BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 50 (1), 186—192 (1977)

A Reductive Elimination of Steroidal Diol Monoesters with Zinc Giving the Corresponding Olefins

Giichi Goto

Central Research Division, Takeda Chemical Industries, Ltd., Yodogawa-ku, Osaka 532

(Received June 5, 1976)

Steroidal *cis*-diol monoacetates (**1**, **9**, **11**, and **13**) were refluxed with zinc powder in acetic acid to give the corresponding olefins (**2**, **10**, **12**, and **14**) in good yield. Under the reaction conditions, no reaction occurred with diol diacetates (**1b**: $R_1=R_2=H$, $R_3=R_4=Ac$ and **1m**: $R_1=C_6H_5$, $R_2=H$, $R_3=R_4=Ac$) and *trans*-diol monoacetates (**15** and **16**). Acyclic erythro and threo diol monoacetates (**17** and **19**) underwent highly stereoselective reduction affording **18** and **20**, respectively. The olefin-forming elimination proceeded with *syn*-elimination of a cyclic orthoacetate intermediate (**21**). The effect of some metals on the reduction and the behavior of a number of esters (**26**) and orthoesters (**27**) were also investigated.

In connection with mechanistic studies on the Serini reaction,[1,2] the addition of a catalytic amount of acetic acid accelerate was reported to the Serini rearrangement.[2] During the course of an investigation of the effect of acetic acid on the rearrangement, it was found that increase in the amount of acetic acid resulted in the formation of olefinic products. Thus, treatment of 16,-17-dihydroxy steroid monoacetates (**1**) with zinc powder in toluene in the presence of an excess acetic acid at 130 °C for 8 h gave the olefinic compounds (**2**) as a major product and a trace of the Serini rearrangement products (**3**). The finding has led to an investigation of the reductive elimination of diol monoesters to olefins. This paper describes the scope of this new reaction using a variety of steroidal diol monoesters.

Results and Discussion

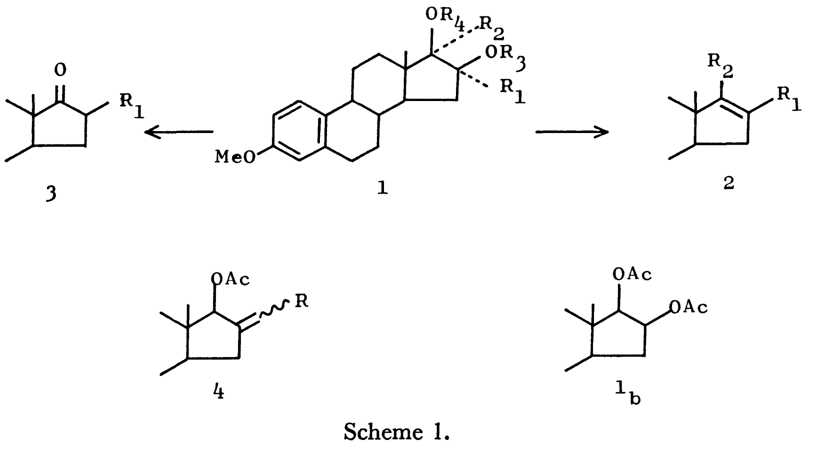
The solution of steroidal 16,17-*cis*-diol monoacetates (**1**)[2] in acetic acid was refluxed with freshly activated zinc powder[3] under nitrogen for 4—6 h. After removal of the zinc by filtration, the filtrates were extracted with ether to give the corresponding steroidal 16-enes (**2**). Of various *cis*-diol monoacetates, secondary-tertiary diol monoesters were smoothly converted into olefins in high yields, together with a small amount ($<5\%$) of the dehydrated compounds (**4**) as a by-product. Secondary-secondary diol monoacetates were reduced in lower yield and a large amount of diacetate (**1b**: $R_1=R_2=H$, $R_3=R_4=Ac$) was formed.[4] The corresponding diacetates (**1b** and **1m**: $R_1=C_6H_5$, $R_2=H$, $R_3=R_4=Ac$) were not affected under the reaction conditions.[6]

In order to investigate the participation of the neighbouring double bond, 16α-vinyl-16β,17β-diol 17-monoacetate (**1i**)[2] was heated with zinc in acetic acid to afford 16-vinyl-16-ene (**2i**) in 25% yield, coupled with 16β-vinyl-17β-acetate (**5**), its 16α-isomer (**6**) and (*E*)-16-ethylidene-17β-acetate (**7**) in 22, 26, and 17% yields, respectively. The (*E*)-configuration of 16-ethylidene group in **7** was confirmed by the conversion (hydrolysis and then oxidation) of **7** into the known (*E*)-16-ethylidene-17-one derivative.[2] An allenium ion intermediate (**8**) leading to the formation of **5**, **6**, and **7** may be involved in this reaction. The results are summarized in Table 1 and the spectral data of **2** are given in Table 2.

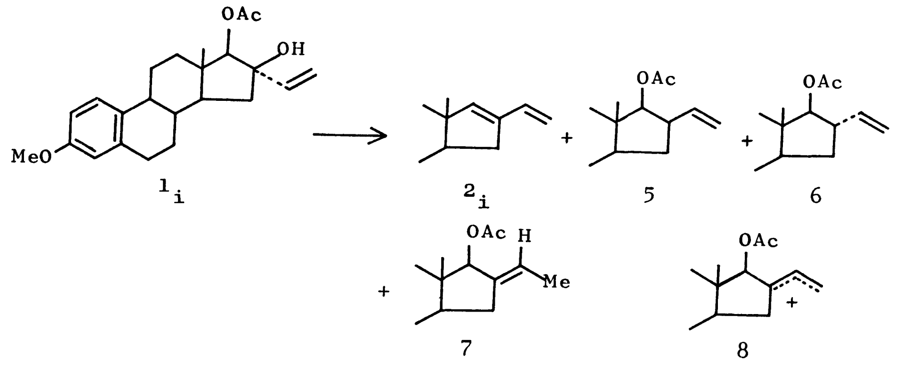
In the androstane series, *cis*-diol monoacetates **9**[2] and **11**[8] were treated with zinc in acetic acid to give the corresponding steroidal olefins **10** and **12**, respectively, without elimination of the 3β-acetyl group. Diol monoacetate (**13**)[2] having a 4-en-3-one system was refluxed with zinc in acetic acid to give 3,16-diene (**14**) accompanied by concomitant Clemmensen type reduction[9] of the system.

On the other hand, when *trans*-diol monoacetates (**15** and **16**)[2] were refluxed with zinc in acetic acid for a prolonged reaction time, most of the starting materials were recovered unchanged, along with a small amount ($<5\%$) of the olefinic products (**2e**: $R_1=H$, $R_2=Me$, and **21**: $R_1=C_6H_5$, $R_2=H$) even after 56 h.

The following results demonstrate that the olefin-



Scheme 1.



Scheme 2.

Table 1. Reductive elimination of 16,17-dihydroxysteroid monoacetates (**1**) to Δ^{16}-steroids (**2**)

Acetates **1**[a)]	R_1	R_2	R_3	R_4	Reaction time (h)	Products **2**	Mp (°C)	Yield[b)] (%)
a	H	H	Ac	H	6	**a**[c)]	63	7
b	H	H	Ac	Ac	56	—	—	—
c	D	H	Ac	H	6	**c**	63	19
d[d)]	Me	H	H	Ac	4	**d**	100	85
e	H	Me	Ac	H	4	**e**	123	88
f	Et	H	H	Ac	4	**f**	74	92
g	Et	H	Ac	H	4	**f**	74	74
h	Et	D	H	Ac	6	**h**	74	83
i	$CH=CH_2$	H	H	Ac	2	**i**	111	25
j	$CH_2CH=CH_2$	H	H	Ac	4	**j**	48	86
k	$(CH_2)_2CH=CH_2$	H	H	Ac	4	**k**	oil[e)]	88
l	C_6H_5	H	H	Ac	4	**l**	154	87
m	C_6H_5	H	Ac	Ac	56	—	—	—

a) Ref. 2. b) The yields given are based on recrystallized products from CH_3OH. c) L. Cagliati and M. Magi, *Tetrahedron*, **19**, 1127 (1963). d) H. Mori and K. Yasuda, *Yakugaku Zasshi*, **80**, 330 (1960). e) Crystallization was unsuccessful.

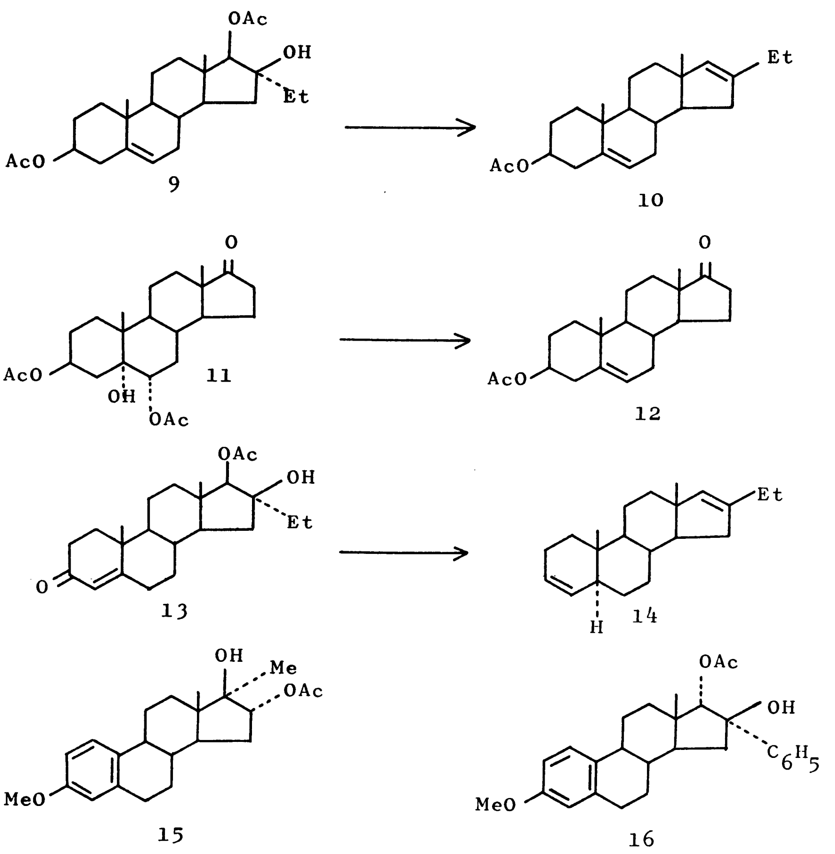
Table 2. Spectral data of Δ^{16}-steroids (**2**)

Δ^{16}-Steroids **2**	R_1	R_2	IR (KBr) $\nu\Delta^{16}$ (cm^{-1})	^1H-NMR ($CDCl_3$) δ (ppm)					MS (m/e)	
				18-Me (3H, s)	O-Me (3H, s)	17-H (1H, s)	Ar-H (3H, m)	Others	M^+	Others
d	Me	H	1625	0.78	3.77	5.50	6.6—7.3	1.73(3H, s, 16-Me)	282	267, 253
e	H	Me	1625	0.74	3.72	—	6.6—7.3	1.65(3H, s, 17-Me), 5.27(1H, m, 16-H)	282	267, 253
f	Et	H	1630	0.78	3.77	5.52	6.6—7.3	1.02(3H, t, J=7 Hz, Me)	296	281, 267
h	Et	D	1635	0.78	3.77	—	6.6—7.3	1.02(3H, t, J=7 Hz, Me)	297	282, 268
i[a)]	$CH=CH_2$	H	1630[b)]	0.81	3.70	5.78	6.6—7.3	4.96(1H, d, J=11 Hz, =CH), 5.04(1H, d, J=17 Hz, =CH), 6.2—6.6(1H, m, -CH=)[c)]	294	279, 265
j	$CH_2CH=CH_2$	H	1625	0.80	3.77	5.53	6.6—7.3	4.8—6.4(3H, m, $-CH=CH_2$)	308	293, 267
k	$(CH_2)_2CH=CH_2$	H	1630[b)]	0.79	3.78	5.55	6.6—7.3	4.8—6.4(3H, m, $-CH=CH_2$)	322	307, 281
l[d)]	C_6H_5	H	1625	0.91	3.73	6.25	6.6—7.3	7.26(5H, m, Ar)	344	329, 213

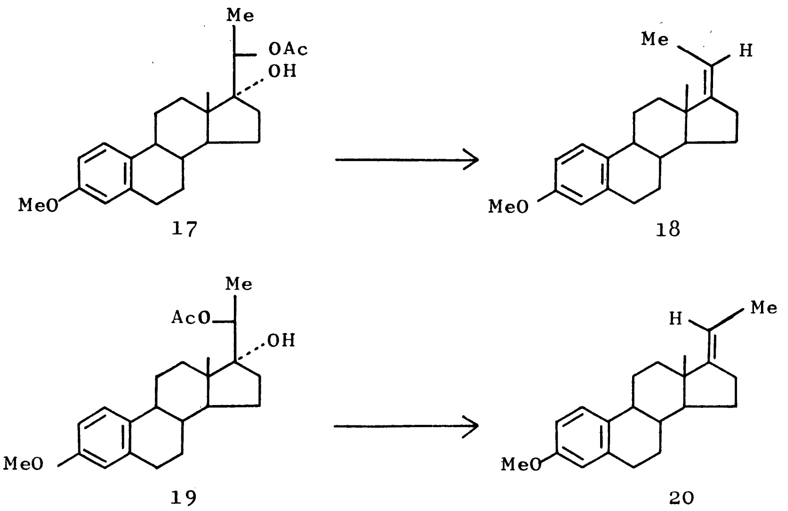
a) UV (EtOH) λ_{max} nm (ε): 221 (12000), 231 (16500), 236 (14000). b) Overlapped with terminal olefinic band. c) Overlapped with aromatic protons. d) UV (EtOH) λ_{max} nm (ε): 220 (13000), 258 (9800).

forming elimination of acyclic erythro and threo diol monoacetates proceeded stereoselectively and in good yield. 17α,20α-Diol monoacetate (**17**), when treated with zinc in acetic acid for 8 h at 120 °C, afforded stereoselectively (93%) (*Z*)-17-ethylidene derivative (**18**)[10)] in 92% yield, whereas 20*β*-epimer (**19**) gave stereoselectively (94%) (*E*)-17-ethylidene isomer (**20**)[11)] in 93% yield.

The results suggest that the dideoxygenation reaction proceeds with reductive *cis*-elimination of a cyclic ortho-



Scheme 3.

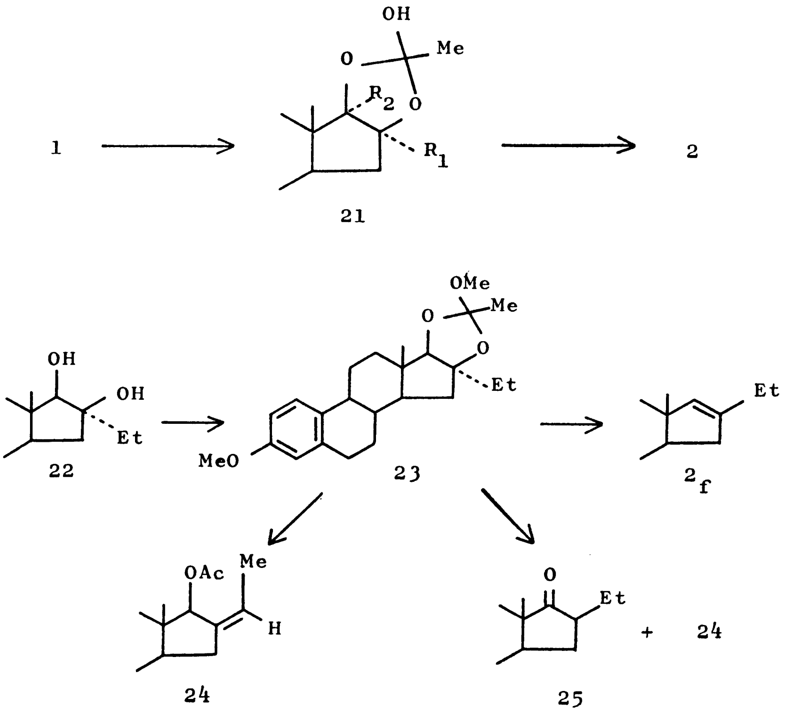


Scheme 4.

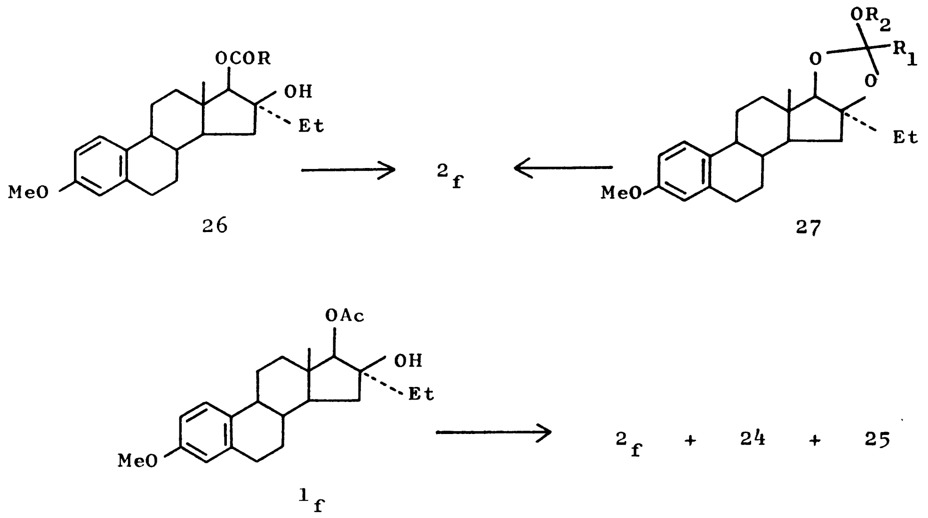
acetate intermediate (**21**),[2] which is in accord with the recent *syn*-elimination[12–14] of 1,3-dioxolan derivatives.

The explanation is supported by the following results. The cyclic orthoacetate (**23**), prepared from diol (**22**)[2] and trimethyl orthoacetate,[15] was refluxed with zinc in acetic acid to yield **2f** in 93% yield. It should be noted that heating of **23** with acetic acid gave (*Z*)-16-ethylidene-17*β*-acetate (**24**)[16] *via trans*-elimination of methanol quantitatively. Furthermore, treatment of **23** under the conditions of the Serini reaction (zinc in toluene)[1] gave 16*β*-ethyl-17-one (**25**) and **24** in 83% yield with a ratio of 1 : 5. Assignment of the configuration of 16-ethylidene group in **24** was made by comparison of the NMR spectrum with that of (*E*)-16-ethylidene isomer (**7**).

In order to investigate the behavior of esters other than acetates, several esters were subjected to the reaction conditions. The esters (**26**) were smoothly converted into the olefin (**2f**) in a range of 70—90% yield. This means that the reaction is not restrict-



Scheme 5.

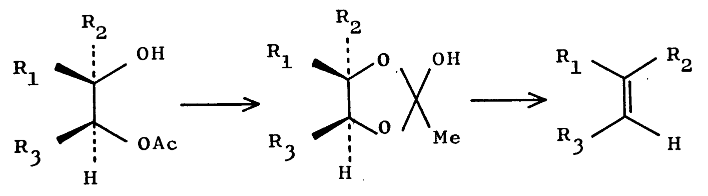


Scheme 6.

Table 3. Reductive elimination of 16,17-dihydroxysteroid monoesters (**26**) and the corresponding orthoesters (**27**) to Δ^{16}-steroid (**2f**)

Esters **26**	R	Mp (°C)	Reaction time (h)	Yield[a] (%)	Ortho-esters[b] **27**	Mp (°C)	R_1	R_2	Reaction time (h)	Yield[1] (%)
a	H	133—134	4	67	**a**	116—118	H	Me	4	69
b	Et	89	6	91	**b**	104—106	H	Et	4	70
c	C_6H_5	137—138	6	83	**c**	oil	Me	Et	4	92
					d	oil	Et	Et	4	90
					e	oil	C_6H_5	Et	6	86

a) The yields given are based on recrystallized product from CH_3OH. b) Isomeric mixture of 1,3-dioxolan derivatives was used.



28

29

Scheme 7.

Table 4. Effect of metal on the reduction of 16,17-dihydroxysteroid monoacetate (**1f**)

Metal used	Solvent	Reaction time (h)	Products (%)[c]		
			2f	**24**	**25**
Zn	AcOH	4	92	2	trace
Sn[a]	AcOH	6	24	17	40
Mg[b]	AcOH–Toluene (1: 3)	2	trace	3	7
Al[2]	AcOH–Toluene (1: 3)	2	7	5	12

a) Sn dust was activated by washing with 5% HCl.
b) Mg and Al powders were washed with 3% NaOH and then water. c) Isolated yield.

ed to acetate. The corresponding orthoesters (**27**) were also reduced into the olefin (**2f**) in a good yield. The results are summarized in Table 3.

The olefin-forming elimination of diol monoesters was also effected by the use of activated tin powder, but considerable amount of by-products were formed. Other metal powders such as magnesium and aluminium gave no satisfactory results. The effect of metals on the reduction is shown in Table 4. We see that zinc is the most suitable reducing agent in this reaction.

The new dideoxygenation reaction is restricted to the case in which one hydroxyl group is tertiary. However, the reaction may be of general applicability to the stereoselective synthesis of trisubstituted olefins (**29**) from diastereomeric trisubstituted 1,2-glycol monoesters (**28**).

Experimental

All melting points were determined on a micro hot-stage apparatus and were uncorrected. UV spectra were measured in EtOH on a Hitachi EPS-3T spectrophotometer, IR spectra on a Hitachi 215 spectrophotometer. NMR spectra were determined on a Varian HA-100 spectrometer using $CDCl_3$ as a solvent, chemical shifts (δ) being given in ppm relative to internal TMS. The mass spectra were determined on a Hitachi RMU-6D mass spectrometer equipped with a direct inlet system. Silicagel GF_{254} (E. Merck) was used for TLC analysis.

Reaction of Diol Monoacetates with Zinc in Acetic Acid. General Procedure: To a solution of **1** in acetic acid was added a 5—10 fold mol of freshly activated zinc powder. The mixture was refluxed on an oil bath (at 150 °C) with stirring under nitrogen for 2—6 h. After cooling, ether was added and the solid was removed by filtration. The ether was successively washed with satd $NaHCO_3$ aq solution, water and satd NaCl aq solution, followed by drying, and then concentrated to give crude crystals. Recrystallization from MeOH afforded pure **2**. The mother liquor was treated with column chromatography using silica gel (E. Merck); eluted with benzene: ether (5: 1) to give **4** in 2—5% yield. The mps of **2** are given in Table 1 and IR, UV and NMR spectral data in Table 2. The results of elemental analyses are as follows.

*16-Methyl-3-methoxyestra-1,3,5(10),16-tetraene (**2d**).* Found: C, 85.09; H, 9.29%. Calcd for $C_{20}H_{26}O$: C, 85.05; H, 9.28%.

*17-Methyl-3-methoxyestra-1,3,5(10),16-tetraene (**2e**).* Found: C, 85.01; H, 9.30%. Calcd for $C_{20}H_{26}O$: C, 85.05; H, 9.28%.

*16-Ethyl-3-methoxyestra-1,3,5(10),16-tetraene (**2f**).* Found: C, 85.07; H, 9.63%. Calcd for $C_{21}H_{28}O$: C, 85.08; H, 9.52%.

*16-Ethyl-17-deuterio-3-methoxyestra-1,3,5(10),16-tetraene (**2h**).* Found: C, 84.81; H, 9.80%. Calcd for $C_{21}H_{27}DO$: C, 84.79; H, 9.83%.

*16-Vinyl-3-methoxyestra-1,3,5(10),16-tetraene (**2i**).* Found: C, 85.58; H, 8.90%. Calcd for $C_{21}H_{26}O$: C, 85.66; H, 8.90%.

*16-Allyl-3-methoxyestra-1,3,5(10),16-tetraene (**2j**).* Found: C, 85.70; H, 9.23%. Calcd for $C_{22}H_{28}O$: C, 85.66; H, 9.15%.

*16-(3-Butenyl)-3-methoxyestra-1,3,5(10),16-tetraene (**2k**).* Found: C, 85.80; H, 9.40%. Calcd for $C_{23}H_{30}O$: C, 85.66; H, 9.38%.

*16-Phenyl-3-methoxyestra-1,3,5(10),16-tetraene (**2l**).* Found: C, 87.14; H, 8.20%. Calcd for $C_{25}H_{28}O$: C, 87.16; H, 8.19%.

*Reaction of **1i** with Zinc in Acetic Acid.* To a solution of **1i** (2.4 g) in acetic acid (25 ml) was added activated zinc powder (4.8 g). The mixture was refluxed under nitrogen for 2 h with stirring. Work-up of the reaction mixture in the same way as for **2** gave a mixture of the products which were separated by preparative TLC impregnated with $AgNO_3$ (developed with hexane: ether 5: 1). The product with R_f value 0.89 was **2i** (477 mg). The other products with R_f values 0.47, 0.43 and 0.33 were **5** (505 mg), **7** (390 mg) and **6** (597 mg), respectively.

*17β-Acetoxy-16β-vinyl-3-methoxyestra-1,3,5(10)-triene (**5**).* Mp 107—108 °C (from petroleum ether); IR (KBr) 1730, 1640, 1610 cm^{-1}; NMR 0.83 (3H, s, 18-Me), 1.96 (3H, s, OAc), 3.73 (3H, s, OMe), 4.72 (1H, d, $J=9$ Hz, 17α-H),[16] 5.0—6.2 (3H, m, vinyl H), 6.6—7.3 (3H, m, Ar); MS *m/e* 354 (M^+), 312, 294. Found: C, 77.90; H, 8.62%. Calcd for $C_{23}H_{30}O_3$: C, 77.93; H, 8.53%.

*17β-Acetoxy-16α-vinyl-3-methoxyestra-1,3,5(10)-triene (**6**).* Mp 109 °C; IR (KBr) 1730, 1640, 1610 cm^{-1}; NMR 0.86 (3H, s, 18-Me), 1.98 (3H, s, OAc), 3.73 (3H, s, OMe), 4.50 (1H, d, $J=7$ Hz, 17α-H),[16] 4.9—6.2 (3H, m, vinyl H), 6.6—7.3 (3H, m, Ar); MS *m/e* 354 (M^+), 312, 294. Found: C, 77.99; H, 8.52%. Calcd for $C_{23}H_{30}O_3$: C, 77.93; H, 8.53%.

*17β-Acetoxy-(E)-16-ethylidene-3-methoxyestra-1,3,5(10)-triene (**7**).* Mp 99—100 °C; IR (KBr) 1730 cm^{-1}; NMR 0.75

(3H, s, 18-Me), 1.50 (3H, d, $J=7$ Hz, =CMe), 2.14 (3H, s, OAc), 3.75 (3H, s, OMe), 5.27 (1H, s, 17α-H), 5.2—5.3 (1H, m, =CH), 6.6—7.3 (3H, m, Ar); MS *m/e* 354 (M^+), 312, 294. Found: C, 77.85; H, 8.31%. Calcd for $C_{23}H_{30}O_3$: C, 77.93; H, 8.53%.

3β-Acetoxy-16-ethylandrosta-5,16-diene (10). Reaction of **9** (3.5 g) with zinc powder (8 g) in acetic acid (25 ml) was carried out by the same procedure as for **2**: **10** (2.6 g), mp 128 °C; IR (KBr) 1730, 1625 cm^{-1}; NMR 0.78 (3H, s, 18-Me), 1.00 (3H, t, $J=6$ Hz, Me), 1.05 (3H, s, 19-Me), 2.01 (3H, s, OAc), 4.4—4.8 (1H, m, 3α-H), 5.3—5.5 (2H, m, 6-H and 16-H); MS *m/e* 342 (M^+), 327, 282, 267. Found: C, 80.60; H, 10.01%. Calcd for $C_{23}H_{34}O_2$: C, 80.65; H, 10.01%.

Stereoselective Conversion of 17α,20-Dihydroxy Monoacetates (17 and 19) into (Z)- and (E)-17-Ethylidene Derivatives (18 and 20). Reaction of diol monoacetates (**17** and **19**) with zinc in acetic acid was carried out by the same procedure as for **1**. The purity of the products was estimated by gas chromatography on a column with 10% OV-17 (2 m, 265 °C).

Preparation of Orthoesters.[15] *General Procedure*: To a solution of diol (**22**) in CH_2Cl_2 was added trialkyl orthoester and a catalytic amount of *p*-TsOH. After being stirred at room temperature for 2 h, the reaction mixture was poured into 5% $NaHCO_3$ aq solution and extracted with CH_2Cl_2. The extracts were washed with water, dried, and concentrated to give a resinous material. Recrystallization from petroleum ether gave the steroidal orthoesters. The following compounds were prepared.

Methyl Orthoacetate of 22 (23). Mp 63 °C; IR (KBr) 1610 cm^{-1}; NMR 0.86 (3H, s, 18-Me), 1.04 (3H, t, $J=7$ Hz, Me), 1.57 (3H, s, Me), 3.25 (3H, s, OMe), 3.73 (3H, s, OMe), 3.84 (1H, s, 17α-H), 6.6—7.3 (3H, m, Ar); MS *m/e* 386 (M^+), 354, 312. Found: C, 74.60; H, 8.80%. Calcd for $C_{24}H_{34}O_4$: C, 74.57; H, 8.87%.

Methyl Orthoformate of 22 (27a). IR (KBr) 1610 cm^{-1}; NMR 0.83 (3H, s, 18-Me), 1.01 (3H, t, $J=7$ Hz, Me), 3.27 (3H, s, OMe), 3.71 (3H, s, OMe), 3.86 (1H, s, 17α-H), 5.74 (1H, s, -OCHO-), 6.6—7.3 (3H, m, Ar); MS *m/e* 372 (M^+), 344, 341. Found: C, 74.20; H, 8.60%. Calcd for $C_{23}H_{32}O_4$: C, 74.16; H, 8.66%.

Ethyl Orthoformate of 22 (27b). IR (KBr) 1610 cm^{-1}; NMR 0.82 (3H, s, 18-Me), 1.00 (3H, t, $J=6$ Hz, Me), 1.20 (3H, t, $J=7$ Hz, Me), 3.52 (2H, q, $J=7$ Hz, $-CH_2-$), 3.73 (3H, s, OMe), 3.78 (1H, s, 17α-H), 5.73 (1H, s, -OCHO-), 6.6—7.3 (3H, m, Ar); MS *m/e* 386 (M^+), 357, 341. Found: C, 74.59; H, 8.90%. Calcd for $C_{24}H_{34}O_4$: C, 74.57; H, 8.87%.

Ethyl Orthoacetate of 22 (27c). IR (Neat) 1610 cm^{-1}; NMR 0.87 (3H, s, 18-Me), 3.56 (2H, q, $J=7$ Hz, $-CH_2-$), 3.72 (3H, s, OMe), 3.80 (1H, s, 17α-H), 6.6—7.3 (3H, m, Ar); MS *m/e* 400 (M^+, $C_{25}H_{36}O_4$ requires: 400), 385, 354.

Ethyl Orthopropionate of 22 (27d). IR (Neat) 1610 cm^{-1}; NMR 0.86 (3H, s, 18-Me), 3.60 (2H, q, $J=7$ Hz, $-CH_2-$), 3.71 (3H, s, OMe), 3.84 (1H, s, 17α-H), 6.6—7.3 (3H, m, Ar); MS *m/e* 414 (M^+, $C_{26}H_{38}O_4$ requires: 414), 399, 368.

Ethyl Orthobenzoate[17] *of 22 (27e).* IR (Neat) 1615, 1610 cm^{-1}; NMR 0.90 (3H, s, 18-Me), 3.70 (3H, s, OMe), 3.72 (2H, q, $J=7$ Hz, $-CH_2-$), 3.93 (1H, s, 17α-H), 6.6—7.6 (8H, m, Ar); MS *m/e* 462 (M^+, $C_{30}H_{33}O_4$ requires: 462), 447, 434.

Treatment of Orthoesters with Zinc in Acetic Acid. General Procedure: To a solution of orthoester (0.4 g) in acetic acid (5 ml) was added activated zinc powder (1.3 g). The mixture was refluxed under nitrogen for 4—6 h with stirring. Work-up of the reaction mixture gave **2f** which was crystallized from MeOH.

17β-Acetoxy-(Z)-16-ethylidene-3-methoxyestra-1,3,5(10)-triene (24). A solution of **23** (0.34 g) in acetic acid (10 ml) was heated under reflux for 30 min. The solvent was evaporated under reduced pressure to give crude crystals. Recrystallization from ether: hexane (5: 1) afforded **24** (0.3 g), mp 161—162 °C; IR (KBr) 1730, 1610 cm^{-1}; NMR 0.81 (3H, s, 18-Me), 1.56 (3H, d, $J=7$ Hz, =CMe), 2.11 (3H, s, OAc), 3.75 (3H, s, OMe), 5.24 (1H, s, 17α-H), 5.49 (1H, m, =CH), 6.6—7.3 (3H, m, Ar); MS *m/e* 354 (M^+), 312, 297, 294. Found: C, 77.85; H, 8.31%. Calcd for $C_{23}H_{30}O_3$: C, 77.93; H, 8.53%.

Treatment of 23 under the Conditions of the Serini Reaction. To a solution of **23** (0.77 g) in dried toluene was added freshly activated zinc powder. The mixture was refluxed for 6 h with stirring. Zinc was removed by filtration. The filtrates were evaporated under vacuum to give a residue which was separated by preparative TLC (developed with benzene: ether 10: 1). The product with higher R_f value (0.42) was **24** (490 mg). The other product with R_f value (0.33) was 16β-ethyl-3-methoxyestra-1,3,5(10)-trien-17-one (**25**)[2] (86 mg).

17β-Formyloxy-16β-hydroxy-16α-ethyl-3-methoxyestra-1,3,5(10)-triene (26a). Formylation of **22** with Ac_2O-HCOOH gave **26a**: IR (KBr) 3500, 1720, 1610 cm^{-1}; NMR 0.97 (3H, s, 18-Me), 3.71 (3H, s, OMe), 4.59 (1H, s, 17α-H), 6.6—7.3 (3H, m, Ar), 8.15 (1H, s, CHO); MS *m/e* 358 (M^+), 312. Found: C, 73.76; H, 8.43%. Calcd for $C_{22}H_{30}O_4$: C, 73.71; H, 8.44%.

17β-Propionyloxy-16β-hydroxy-16α-ethyl-3-methoxyestra-1,3,5(10)-triene (26b). Treatment of **22** with propionic anhydride in pyridine gave **26b**: IR (KBr) 3500, 1730, 1610 cm^{-1}; NMR 0.98 (3H, s, 18-Me), 3.75 (3H, s, OMe), 4.58 (1H, s, 17α-H), 6.6—7.3 (3H, m, Ar); MS *m/e* 386 (M^+), 357, 312. Found: C, 74.59; H, 8.80%. Calcd for $C_{24}H_{34}O_4$: C, 74.57; H, 8.87%.

17β-Benzoyloxy-16β-hydroxy-16α-ethyl-2-methoxyestra-1,3,5(10)-triene (26c). Treatment of **22** with benzoyl chloride in pyridine afforded **26c**: IR (KBr) 3350, 1695, 1610, 1600 cm^{-1}; NMR 0.95 (3H, t, $J=7$ Hz, Me), 1.08 (3H, s, 18-Me), 3.74 (3H, s, OMe), 4.85 (1H, s, 17α-H), 6.6—7.3 (3H, m, Ar), 7.4—8.3 (5H, m, Ar); MS *m/e* 434 (M^+), 312. Found: C, 77.40; H, 7.80%. Calcd for $C_{28}H_{34}O_4$: C, 77.39; H, 7.89%.

Reaction of 26 with Zinc in Acetic Acid. General Procedure: To a solution of **26** in acetic acid was added freshly activated zinc powder. The mixture was refluxed under nitrogen for 4—6 h with stirring. Work-up by the usual procedure gave **2f**.

Reaction of 1f with Tin in Acetic Acid. To a solution of **1f** (1.2 g) in acetic acid (15 ml) was added tin powder (3 g) which had been washed with acid. The mixture was heated under reflux for 6 h. To the cooled solution was added ether (200 ml) and the solid was removed by filtration. The filtrate was washed with satd $NaHCO_3$ aq, satd NaCl aq solution in succession and then dried. The ether was concentrated to give a residue which was separated by preparative TLC using benzene: ether (10: 1) as an eluent. The product with R_f value 0.86 was **2f** (229 mg). The other products with R_f values 0.42 and 0.33 were **24** (194 mg) and **25** (403 mg), respectively.

The author would like to thank Drs. E. Ohmura, H. Morimoto, T. Miki, and K. Hiraga of this Division for their advice and encouragement.

References

1) a) A. Serini, W. Logemann, and W. Hildebrand, *Ber.*, **72**, 391 (1939); b) T. Goto and L. F. Fieser, *J. Am. Chem. Soc.*, **83**, 251 (1961); c) E. Ghera, *Chem. Commun.*,

1968, 1639; E. Ghera, *J. Org. Chem.*, **35**, 660 (1970).

2) G. Goto, K. Yoshioka, and K. Hiraga, *Tetrahedron*, **30**, 2107 (1974).

3) Zinc powder was treated with dil HCl, followed by washing with distilled water and then dried over P_2O_5 at 100 °C.

4) The facile formation of the diacetate (**1b**) is due to a neighbouring group particitipation5) of the 16β-acetoxyl group.

5) a) R. Boschan and S. Winstein, *J. Am. Chem. Soc.*, **78**, 4921 (1956); b) J. F. King and A. D. Allbutt, *Tetrahedron Lett.*, **1967**, 49.

6) Reductive elimination of cholestane diacetates by lithium (or calcium) in liquid ammonia was known7) to occur only when one ester is tertiary and both ester groups are *trans*-diaxial.

7) D. H. R. Barton, P. G. Sammes, and M. Silva, *Tetrahedron Suppl.*, **7**, 57 (1966).

8) J. S. Baran, *J. Org. Chem.*, **25**, 257 (1960).

9) a) J. McKenna, J. K. Norymberski, and R. D. Stubbs, *J. Chem. Soc.*, **1959**, 2502; b) G. M. L. Cragg, C. W. Davey, D. N. Hall, G. D. Meakins, E. E. Kichards, and T. L. Whateley, *J. Chem. Soc., C*, **1966**, 1266; c) B. R. Davis and P. D. Woodgate, *ibid.*, **1966**, 2006.

10) A. M. Krubiner and E. P. Oliveto, *J. Org. Chem.*, **31**, 24 (1966).

11) H. Schick, *Pharmazie*, **30**, 30 (1975).

12) a) E. J. Corey and R. A. E. Winter, *J. Am. Chem. Soc.*, **85**, 2677 (1963); b) E. J. Corey, F. A. Carey, and R. A. E. Winter, *ibid.*, **87**, 934 (1965); c) E. J. Corey and R. A. E. Winter, *Chem. Commun.*, **1965**, 208; d) D. Horton and W. N. Turner, *Tetrahedron Lett.*, **1964**, 2531; e) R. Hull and R. Farrand, *Chem. Commun.*, **1965**, 164; f) E. J. Corey and J. I. Shulman, *Tetrahedron Lett.*, **1968**, 3655; g) M. Tichy and J. Sicher, *ibid.*, **1969**, 4609; h) M. F. Semmelhack and R. D. Stauffer, *ibid.*, **1973**, 2667.

13) a) G. Crank and F. W. Eastwood, *Aust. J. Chem.*, **17**, 1392 (1964); b) J. S. Josan and F. W. Eastwood, *Carbohydr. Res.*, **7**, 161 (1963); c) G. I. Moss, G. Crank, and F. W. Eastwood, *J. Chem. Soc., D*, **1970**, 206; d) J. W. Scheeren, A. P. M. van der Veek, and W. Stevens, *Recl. Trav. Chim. Pays-Bas*, **88**, 165 (1969); e) A. P. M. van der Veek and F. H. Putten, *Tetrahedron Lett.*, **1970**, 3951; f) T. Hiyama and H. Nozaki, *Bull. Chem. Soc. Jpn.*, **46**, 2248 (1973); g) R. A. Braun, *J. Org. Chem.*, **31**, 1147 (1966); h) F. W. Eastwood, K. J. Harrington, J. S. Josan, and J. J. Pura, *Tetrahedron Lett.*, **1970**, 5223.

14) a) P. S. Wharton, G. A. Hiegel, and S. Ramaswami, *J. Org. Chem.*, **29**, 2441 (1964); b) J. S. Josan and F. W. Eastwood, *Aust. J. Chem.*, **21**, 2013 (1968); c) J. N. Hines, M. J. Peagran, G. H. Whitham, and M. Wright, *Chem. Commun.*, **1968**, 1593; d) J. N. Hines, M. J. Peagran, E. J. Thomas, and G. H. Whithan, *J. Chem. Soc. Perkin Trans. 1*, **1973**, 2332.

15) R. H. DeWolfe, "Carboxylic Ortho Acid Derivatives," Academic Press, New York and London (1970).

16) G. Goto, K. Yoshioka, K. Hiraga, and T. Miki, *Chem Pharm. Bull.*, **21**, 1393 (1973).

17) a) L. G. S. Brooker and F. L. White, *J. Am. Chem. Soc.*, **57**, 2480 (1935); b) A. Kiprianov, Z. P. Suitnik, and E. D. Suich, *Zh. Obshch. Khim.*, **6**, 42 (1936).