduced pressure and the brown residue was chromatographed on silica (deactivated with water 15% w/w). Elution with toluene gave 18-*formyloxyaphidicola*-2,16-*diene* (22 mg) as a white powder, m.p. 89—92 °C (Found: C, 79.8; H, 10.0. $C_{21}H_{30}O_2$ requires C, 80.2; H, 9.6%); $\nu_{max.}$ 3 070, 1 735, 1 660, 1 650, 885, and 720 cm^{-1}; δ 1.00 and 1.03 (each 3 H, s, 20- and 19-H_3), 3.92 (2 H, s, 18-H), 4.48 (2 H, m, 17-H), 5.2 and 5.7 (each 1 H, m, 2- and 3-H), and 8.02 (1 H, s, OCHO).

(*b*) Aphidicolin (300 mg) was heated in DMFDMA (15 ml) under reflux under nitrogen for 30 min. The reagent was removed under reduced pressure to yield a gum, which showed ^{1}H n.m.r. signals at δ 0.7 (3 H, s, 20-H_3), 1.00 (3 H, s, 19-H_3), 2.33 and 2.36 (each 3 H, s, NMe_2), 2.43 (6 H, s, 2 × NMe_2), 3.00 and 3.95 (each 1 H, d, *J* 12 Hz, CH_2O), 3.37 and 3.70 (each 1 H, d, *J* 8.4 Hz, CH_2O), 4.85 (1 H, m, 3-H), and 5.42 and 5.52 (each 1 H, s, C*H*NMe_2); *m*/*z* 448 (M^+, 1%), 447 (M − H, 2), 433 (5), 418 (1), 404 (40), 359 (10), 331 (38), 285 (40), 142 (50), and 74 (100).

Chromatography of the remaining acetal (280 mg) on silica in toluene–ethyl acetate (1:1) gave a mixture of diformates, δ 1.0 (3 H, s, 20-H_3), 1.11 (3 H, s, 19-H_3), 3.4 (*ca.* 1 H, s, CH_2OH), 3.7 (*ca.* 0.7 H, m, 3-H), 4.14 (*ca.* 3 H, CH_2OCHO), 4.97 (*ca.* 0.3 H, m, 3-H), and 8.2 (2 H, s, OC*H*O). Hydrolysis of the mixture (182 mg) with 0.1M methanolic sodium hydroxide (1 ml) for 10 min and recovery of the product gave aphidicolin (**2**) (22 mg), m.p. 231—233 °C (lit.,[7] 227—233 °C), identified by its n.m.r. spectrum and by the formation of its isopropylidene derivative, m.p. 146—148 °C (lit.,[7] 145—147 °C).

Reaction of Foliol (**9**) *with DMFDMA*.—Foliol (110 mg) was heated in DMFDMA (6 ml) under reflux for 30 min. The reagent was removed under reduced pressure, and toluene (2 ml) and methyl iodide (1 ml) were added. The mixture was left at room temperature for 1 h. The product was chromatographed on silica to give a powder (74 mg), which was recrystallized from ethyl acetate to afford ent- 7α,18-*diformyloxy*-3β-*hydroxykaur*-16-*ene* (**10**) as white needles, m.p. 208—210 °C (Found: C, 69.8; H, 8.3. $C_{22}H_{32}O_5$ requires C, 70.2; H, 8.6%); $\nu_{max.}$ 3 500, 1 725, and 1 660 cm^{-1}; δ 0.8 (3 H, s, 20-H_3), 1.1 (3 H, s, 19-H_3), 3.45 (1 H, m, 3-H), 3.75 and 4.3 (2 H, d, *J* 11.5 Hz, 18-H_2), 4.8 (3 H, m, 7-H and 17-H_2), and 8.1 (2 H, s, 2 × OCHO).

Reaction of 3α,5α-*Dihydroxyandrostane* (**12**) *with DMFDMA*.—The steroid[9] (110 mg) was heated in DMFDMA under reflux for 1 h. The reagent was removed under reduced

pressure and the residue was treated with toluene (5 ml) and methyl iodide (1 ml) for 1 h. The solvent was evaporated off, fresh toluene (10 ml) was added, and the mixture was heated under reflux for 2 h. The solvent was then evaporated off, the mixture was taken up in chloroform, and the solution was washed successively with dil. hydrochloric acid, aqueous sodium hydrogen carbonate, and aqueous sodium chloride. The organic phase was dried and the solvent was evaporated off to give a gum (130 mg), which was chromatographed on silica. Elution with toluene gave 3α-*formyloxyandrost-5-ene* (**20**) (63 mg), m.p. 108—110 °C (Found: M^+, 304.226. $C_{20}H_{30}O_2$ requires M, 304.244); $\nu_{max.}$ 1 730 cm^{-1}; δ 0.72 (3 H, s, 18-H_3), 1.03 (3 H, s, 19-H_3), 5.17 and 5.34 (each 1 H, m, 3- and 6-H), and 8.05 (1 H, s, OCHO).

Further elution with toluene–ethyl acetate (9:1) gave 3α-*formyloxy-5α-hydroxyandrostane* (**13**) (28 mg), m.p. 119—122 °C (Found: C, 74.7; H, 9.9. $C_{20}H_{32}O_3$ requires C, 75.0; H, 10.0%); $\nu_{max.}$ 3 560, 3 450, and 1 725 cm^{-1}; δ 0.70 (3 H, s, 18-H), 0.97 (3 H, s, 19-H_3), 5.35 (1 H, m, 3-H), and 8.06 (1 H, s, OCHO); *m/z* (C.I., NH_3) 338 ($M^+ + NH_4$, 20%), 320 (15), 303 (45), and 257 (100).

Hydrolysis of the Formates.—(*a*) A solution of the formate (**20**) (10 mg) in methanol (10 ml) was treated with 3M sodium hydroxide (1 ml) for 15 min at room temperature. The solution was concentrated, and acidified with dil. hydrochloric acid, and the product was recovered in ether. The extract was washed with water, dried (Na_2SO_4), and evaporated to afford 3α-hydroxyandrost-5-ene (**22**), which crystallized from ether–hexane as needles, m.p. 134—136 °C (lit.,[9] 138—139 °C), identified by comparison of its i.r. spectrum with that of an authentic sample.

(*b*) A solution of the hydroxy formate (**13**) (20 mg) in methanol (5 ml) was treated with aqueous sodium hydroxide (10%; 0.5 ml) at room temperature for 2 h. The product was recovered as above in ether to afford 3α,5α-dihydroxyandrostane (**12**), which crystallized from ethyl acetate as needles, m.p. 171—172 °C (lit.,[9] 171—172 °C), identified by its i.r. spectrum.

Reaction of 4α,6α-*Dihydroxy-5α-androstane* (**14**) *with DMFDMA.*—The steroid (**14**)[12] (100 mg) was heated in DMFDMA (4 ml) under reflux under nitrogen for 1 h. The solvent was removed under reduced pressure to afford 4α,6α-*O*-[(dimethylamino)methylene]-5α-androstane as an amorphous white solid, δ 0.63 (3 H, s, 18-H_3), 0.83 (3 H, s, 19-H_3), 2.3 (6 H, s, NMe_2), and 5.33 (1 H, s, C*H*NMe_2). The solid was dissolved in toluene (5 ml) containing methyl iodide (1 ml) and the mixture was kept at room temperature for 30 min. The solvent was removed under reduced pressure and the residue was heated under reflux in fresh toluene (5 ml) for 2 h. The solvent was evaporated off, the residue was taken up in ethyl acetate, and the solution was washed successively with dil. hydrochloric acid, aqueous sodium hydrogen carbonate, aqueous sodium chloride, and then dried. The solvent was evaporated off and the residue was chromatographed on silica to afford a mixture of the 4α- and 6α-monoformates of 4α,6α-dihydroxy-5α-androstane [compounds (**15**) and (**16**) respectively] (95 mg), $\nu_{max.}$ 3 390 and 1 720 cm^{-1}; δ 0.62 (3 H, s, 18-H_3), 0.81 (3 H, s, 19-H_3), 3.72 and 3.78, and 5.12 and 5.18 (total 2 H, each doublet of triplets, *J* 5, 10, and 10 Hz), and 8.02 (1 H, s, OCHO). The mixture (50 mg) was dissolved in methanol (10 ml) and the solution was treated with 10% aqueous sodium hydroxide (6 drops) overnight. The solvent was evaporated off and the product was recovered in ethyl acetate to afford 4α,6α-dihydroxy-5α-androstane (**14**) (31 mg), m.p. and mixed m.p. 213—214 °C, identical (i.r.) with an authentic sample.[12]

Reaction of 5β-17β-*Dihydroxy*-3β-*hydroxymethyl*-A-*nor-androstane* (**17**) *with DMFDMA.*—The triol (**17**)[12] (120 mg) was heated in DMFDMA (8 ml) under reflux under nitrogen for 1 h. The reagent was evaporated off and the residual gum was treated with toluene (5 ml) containing methyl iodide (1 ml) for 1 h. The solvent was evaporated off, fresh toluene (10 ml) was added, and the solution was heated under reflux for 3 h. The solvent was evaporated off, the residue was taken up in ethyl acetate, and the solution was washed successively with dil. hydrochloric acid, aqueous sodium hydrogen carbonate, and water and dried. The solvent was evaporated off and the residue was chromatographed on silica. Elution with ethyl acetate–light petroleum (1:4) gave the diformate (**23**) of 17β-hydroxy-3-hydroxymethyl-A-norandrost-3(5)-ene (9 mg) as a waxy solid, $\nu_{max.}$ 1 731 and 1 722 cm^{-1}; δ 0.84 (3 H, s, 18-H_3), 0.95 (3 H, s, 19-H_3), 4.69 (1 H, t, *J* 9 Hz, 17-H), 4.64 and 4.75 (each 1 H, d, *J* 12 Hz, CH_2O), and 8.08 (2 H, s, OCHO); *m/z* 346 (10%), 331 (15), 300 (20), and 287 (100). The compound was identical (i.r. and n.m.r.) with the product of reaction of 17β-hydroxy-3β-hydroxymethyl-A-norandrost-3(5)-ene with acetic anhydride and formic acid.

Further elution gave a mixture of 3-formyloxymethyl-17β-hydroxy-A-norandrost-3(5)-ene (**24**) and 17β-formyloxy-3β-formyloxymethyl-5β-hydroxy-A-norandrostane (**18**) (56 mg), δ 0.77, 0.82, 0.91, and 0.95 (CMe signals), 3.61 [t, *J* 7 Hz, 17-H in (**24**)], 4.17 and 4.41 [m, CH_2O of (**18**)], and 4.66 [m, CH_2O of (**24**) and t, *J* 7 Hz, 17-H of (**18**)].

Further elution gave 3β-*formyloxymethyl*-5β,17β-*dihydroxy*-A-*norandrostane* (**19**) (38 mg), m.p. 138—139 °C (Found: C, 71.7; H, 9.2. $C_{20}H_{32}O_4$ requires C, 71.4; H, 9.6%); $\nu_{max.}$ 3 520, 3 400, and 1 715 cm^{-1}; δ 0.78 (3 H, s, 18-H_3), 0.92 (3 H, s, 19-H_3), 3.61 (1 H, t, *J* 8 Hz, 17-H), 4.17 and 4.41 (2 H, ABX double doublets, *J* 7 and 12 Hz, CHCH_2O), and 8.0 (1 H, s, OCHO).

Hydrolysis of the Mixed Formates (**18**) *and* (**24**).—The mixture (50 mg) was dissolved in methanol (10 ml) and the solution was treated with 10% aqueous sodium hydroxide (6 drops) at room temperature overnight. The products were recovered in ethyl acetate and chromatographed on silica to afford 17β-hydroxy-3-hydroxymethyl-A-norandrost-3(5)-ene (**25**) (15 mg), m.p. 175—177 °C (lit.,[11] 176—177 °C) and 5β,17β-dihydroxy-3β-hydroxymethyl-A-norandrostane (**17**) (27 mg), m.p. and mixed m.p. 189—191 °C, both identified by their i.r. and n.m.r. spectra.

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