lowed to cool and poured into an ice–water mixture (1.5 l.) with stirring. The mixture was refrigerated for 30 min and the product was collected by filtration, washed with water, and dried. Recrystallization of the crude product (31.2 g) from acetone–hexane gave a first crop (23.0 g) melting at 137.5–140° and a second crop (5.0 g) melting at 132–135°. Recrystallization of a sample from methylene chloride–hexane gave pure XIa: mp 138–140°; $[\alpha]^{26}D$ +152.5°; nmr 54 (C-18 methyl), 228 (C-19 methylene), and 341–343 cps (C-2, C-3 protons).

Anal. Calcd for $C_{19}H_{28}O_2$: C, 79.12; H, 9.79. Found: C, 78.83; H, 9.67.

5α-Androst-2-ene-17β,19-diol (XIb).—A solution of Xb (0.3 g) and KOH (0.5 g) in methanol (10 ml) and water (4 ml) was refluxed for 1.5 hr. The mixture was filtered while still hot and the filtrate was poured slowly with stirring into cold water. The precipitate was collected, washed with water, and air dried. Recrystallization from acetone–hexane gave pure XIb (0.25 g), mp 152–152.5°, $[\alpha]^{26}D$ +76°.

Anal. Calcd for $C_{19}H_{30}O_2$: C, 78.59; H, 10.41. Found: C, 78.71; H, 10.65.

17α-Methyl-5α-androst-2-ene-17β,19-diol (XId).—To a refluxing mixture of 3 *M* methylmagnesium bromide in *n*-butyl ether (30 ml) and THF (50 ml) was added dropwise with stirring a solution of XIa (1.45 g) in THF (50 ml). The entire process was performed under an atmosphere of nitrogen. The mixture was then refluxed with stirring for 7 hr and allowed to stand at room temperature overnight. The vessel was surrounded with an ice–water bath and 10% NH_4Cl solution (50 ml) was added dropwise with stirring. The contents was transferred to a separatory funnel, ether (10 ml) was added, and the aqueous phase separated. The ether solution was washed successively with dilute HCl (1:4, 75 ml) and two 75-ml portions of water and dried (Na_2SO_4, Darco). The solvent was removed under reduced pressure and the solid residue (1.4 g) was recrystallized from ethyl acetate. This gave pure XId (0.66 g), mp 165–166°, $[\alpha]^{27}D$ +26.3°. A second crop (0.44 g) was also obtained, mp 163–166°.

Anal. Calcd for $C_{20}H_{32}O_2$: C, 78.89; H, 10.59. Found: C, 78.76; H, 10.63.

19-Hydroxy-5α-androst-2-en-17-one *p*-Toluenesulfonate (XIIa).—A solution of XIa (10 g) and *p*-toluenesulfonyl chloride (7.0 g) in pyridine (100 ml) was warmed on the steam bath for 4 hr and allowed to stand at room temperature for 48 hr. The solution was poured into water (600 ml) and the mixture was allowed to stand for 30 min whereupon the initial oil crystallized. The mixture was refrigerated for 1 hr and the product was collected. After washing the product successively with water, dilute HCl (1:10), and water, it was recrystallized from acetone–water to give XIIa as needles (12.0 g), mp 145.5–147.5°. Recrystallization of a sample from acetone–hexane gave pure XIIa, mp 145–147.5°, $[\alpha]^{26}D$ 67.5°, λ_{max} 225 mμ (log ε 4.09).

Anal. Calcd for $C_{26}H_{34}O_4S$: C, 70.55; H, 7.74. Found: C, 70.20; H, 7.72.

19-Hydroxy-5α-androst-2-en-17-one Methanesulfonate (XIIIa).—A solution of XIa (10 g) in methanesulfonyl chloride (15 ml) and pyridine (160 ml) was stirred for 5 hr and allowed to stand at room temperature for 48 hr. The mixture was poured into water (600 ml) and allowed to stand at room temperature for 30 min whereupon the initial oil became crystalline. The mixture was refrigerated for 1 hr. The product was collected and washed with water, dilute HCl (1:10), and water. The brown product was dissolved in ether and the solution was decolorized with Darco. The solvent was removed *in vacuo* and the oily residue crystallized from ether–pentane to give XIIIa (9.5 g), mp 117.5–119°. Recrystallization of a sample from acetone–hexane afforded pure XIIIa, mp 120–122°, $[\alpha]^{27}D$ +91°.

Anal. Calcd for $C_{20}H_{30}O_4S$: C, 65.54; H, 8.25. Found: C, 65.68; H, 8.42.

Chemical and Biological Properties of Some 17-Substituted Estradiol Derivatives

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Received March 12, 1966

A series of 17-substituted estradiol derivatives were prepared with the hope of introducing progestational properties into an estrogenic molecule. The methods for synthesizing these compounds are described along with some of the striking biological properties exhibited by some of the derivatives.

It has been known for many years that some of the naturally occurring sex hormones such as testosterone, progesterone, and estrone are capable of inhibiting ovulation in women. For various reasons, however, these hormones are unsuitable for clinical use as oral contraceptives. In an effort to overcome some of the shortcomings associated with these substances, various laboratories have been involved in extensive programs directed toward the chemical modification of natural hormones.[2] In most instances, these modifications have dealt with testosterone (*e.g.*, 17α-ethynyltestosterone and 19-nor analogs) and progesterone (*e.g.*, 17-acetoxyprogesterones). On the other hand, few investigations have involved modification of estrogens such as estrone. This is true despite the fact that estrogens such as ethynylestradiol or its 3-methyl ether are components of most contraceptive medications. Moreover, it has been noted that these estrogens when given alone have ovulation inhibitory properties in women.[3]

Clinical experience indicates that the estrogen–progestin combination therapy provides the most effective means for control of fertility.[4] As a result, our attempts to find a single agent useful for fertility control has involved a search for substances that would mimic the biological effects produced by the estrogen–progestin combinations.

In 1957, studies by Saunders, *et al.*,[5] dealing with 17-alkylated 19-nortestosterone derivatives indicated that progestational activity was related to the length of the side chain at C-17. Maximum activity was achieved with the 17-(2-methylallyl)-substituted compounds. It seemed reasonable, therefore, that one might be able to incorporate progestational activity into the estradiol molecule by alkylating at C-17 with appropriate groups. To test this hypothesis, a series

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(2) *Cf.* F. B. Colton and P. D. Klimstra, "Encyclopedia of Chemical Technology," Vol. 6, John Wiley and Sons, Inc., New York, N. Y., 1965, p 60.

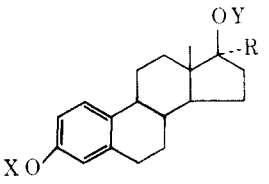
(3) M. C. N. Jackson, *J. Reprod. Fertility*, **6**, 153 (1963).

(4) G. Pincus, Advances in Chemistry Series, No. 45, American Chemical Society, Washington, D. C., 1964, p 201.

(5) F. J. Saunders F. B. Colton, and V. A. Drill, *Proc. Soc. Exptl. Biol. Med.*, **94**, 717 (1957).

TABLE I

ESTRADIOL DERIVATIVES



R	X	Y	Mp, °C	$[\alpha]^{23-25}$D, deg	Recrystn media[a]	Carbon, % Calcd	Carbon, % Found	Hydrogen, % Calcd	Hydrogen, % Found
$CH{=}CH_2$	H[b]	H	170–171	+53	i	80.49	81.49	8.78	8.78
	Ac[c]	H	129.5–131.5	+37	ii	77.61	77.85	8.29	8.64
CH_2CH_3	H	H	169–170	+66	iii	79.95	80.03	9.39	9.27
	Ac	H	105.5–107	+41.5	iv	77.15	77.09	8.83	8.77
$CH_2C{\equiv}CH$	H	H	163–166	+44	ii	81.25	81.37	8.44	8.33
	Ac	H	167–169	+38	ii	78.37	78.51	8.01	7.86
	Ac	Ac	140–141	+26	i	76.11	76.03	7.67	7.68
$CH_2CH{=}CH_2$	H	H	82–85[d]	+54	ii	80.73	80.25	9.03	9.00
	Ac	H	126–128	+52	iv	77.93	77.94	8.53	8.54
	Ac	Ac	120–121	+26	i	75.72	75.62	8.13	8.16
	H	Ac	171–174	+35.5	v	77.93	77.63	8.53	8.60
$CH_2CH_2CH_3$	H	H	167–168	+56	i	80.21	80.14	9.62	9.81
	Ac	H	90–92	+47.5	vi	77.49	77.48	9.05	9.04
$CH_2C{\equiv}CCH_3$	H	H	181–182.5	+33.5	ii	81.44	81.18	8.70	8.50
	Ac	H	159–161	+35.5	ii	78.65	78.86	8.25	8.27
	Ac	Ac	165–167	+28	i	76.44	76.48	7.90	7.97
$CH_2CH{=}CHCH_3$	H	H	[e]	+55		80.93	80.40	9.26	9.10
	Ac	H	85–86	+48	viii	78.22	78.33	8.75	8.90
$CH_2C(CH_3){=}CH_2$	H[f]	H	165–166	+69.5	viii	80.93	80.92	9.26	9.06
	Ac	H	118–120	+59.5	vii	78.22	78.43	8.75	8.43
	Ac	Ac	109–111	+21	ix	76.06	76.01	8.34	8.15
	H	Ac	153.5–154.5	+72.5	ix	78.22	78.50	8.75	8.82
$CH_2CH_2CH_2CH_3$	H	H	124–126	+44	ii	80.44	80.43	9.83	9.73
	Ac	H	67–69	+37	ix	77.80	77.91	9.25	9.18
$CH_2CH(CH_3)_2$	H	H	150.5–151.5	+49	x	80.44	80.42	9.83	9.52
	Ac	H	80.5–82.5	+5	vii	77.05	77.25	9.56	9.16

[a] i, methanol; ii, acetone–hexane; iii, ethyl acetate; iv, acetone–H_2O; v, ethanol; vi, ether–hexane; vii, heptane; viii, ethyl acetate–heptane; ix, methanol–H_2O; x, benzene–heptane. [b] Lit.[9a] mp 142–147°, $[\alpha]^{25}$D +59.5° (dioxane). [c] Lit.[9a] mp 126–127.5°, $[\alpha]^{25}$D +61.2° (dioxane). [d] Sublimed. Sample from ethyl acetate crystallizes as a solvate, mp 110–112°. [e] An oil which resisted crystallization from a variety of solvents. [f] The 17-epimer, 17-(2-methylallyl)estra-1,3,5(10)-triene-3,17α-diol, was isolated by chromatography; mp 141–143°, $[\alpha]$D +31.5°. *Anal.* Found: C, 80.68; H, 9.08.

of 17-alkanyl, alkenyl, and alkynyl analogs of estradiol [estra-1,3,5(10)-triene-3,17β-diol] were synthesized and evaluated biologically.[6]

Of the compounds of interest to us for biological testing, 17-methyl-,[7] 17-ethynyl-,[8] and 17-vinylestradiol[8,9] had been previously described. The melting points reported for 17-vinylestradiol have varied from 142–147 to 155–156° as compared to 170–171° observed in this study. This discrepancy is most likely due to solvate formation similar to that noted for 17-ethynylestradiol,[10] since our earlier preparation had mp 146–148° and lost solvent to remelt at 170–171°. The formation of crystalline solvates was observed for several of the other 17-substituted estradiols prepared during this study. The corresponding acetates, however, showed no tendency to solvate and were readily characterized.

The other 17-substituted estradiols required for this study were readily obtained from estrone by conventional methods.[11] An improvement in the synthesis of some of these compounds involved conversion of estrone to its tetrahydropyranyl ether prior to alkylation to overcome the low solubility of the former in organic solvents.[12] In cases where alkylation was found to be incomplete by thin layer chromatography, the starting ketone was readily removed by treatment of the crude reaction mixture with Girard-T reagent. In one case, chromatographic purification of 17-(2-methylallyl)-estradiol furnished a trace of the C-17 epimer. Acetylation of the diols at room temperature by means of pyridine and acetic anhydride afforded the 3-acetates whereas treatment with isopropenyl acetate under acid catalysis gave the 3,17-diacetates. Saponification of the 3,17-diacetates with methanolic potassium carbonate produced the 17-acetates. Physical constants

(6) A preliminary description of this work has appeared: R. E. Counsell, U. S. Patent 3,107,257 (1963); *Chem. Abstr.*, **60**, 3038 (1964). Since completion of this work, 17-butadiynylestradiol has been reported to exhibit potent contraceptive and estrogen properties in rats: J. Gardner, D. Gnoj, A. S. Watnick, and J. Gibson, *Steroids*, **4**, 801 (1964).

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(8) H. Inhoffen, W. Logemann, W. Holdweg, and A. Serini, *Ber.*, **71**, 1024 (1938).

(9) (a) C. Djerassi and C. B. Scholz, *J. Am. Chem. Soc.*, **71**, 3962 (1949); (b) J. Kathol, German Patent 870,099 (1953); *Chem. Abstr.*, **52**, 15605h (1958).

(10) R. Pheasant, *J. Am. Chem. Soc.*, **72**, 4303 (1950).

(11) M. S. Kharasch and D. Reinmuth, "Grignard Reactions of Non-Metallic Substances," Prentice Hall, New York, N. Y., 1954.

(12) We wish to acknowledge Messrs. W. Aksamit, B. Smith, and J. Yen and Dr. W. Hoehn for their assistance in the development of this improved synthesis.

Table II

Estrogenic and Deciduogenic Effects of Some Substituted Estradiols

R	X	Y	Estrogenic activity, Oral	Estrogenic activity, Sc	Deciduogenic activity
Estrone			≤5	100[a]	
C≡CH	H	H	100[a]	1250	Inactive
C≡CH[b]	Ac	H	100	1000	Active
C≡CH[c]	Ac	Ac		330	Inactive
$CH_2C{\equiv}CH$	Ac	H	20	80	Weakly active
$CH_2C{\equiv}CCH_3$	Ac	H	680	1250	Active[d]
$CH_2C{\equiv}CCH_3$	Ac	Ac	~5	~5	Inactive
$CH{=}CH_2$	Ac	H	20	250	Weakly active
$CH_2CH{=}CH_2$	Ac	H	0.3	2.5	Active
$CH_2CH{=}CH_2$	Ac	Ac	0.25	<0.1	
$CH_2C(CH_3){=}CH_2$	Ac	H	2.8	2.5	Active[d]
$CH_2C(CH_3){=}CH_2$	Ac	Ac	<0.01	<0.25	
$CH_2CH{=}CHCH_3$	Ac	H	2.8	3.3	Active
CH_3	Ac	H	160	1000	Inactive
CH_2CH_3	Ac	H	<1	2	Weakly active
$CH_2CH_2CH_3$	Ac	H	0.7	1	Inactive
$CH_2CH(CH_3)_2$	Ac	H	1	3	Weakly active
$CH_2CH_2CH_2CH_3$	Ac	H	<0.25	0.25	Inactive
Ethynodiol diacetate			1.7	4[e]	Active

[a] Standards. [b] K. Junkmann, *Arch. Exptl. Pathol. Pharmakol.*, **220**, 358 (1953); *Chem. Abstr.*, **48**, 2917 (1954). [c] J. S. Mills, H. J. Ringold, and C. Djerassi, *J. Am. Chem. Soc.*, **80**, 6118 (1958). [d] The most active deciduogenic agents of this series as measured by decidual cell formation at the 1, 2, 4, and 10 mg/day dose in rabbits.[11] [e] R. L. Elton and E. F. Nutting, *Proc. Soc. Exptl. Biol. Med.*, **107**, 991 (1961).

and analytical data for the various derivatives are summarized in Table I.

Preliminary Biological Results.—The estrogenic properties for some of the substituted estradiols are compared in Table II. The estrogenic activity was determined in rats using cornification of the vaginal epithelium as the end point.[13] The compounds were administered subcutaneously or intragastrically as solutions or suspensions in corn oil. The alkynyl-substituted analogs were, in general, the most potent estrogens with activity decreasing with saturation in the order alkynyl > alkenyl > alkyl. The 17-methyl derivative, however, displayed considerable estrogenic activity and was more potent than the standard in the rat vaginal smear assay. This activity was sharply decreased by increasing chain length. A similar decrease in potency was noted in going from ethynyl to propargyl; however, this effect was reversed upon conversion to the butynyl analog. In fact, the 17-(2-butynyl) derivative was the most potent estrogen tested by the oral route of administration.

It is interesting to point out that while acetylation of the phenolic hydroxyl group had little effect on estrogenic activity, esterification of the 17-hydroxyl group markedly lowered activity by both the subcutaneous and oral routes of administration. On the other hand, Cross and co-workers[14] have reported that the 17-tetrahydropyranyl ether of ethynylestradiol 3-methyl ether dramatically increased the estrogenic activity of the latter following subcutaneous administration, while the oral estrogenic activity greatly decreased.

An attempt was made to determine the progestational activity of these estradiol derivatives using arborization of the rabbit uterine epithelium as the index of activity.[15] Unfortunately, only 17-(2-methylallyl)estradiol and its 3-acetate exhibited progestational activity, being approximately one-twentieth of the potency of progesterone by subcutaneous administration. However, to our knowledge apparently this is the first time that a steroid possessing an aromatic A ring has been shown to have progesterone-like properties. While this activity was not observed with any of the other 17-substituted estradiols, it is possible that the high estrogenic property of some of the compounds [*e.g.*, 17-(2-butynyl)estradiol 3-acetate] masked the progestational effects which may have been present.

In the 19-nortestosterone and 17α-hydroxyprogesterone series, preparation of the 17-acetates is known to enhance the progestational properties of the compounds.[2] On the other hand, conversion of 17-(2-methylallyl)estradiol to its 3,17-diacetate completely eliminated the progestational effects displayed by its unacetylated progenitor. This would tend to indicate that the mechanism whereby these substances exert their progestational effects may be different from that for the testosterone and progesterone analogs.

The ability of some of the substituted estradiols to stimulate decidual cell formation in the endometrium of rabbits served as another parameter for assessing their intrinsic progestational properties. The decidual response is observed in rabbits given an estrogen and a progestin but not when these substances are administered separately.[16,17] It has been shown that agents such as norethynodrel (17α-ethynyl-17β-hydroxyestr-5(10)-en-3-one) and ethynodiol diacetate (17α-ethynylestr-4-ene-3β,17β-diol diacetate) readily produce decidual cell responses in rabbits[17] and in humans.[18] However, when used in women, additional estrogen is required to obtain the desired uterine responses.[4] Table II shows that many of the 17-substituted estra-

(13) (a) R. A. Edgren and D. W. Calhoun, *Am. J. Physiol.*, **189**, 355 (1957); (b) R. A. Edgren, D. W. Calhoun, R. L. Elton, and F. B. Colton, *Endocrinology*, **65**, 265 (1959).

(14) A. D. Cross, I. T. Harrison, F. A. Kind, E. Farkas, R. Kraay, and R. I. Dorfman, *Steroids*, **4**, 423 (1964).

(15) R. L. Elton and R. A. Edgren, *Endocrinology*, **63**, 464 (1958).

(16) R. L. Elton, D. W. Calhoun, and E. F. Nutting, submitted for publication.

(17) R. L. Elton, P. D. Klimstra, F. B. Colton, and V. A. Drill, submitted for publication.

(18) M. Roland, M. J. Clyman, A. Decker, and W. B. Ober, *Fertility Sterility*, **15**, 143 (1964).

diol derivatives are capable of inducing deciduogenesis in the rabbit. The most potent compounds in this regard were the 17-allyl, 17-(2-methylallyl), and 17-(2-butynyl) derivatives. It is interesting to note that while both 17-(2-butynyl)estradiol 3-acetate and the 17-(2-methylallyl) derivative were active as deciduogens, their estrogenic activities were markedly different. As yet, there is no suitable explanation for this disparity. Because of its unique properties, 17-(2-butynyl)estradiol 3-acetate is currently undergoing clinical evaluation for the treatment of menstrual disorders and for controlling ovulation.

As anticipated, the C-17 epimer, 17-(2-methylallyl)-estra-1,3,5(10)-triene-3,17α-diol, was totally devoid of activity in all of the above categories.

A more detailed biological description of the estradiol derivatives will be reported elsewhere in the near future.[19]

Experimental Section[20]

17-Substituted Estra-1,3,5(10)-triene-3,17β-diols. Method A. From Estrone.—A solution of propargyl bromide (24 g) in anhydrous ether (50 ml) was added dropwise with stirring under an atmosphere of nitrogen to Mg turnings (5.4 g) and $HgCl_2$ (0.27 g) in anhydrous ether (200 ml). The reaction mixture was kept cool with a cold-water bath. A solution of estrone (13.5 g) in anhydrous tetrahydrofuran (THF) (400 ml) was added dropwise with stirring and cooling to the reaction mixture. The mixture was refluxed for 3 hr and allowed to cool. A solution of NH_4Cl (30%, 50 ml) was added dropwise with stirring. Anhydrous Na_2SO_4 (30 g) was added and the mixture was filtered. The filtrate was evaporated to dryness *in vacuo* and the crude residue was dissolved in ethanol–acetic acid (9:1, 100 ml). Girard-T reagent (5 g) was added and the mixture was heated on the steam bath for 30 min. The solution was cooled, poured into ice–water, and extracted with CH_2Cl_2. The organic phase was washed with water, dried (Na_2SO_4), and concentrated to dryness *in vacuo*. The residue was dissolved in ether and treated with Darco, and the solvent was removed. The resulting solid was recrystallized from acetone–hexane to give pure 17-(2-propynyl)-estra-1,3,5(10)-triene-3,17β-diol (3.7 g), $\epsilon_{280.5}$ 1980. Chromatography of the residual mother liquors over silica gel afforded additional product (2.4 g), mp 162–165°.

Method B. From Estrone 3-Tetrahydropyranyl Ether.—Estrone (27 g) was converted to the pyranyl ether in a manner similar to that recently described by Cross and associates.[14] The crude ether was dissolved in THF (250 ml) and added dropwise with stirring to the Grignard reagent prepared from β-methallyl chloride (54 g) and Mg (turnings 116 g) in anhydrous ether (150 ml). The reaction temperature was maintained below 10° during the addition. The mixture was allowed to come to room temperature and stirred for an additional 2 hr. Saturated NH_4Cl solution (165 ml) was added with stirring followed by solid anhydrous Na_2SO_4 (20 g). The salts were removed by filtration and washed with THF (125 ml). *p*-Toluenesulfonic acid monohydrate (0.1 g) was added to the filtrate and the solution was stirred at room temperature for 1 hr. The solvent was removed *in vacuo* and the resulting solid recrystallized from ethyl acetate–heptane to give 17-(2-methylallyl)estra-1,3,5(10)-triene-3,17β-diol (20 g), $\epsilon_{280.5}$ 2300.

Method C. By Hydrogenation.—A solution of 17-ethynylestradiol (2.0 g) in pyridine (60 ml) was hydrogenated over 5% Pd–C (0.3 g) at room temperature and atmospheric pressure. After the theoretical uptake had been achieved, the catalyst was removed by filtration and washed with pyridine. The filtrate was concentrated to dryness *in vacuo* and the oily residue was triturated with ether–hexane to afford crystallization. Recrystallization from methanol gave 17-vinylestradiol (1.6 g), mp 146–148°, remelting at 170–171°.

Method D. By Hydrogenation.—A solution of 17-(2-propenyl)estra-1,3,5(10)-triene-3,17β-diol (10 g) in ethanol (250 ml) was hydrogenated over 5% Pd–C (0.15 g) as above. The catalyst and solvent were removed and the residue crystallized from methanol to give 17-propylestra-1,3,5(10)-triene-3,17β-diol (9.6 g) as the monomethanolate. Drying *in vacuo* at 140° gave an analytical sample, $\epsilon_{280.5}$ 2080.

3-Acetates. General Method.—The substituted estradiols (2.5 g) were dissolved in a mixture of pyridine (15 ml) and acetic anhydride (2.5 ml) and allowed to stand at room temperature for 4 hr. The solution was poured into cold water, and the mixture was allowed to stand at room temperature for 1 hr. The resulting precipitate was collected by filtration and washed well with water. If an oil resulted at this stage, it was extracted with ether. The extract was washed with 10% HCl, 5% $NaHCO_3$ solution, and water. The solution was dried (Na_2SO_4) and the solvent was removed under reduced pressure. Recrystallization from the appropriate solvents afforded pure monoacetates, ϵ_{280} 750 ± 20 and ϵ_{275} 720 ± 20.

3,17-Diacetates. General Method.—To a solution of the 17-substituted estradiol (5.0 g) in isopropenyl acetate (100 ml) was added *p*-toluenesulfonic acid monohydrate (0.75 g). The solution was heated at reflux under a Vigreux column and the acetone was allowed to slowly distil for a period of 6 hr. The solution was allowed to cool, ether (200 ml) was added, and the solution was washed with three 50-ml portions of water, two 50-ml portions of 10% $NaHCO_3$ solution, and water (50 ml). The organic phase was dried ($NaSO_4$ and Darco) and the solvent was removed by distillation. Crystallization of the residual oils afforded the diacetates.

17-Acetates. General Method.—To a solution of the 3,17-diacetate (2.0 g) in 10% aqueous methanol or dioxane (50 ml) was added K_2CO_3 (1.0 g) and the mixture was stirred at room temperature for 1 hr. The solution was poured slowly into ice–water and resulting product was extracted with ether. The ether solution was washed with water and dried, and the solvent was removed under reduced pressure. The resulting residue was recrystallized from the appropriate solvent system.

(19) R. L. Elton, R. E. Counsell, P. D. Klimstra, and E. F. Nutting, *Experientia*, in press.

(20) The elemental analyses, optical rotations, and ultraviolet spectra were furnished by Dr. R. T. Dillon, Mr. E. Zielinski, and Mr. J. Damascos of our analytical department. The rotations were obtained in chloroform and the ultraviolet spectra in methanol. The melting points were taken on a Fisher-Johns apparatus and are corrected.