21690-26-6; **2**, 21748-36-7; **4a**, 21690-24-4; **4b**, 21690-25-5; **5**, 21690-27-7; **8**, 6285-99-0; **9**, 21690-29-9; **10a**, 21690-30-2; **10b**, 21690-31-3; **11**, 21690-32-4; **13**, 21690-33-5; **15**, 21690-34-6; **16**, 21690-35-7; **17**, 21690-36-8; **18**, 21690-37-9; **19**, 21690-38-0; **21**, 21690-63-1.

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The Reformatsky Reaction with Halolactones. II. Reaction with Steroid Ketones

HOUSHANG TORABI, ROY L. EVANS,[1] AND HOMER E. STAVELY[2]

Department of Biological Chemistry, Mead Johnson Research Center, Evansville, Indiana 47721

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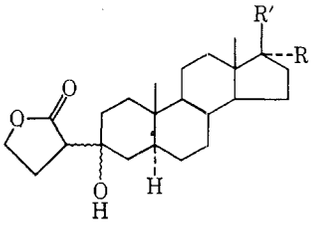
Steroids with 3-, 17- and 20-ketone groups have been condensed with α-bromo-γ-butyrolactone to form hydroxylactonyl addition products or the corresponding dehydrated substances. When Δ^4-3-keto steroids are condensed mixtures of the addition product and $\Delta^{3,5}$- and/or $\Delta^{3(3')4}$-dienes are obtained. The $\Delta^{3(3')4}$-diene is the end product of acid treatment. For obvious steric reasons, the C_{20}-ketone group of pregnenolone is totally unreactive, but 16-dehydropregnenolone reacts normally. The C_{17} ketone in steroids is also unreactive but low yields of a normal condensation product can be obtained.

It has been found that α-bromo-γ-butyrolactone is a suitable reactant, in place of α-bromo ester, in the Reformatsky reaction with aromatic carbonyl compounds.[3] In this paper we wish to report the condensation between α-bromo-γbutyrolactone and steroidal 3, 17, and 20 ketones.[4]

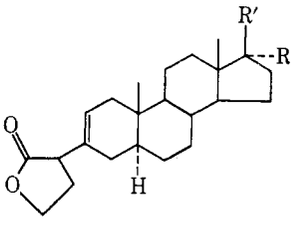
Condensations were carried out with two saturated 3-keto steroids, cholestanone, and 17α-methyldihydrotestosterone acetate. In both cases the primary addition products corresponding to structure **1** were isolated.

A priori it was expected that the bulky lactonyl group in **1a** and **1b** would be equatorial. The nmr spectrum of the dehydration product of **1a** showed the presence of an olefinic proton (δ 5.55 ppm) with an intensity equal to 0.35 that of CH_2–O (δ 4.31 ppm). This corresponds to 70% **2a** (or its Δ^3 isomer) and 30% **3a**. Structure **2a** would be expected from the epimer possessing an axial (3α) hydroxy group, while the 3β-hydroxy epimer would favor structure **3a**. Therefore, it seems justified to conclude either that the product (**1a**), as isolated, is a mixture of the two hydroxy epimers in which the 3α-hydroxy epimer predominates, or that **1a** is essentially only the 3α-hydroxy epimer, which yields an equilibrium mixture of **2a** and **3a** on dehydration.[5]

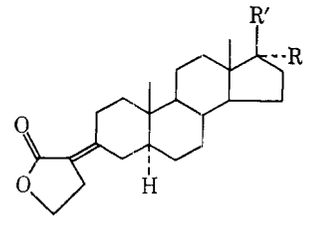
Reformatsky reactions carried out with steroids having a Δ^4-3-keto system were more complicated. When iodine was used to catalyze the reaction the hydroxy addition product **4** was partially or totally dehydrated, but with catalytic mercuric chloride instead of iodine less dehydration occurred. Three dehydrated products are possible (**5**, **6**, and **7**). No evidence for the



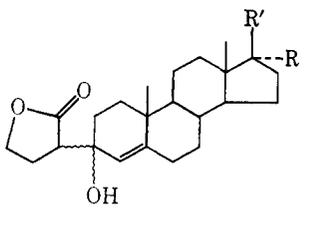
1a, R = H; R′ = C_8H_{17}
b, R = CH_3; R′ = $OCOCH_3$



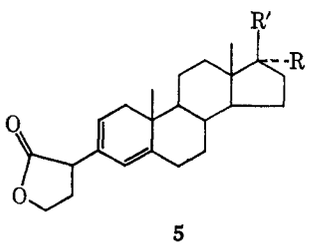
2a, R = H; R′ = C_8H_{17}
b, R = CH_3; R′ = $OCOCH_3$



3a, R = H; R′ = C_8H_{17}
b, R = CH_3; R′ = $OCOCH_3$



4a, R = H; R′ = $OCOCH_3$
b, R = H; R′ = $COCH_3$
c, R = CH_3; R′ = $OCOCH_3$



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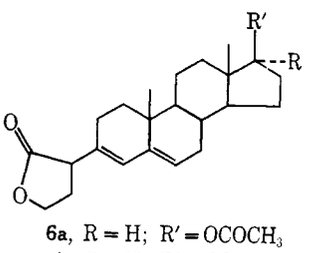
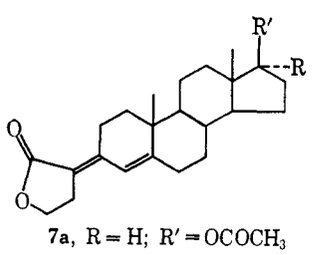
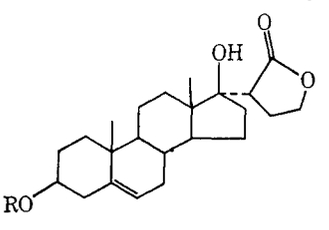


6a, R = H; R′ = $OCOCH_3$
b, R = H; R′ = $COCH_3$
c, R = CH_3; R′ = $OCOCH_3$



7a, R = H; R′ = $OCOCH_3$
b, R = H; R′ = $COCH_3$
c, R = CH_3; R′ = $OCOCH_3$



8a, R = $COCH_3$
b, R = H

(1) Deceased.

(2) To whom correspondence should be addressed: Medical College of Ohio at Toledo, Toledo, Ohio 43614.

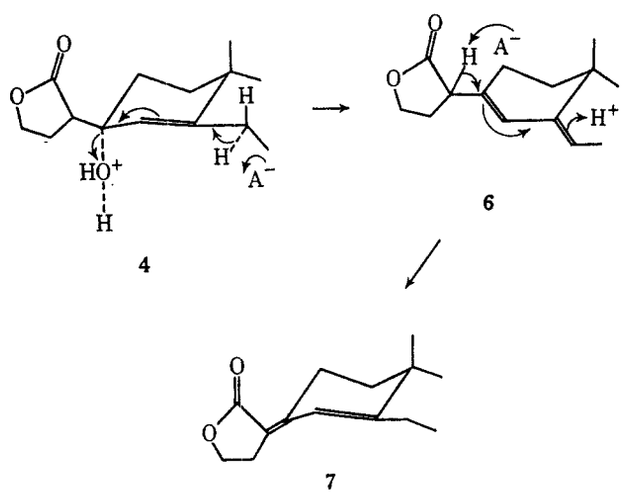
(3) H. Torabi, R. L. Evans, and H. E. Stavely, *J. Org. Chem.* **34**, 3792 (1969).

(4) R. L. Evans and H. E. Stavely, U. S. Patent 3,248,393 (1969).

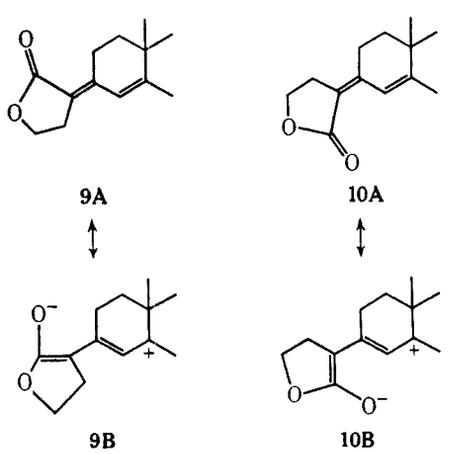
(5) Since the preparation of this manuscript, L. Rand and C. S. Rao [*J. Org. Chem.*, **33**, 2704 (1968)] reported that the Reformatsky reaction of cholestanone with ethyl bromoacetate afforded a mixture of 3α- and 3β-hydroxy epimers in a 3:2 ratio.

formation of **5** was found.[6] Steroids with structures **6** and **7**, however, were present in every case. Structural assignment for the compounds having structure **6** was made on the basis of nmr and ultraviolet spectroscopy. These compounds possess two olefinic protons in the nmr and exhibit ultraviolet absorption maxima at 239 mμ (ε ~ 24,000). The compounds having structure **7**, on the other hand, possess only one olefinic proton and maxima at 293 mμ (ε ~27,000). It was noticed that a reaction catalyzed with mercuric chloride or a reaction which did not undergo a subsequent extended acid catalysis yielded a higher proportion of **6**. This suggests that dehydration of the hydroxy addition product may proceed according to Scheme I. There is conclusive evidence that **6** is converted into **7** on extended acid catalysis.

SCHEME I

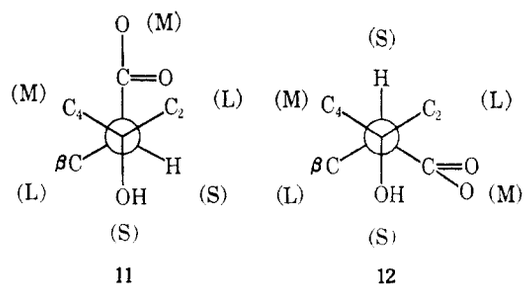


In deciding between the two geometric isomers of the 3(3′),4-diene structure, ultraviolet data are consistent with the structure **9A**, in which the lactone carbonyl is adjacent to steroid C_2. As shown in **9B** and **10B** the dipolar excited state in **9B** (corresponding to **7**) is *s-trans*, whereas in **10B** it is *s-cis*. It is known



that ultraviolet absorption bands arise from transitions to excited states, and that *s-trans* structures of either the ground or excited states have maxima which appear at different wavelengths and are of higher intensity than those of *s-cis* structures. Experimentally, for compounds **7**, **15**, and **17**, ε values of 25,000–27,000 (λ 292 mμ) were obtained. These values are consistent for the structure **9A**, whereas an ε value of about 14,000 is expected for its geometrical isomer **10A**.[7]

There is no agreement concerning the mechanism of the Reformatsky reaction,[8] and speculation concerning the mechanism or the degree to which the reaction is under kinetic or equilibrium control is not pertinent here. On the assumption that the activation energies for the two transition states corresponding to the two possible diastereoisomeric products (both with axial 3α-OH groups) are about the same, the relative stability of the two diastereoisomers may influence which of them will predominate. On the basis of free-energy considerations the diastereoisomer of **4** corresponding to the Newman projection (showing the bond between steroid C_3 and lactone) shown in **12** would be favored over **11**.[9]



(S, M, and L refer to the size of the groups, small, medium, and large, determined by atomic volumes and bond lengths rather than by weight)

Dehydration of the favored diastereoisomer **12** would result in a structure **9A** in which the lactone carbonyl is adjacent to steroid C_2. A similar Newman projection can be depicted for the two possible diastereoisomers of the 3β-hydroxy addition product. The energetically favored diastereoisomer in this case is also the one which leads to the structure **9A**. Thus, although unequivocal proof is lacking, we prefer structure **9A** (corresponding to **7**, **15**, and **17**) for the dehydration product, and the diasteroisomer corresponding to the Newman projection **12** for the 3-hydroxy-3-lactonyl steroids.

Reaction was effected between α-bromo-γ-butyrolactone and the 17-keto group of dehydroisoandrosterone acetate, but in this case the yield of **8a** was quite low, perhaps owing to the presence of the adjacent, bulky β-axial C_{13}-methyl group.

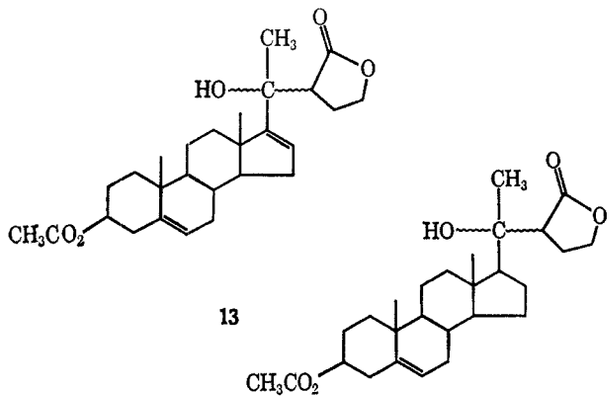
The attempted reaction of the C_{20}-keto group in pregnenolone acetate with the same bromolactone failed completely. In this case the steric factors due to the adjacent β-axial C_{13} CH_3 and the β-C_{17} $COCH_3$ group are

(6) $\Delta^{2,4}$ steroids isomerize into $\Delta^{3,5}$ steroids by acid treatment: H. E. Stavely and W. Bergmann, *J. Org. Chem.*, **1**, 575 (1936).

(7) These conclusions are from the work of E. A. Braude and coworkers. For a discussion of this topic and references see W. Klyne, "Progress in Stereochemistry," Butterworth and Co. (Publishers) Ltd., London, 1954, pp 128–155. In comparing *s-cis* and *s-trans* pairs, ε values of the latter are two to three times larger than those of the *s-cis* compound, and are usually in the 20,000–30,000 range. It has been shown that the intensity of absorption is approximately proportional to the square of the length of the dipole. For the two geometric isomers in **9** and **10** the dipole distances (measured on Dreiding models) are 5.6 and 4.0 Å, respectively. Therefore, from the relationship ϵa^2 the intensity of the maxima for **9A** should be approximately twice as great as for **10A**.

(8) It has been suggested by W. R. Vaughn, *et al.*, *J. Org. Chem.*, **30**, 1790 (1965), that the active agent is the bromozinc enolate, rather than a substance containing a C–Zn–Br group.

(9) E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, p 138. Here only steric effects are considered, as models indicate little possibility of hydrogen bond formation between the 3α-OH proton and the lactonyl carbonyl group.



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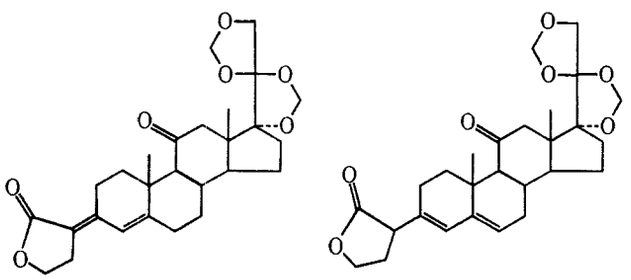
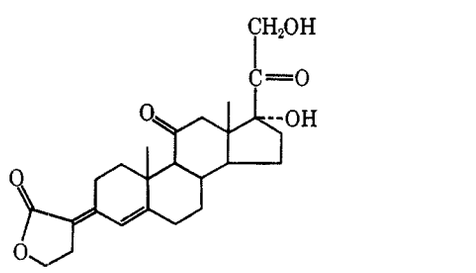
14



15 16



17

insurmountable.[10] This steric crowding is much decreased in the case of 16-dehydropregnenolone acetate; in this compound the $C_{17}COCH_3$ is situated at approximately a 90° angle to the $C_{13}CH_3$ group. With this substance a Reformatsky reaction with α-bromo-γ-butyrolactone afforded two isomeric products whose elemental analysis and spectral data were consistent for structure **13**. No attempts were made to determine the stereochemistry of the two C_{20} epimers. The product isolated was shown to be a mixture of C_{20} epimers by chromatographic separation of the two. Hydrogenation of **13** with Pd in ethanol, which with other Δ^{16} steroids reduces the Δ^{16} bond selectively,[11] gave dihydro product **14**, the normal Reformatsky product to be expected from pregnenolone acetate if steric factors do not interfere with the reaction.

Reaction of the bismethylenedioxy derivative of cortisone afforded the normal products **15** and **16**. On hydrolysis with formic acid **15** was converted into the cortisone derivative **17**.

(10) M. Mousseron-Canet and Y. Beziat [*Bull. Soc. Chim. Fr.*, **6**, 2572 (1968)] have recently reported a conventional Reformatsky reaction of a 20-keto steroids with ethyl α-bromoacetate or propionate.

(11) R. E. Marker, R. B. Wagner, P. R. Ulshafer, E. L. Wittbecker, D. P. Goldsmith, and C. H. Ruof, *J. Amer. Chem. Soc.*, **69**, 2167 (1947). It is presumed that the stereochemistry at C_{17} is α.

Experimental Section

Activated zinc for use in Reformatsky reactions was prepared from reagent grade 30 mesh zinc by the method of Rubin and Blossey.[12] All glassware and solid reagents were oven dried. All liquid reagents were A. R. grade except tetrahydrofuran, which was distilled over lithium aluminum hydride. Nmr spectra were measured in deuteriochloroform solution using tetramethylsilane as internal reference on a Varian Associates A-60 nmr spectrometer.

General Procedure for the Reaction of Steroidal Ketone with α-Bromo-γ-butyrolactone.—The reacting materials were brought in contact by one of two methods. In the first method (a) a solution of α-bromo-γ-butyrolactone (3 mol/1 mol of steroid) in a proper solvent (2–3 l./1 mol of steroid) was added dropwise over 30 min to 1 hr to a flask containing steroidal ketone, freshly activated zinc (about 7.5 g-atom/1 mol of steroid), and a crystal of iodine covered with an equal portion of the same solvent. Most of the reactions recorded in this report have been carried out by this method.

In the second method (b) the solution of bromobutyrolactone and steroidal ketone in the solvent was added dropwise to a flask containing activated zinc and iodine crystal covered with the same solvent. The material ratio was as in method a.

In both cases the reaction was performed under nitrogen and a gentle heat was supplied externally during the course of addition. The reaction mixture was then refluxed for an additional 3 hr, during which portions of activated zinc (an additional total of 7.5 g-atom) was added. The unreacted zinc was usually removed mechanically and the reaction mixture was then treated with dilute hydrochloric or sulfuric acid and extracted with benzene, ethyl acetate, or a mixture of the two. The organic extract was washed with several portions of water, dried over magnesium sulfate, and evaporated under reduced pressure to give a crude reaction product. Purification of this crude product will be discussed individually.

3ξ-(4,5-Dihydro-2-oxo-3-furyl)-3ξ-hydroxy-5α-cholestane, 1a.—Cholestanone (3.8 g, 0.01 mol) and α-bromo-γ-butyrolactone (2.5 g) in benzene as solvent were reacted according to the general procedure, method b. The crude solid product was washed with ether and crystallized from ethanol (0.65 g, 14%), mp 174–177°. The ir and nmr spectra were consistent for structure **1a**.

Anal. Calcd for $C_{31}H_{52}O_3$: C, 78.76; H, 11.09; O, 10.15. Found: C, 78.93; H, 11.24; O, 10.14.

Dehydration of Compound 1a.—Compound **1a** (0.3 g, 0.63 mol) was dissolved in benzene (50 ml) containing *p*-toluenesulfonic acid (30 mg). The mixture was refluxed for 3 hr with removal of water in a Dean–Stark trap. The benzene solution was washed with water, dried over $MgSO_4$, and evaporated. The residue was crystallized from ether to give 0.17 g of the dehydrated material, mp 190–195°. The ir and elemental analysis were consistent with the dehydrated structure.

Anal. Calcd for $C_{31}H_{50}O_2$: C, 81.88; H, 11.08; O, 7.04. Found: C, 82.07; H, 11.36; O, 7.26.

17β-Acetoxy-3ξ-(4,5-dihydro-2-oxo-3-furyl)-17α-methyl-5α-androstan-3ξ-ol, 1b.—The reaction of 17α-methyldihydrotestosterone acetate (4.88 g, 0.016 mol) and α-bromo-γ-butyrolactone (8 g) in benzene was accomplished according to the general procedure, method b. The crude product was chromatographed on acid-washed alumina. Crystallization from ethanol gave 1.3 g of **1b**, mp 223–227°. The ir, uv, and nmr spectra were consistent for this structure.

Anal. Calcd for $C_{26}H_{40}O_5$: C, 72.19; H, 9.32; O, 18.49. Found: C, 71.92; H, 9.39; O, 18.21.

17β-Acetoxy-3-(4,5-dihydro-2-oxo-3-furylidene)androst-4-ene, 7a.—The reaction of testosterone acetate (3.30 g, 0.01 mol) and α-bromo-γ-butyrolactone (5.0 g) in 1:1 ether–benzene was accomplished according to the general procedure, method a. The total crude product was subjected to dehydration as in **1a**. The resulting crude product was crystallized from ether to give 1.5 g crystalline solid which after several recrystallizations from ether (50% recovery) gave a sample of mp 171–178°, $[\alpha]^{25}D$ 149.3° (*c* 1%, $CHCl_3$). The nmr, ir, and uv (λ 293 mμ, ε 27,000) spectra were consistent for the 3(3′),4-diene structure **7a**.

Anal. Calcd for $C_{25}H_{34}O_4$: C, 75.34; H, 8.60; O, 16.06. Found: C, 75.60; H, 8.46; O, 16.23.

3-(4,5-Dihydro-2-oxo-3-furylidene)pregn-4-en-20-one, 7b, and Its 3,5-Diene Isomer, 6b. A.—A reaction was carried out with

(12) M. B. Rubin and E. C. Blossey, *Steroids*, **1**, 453 (1963).

progesterone (6.2 g, 0.02 mol) and α-bromo-γ-butyrolactone (9.9 g) in THF as solvent according to the general procedure, method a (7-hr reflux period). The crude product was crystallized in methanol upon refrigeration to give *ca.* 1.4 g of a solid having ultraviolet absorption maxima at 239 mμ. By column chromatography on Mallinckrodt silicic acid two isomeric products were obtained. The material eluted first was recrystallized a few times from methanol to give *ca.* 0.25 g of 3,5-diene product, **6b**: mp 229–231°; uv max (EtOH) 239 mμ (ε 25,000 shoulder); nmr δ 0.66 (s, 3, 18-methyl), 0.94 (s, 3, 19-methyl), 2.12 (s, 3, CH_3CO), 4.30 (t, 2, CH_2O), 5.36 (1, C=CH, C_6), and 5.61 (s, 1, C=CH, C_4); ir consistent.

Anal. Calcd for $C_{25}H_{34}O_3$: C, 78.49; H, 8.96. Found: C, 77.78; H, 8.64.

The second chromatographic component, *ca.* 0.3 g was recrystallized from methanol to give the isomer **6a**, mp 177–182°. The ir, uv (λ 293 mμ, ε 27,300), and nmr spectra were consistent for this structure.

Anal. Found: C, 78.13; H, 8.83.

B.—A similar reaction was performed in 1:1 benzene–ether (3-hr reflux period). From crude product by crystallization alone 0.8 g of analytically pure **6a** was obtained. The mother liquor indicated the presence of the isomer **6b** (λ 239), but no attempt for isolation was made.

C.—In another similar reaction in THF where 0.3 g of mercuric chloride was used as a catalyst the isomer **6b** was obtained as the main product. This was converted into its isomer **6a** by overnight treatment with methanolic hydrochloric acid.

17β-Acetoxy-3-(4,5-dihydro-2-oxo-3-furylidene)-17α-methylandrost-4-ene, 7c.—The title product was obtained by the reaction of 17α-methyltestosterone acetate (5.17 g, 0.015 mol) and α-bromo-γ-butyrolactone (7.4 g) dissolved in benzene according to the general procedure, method b. Chromatography of the crude product on acid-washed alumina by recrystallization from benzene and finally from ether gave 2.8 g, mp 205–210°, whose ultraviolet spectrum suggested the presence of **6c** and **7c**. Compound **7c** was isolated by further chromatography on acid-washed alumina and subsequent recrystallization from ethanol. The yield was about 1.4 g: mp 210–222°; λ_{max} 295 mμ (ε 25,800).

Anal. Calcd for $C_{26}H_{36}O_4$: C, 75.69; H, 8.80; O, 15.51. Found: C, 75.48; H, 8.98; O, 15.38.

3β-Acetoxy-17α-(4,5-dihydro-2-oxo-3-furyl)androst-5-en-17β-ol, 8a.—The title compound was obtained by the reaction of testosterone acetate (6.6 g, 0.02 mol) and α-bromo-γ-butyrolactone (9.9 g) in 1:1 ether–benzene according to the general procedure, method a. The crude product was chromatographed on an acid-washed alumina column to yield pure starting material with better than 90% recovery. A second fraction was also obtained which was recrystallized several times from ethanol to give 0.33 g of **8a**, mp 205–207°, $[\alpha]^{25}D$ −49.6° (*c* 1%, $CHCl_3$). The spectral data were consistent with this structure.

Anal. Calcd for $C_{25}H_{36}O_5$: C, 72.08; H, 8.71; O, 19.21. Found: C, 72.05; H, 8.68; O, 19.05.

Deacetylation of Compound 8a.—The steroid acetate **8a** was subjected to hydrolysis with methanolic KOH. The solution was acidified and the product was extracted with ethyl acetate. From the acetate extract a crude product was obtained which was recrystallized several times from methanol to give **8b** (*ca.* 60% yield), mp 210–218°. The ir and nmr spectra were consistent for this structure.

Anal. Calcd for $C_{23}H_{34}O_4$: C, 73.76; H, 9.15; O, 17.09. Found: C, 73.20; H, 8.85; O, 16.90.

20ξ-(4,5-Dihydro-2-oxo-3-furyl)-3β,20ξ-dihydroxypregn-5,16-diene 3β-Acetate, 13.—16-Dehydropregnenolone acetate (7.12 g, 0.02 mol) was treated with α-bromo-γ-butyrolactone (9.3 g) in 1:1 benzene–ether according to the general procedure, method a. The crude reaction product was subjected to column chromatography on silicic acid. Two isomeric products were obtained whose elemental analysis were consistent for the structure **13**. The product eluted first had mp 198–201° (ether); $[\alpha]^{25}D$ −87.5° (*c* 1%, $CHCl_3$); nmr δ 0.99 (*s*, 3, 18-methyl), 1.07 (s, 3, 19-methyl), 1.64 (s, 3, 21-methyl), 2.08 (s, 3, CH_3CO), 2.67 (s, 1, OH), 4.38 (2, CH_2O), 5.52 (1, C=CH, C_6), and 5.69 ppm (1, C=CH, C_{16}).

The second product eluted from the column had mp 185–187° (ethanol); $[\alpha]^{25}D$ −58.4° (*c* 1%, $CHCl_3$); nmr δ 1.06 (s, 3, 18-methyl), 1.07 (s, 3, 19-methyl), 1.43 (s, 3, 21-methyl), 2.04 (s, 3, CH_3CO), 3.88 (s, 1, OH), 4.30 (2, CH_2O), 5.45 (1, C=CH, C_6), and 5.57 (1, C=CH, C_{16}).

Anal. Calcd for $C_{27}H_{38}O_5$: C, 73.27; H, 8.65. Found for first product: C, 72.77; H, 8.72. Found for second product: C, 73.27; H, 8.65.

Hydrogenation of Compound 13.—A small portion of the isomeric mixture **13** was hydrogenated at atmospheric pressure in absolute ethanol with 5% palladium on charcoal. After 2 hr ~1 equiv of H_2 had been used. The hydrogenation product was purified on a preparative tlc plate and recrystallized from ethyl acetate to give compound **14**: mp 246–248.5; $[\alpha]^{26}D$ −52.3° (*c* 1%, $CHCl_3$); ir consistent; nmr δ 0.95 (s, 3, 18-methyl), 1.04 (s, 3, 19-methyl), 1.17 (s, 3, 21-methyl), 2.03 (s, 3, CH_3CO), 4.25 (m, 2, CH_2O), 4.57 (1, CHO), and 5.40 ppm (1, C=CH, C_6).

Anal. Calcd for $C_{27}H_{40}O_5$: C, 72.94; H, 9.07. Found: C, 73.05; H, 9.14.

17α,20:20,21-Bismethylenedioxy-3-(4,5-dihydro-2-oxo-3-furylidene)pregn-4-ene-3,11-dione, 15, and Its Diene Isomer, 16.—Cortisone BMD[13] (16.1 g, 0.04 mol), α-bromo-γ-butyrolactone (19.8 g) in 1:1 benzene–ether (400 ml) was reacted according to the general procedure, method a (5-hr reflux period). The crude product was crystallized from methanol to yield a crystalline solid (13.8 g) which, by tlc, consisted mainly of two products and the starting material. By repeated recrystallization a pure product corresponding to structure **16** (4.5 g) was obtained: mp 233.5–235.5°; ir consistent; uv max. (EtOH) 233, 240 mμ (ε 21,200, 21,700 shoulders); nmr δ 0.83 (s, 3, 18-methyl), 1.15 (s, 3, 19-methyl), 4.02 (s, 2, CH_2O, BMD), 4.53 (t, 2, CH_2O, lactone), 5.03 (d, J = 3 Hz, OCH_2O), 5.13 (d, J = 8 Hz, OCH_2O), 5.48 (1, C=CH, C_6), and 5.95 ppm (1, C=CH, C_4).

Anal. Calcd for $C_{27}H_{34}O_7$: C, 68.92; H, 7.28. Found: C, 68.94; H, 7.29.

The total mother liquor was evaporated and chromatographed on silicic acid. Elution with 3:7 benzene–chloroform gave 5.5 g of a crystalline solid which was shown by uv to be a mixture of about 2 g of compound **16** and 3.5 g of its 3(3′),4-diene isomer **15**. This mixture was subjected to acid-catalyzed rearrangement according to the procedure described below to give 4.2 g of **15**, mp 246.5–247.5°.

Rearrangement of 16 into 15.—Compound **16** (0.5 g), and *p*-toluenesulfonic acid (0.2 g) in dry benzene (200 ml) were refluxed for 20 hr. The supernatant was washed with water, dried and evaporated to give 0.447 g solid, mp 238–242°. This was dissolved in ethyl acetate, decolorized over active carbon and recrystallized to give 0.3 g of compound **15**: mp 246.5–247.5°; ir consistent; uv max (EtOH) 292 mμ (ε 27,200); nmr δ 0.81 (s, 3, 18-methyl), 1.29 (s, 3, 19-methyl), 3.95 (s, 2, CH_2O, BMD), 4.30 (t, 2, CH_2O, lactone), 5.03 (d, J = 3 Hz, OCH_2O), 5.13 (d, J = 8 Hz, OCH_2O), and 7.43 ppm (s, 1, C=CH).

Anal. Calcd for $C_{27}H_{34}O_7$: C, 68.92; H, 7.28. Found: C, 68.84; H, 7.30.

3-(4,5-Dihydro-2-oxo-3-furylidene)-17α,21-dihydroxypregn-4-ene-11,20-dione, 17.—The BMD derivative **15** (1.0 g) was dissolved in formic acid (40 ml) and heated on a steam bath for 2 min. Then 50 ml water was added and heating was continued for 45 min. The mixture was poured in water and the solid formed was separated by filtration and chromatographed on silicic acid. The fraction obtained by eluting with a mixture of 15% acetone and 85% benzene was evaporated and recrystallized from acetone–methanol to give 0.2 g of compound **17**, mp 242–243°. The ir, uv [λ max. 292 mμ (ε 25,400)], and nmr spectra were consistent with the assigned structure.

Anal. Calcd for $C_{25}H_{32}O_6$: C, 70.07; H, 7.53. Found: C, 69.82; H, 7.53.

Registry No.—**1a**, 6194-01-0; **1b**, 6194-06-5; **6a**, 21727-62-8; **6b**, 21727-63-9; **7a**, 6194-08-7; **7c**, 6194-05-4; **8a**, 21813-04-7; **8b**, 21727-66-2; **13**(20*R*), 21727-67-3; **13** (20*S*), 21727-92-4; **14**, 6841-27-6; **15**, 21766-48-3; **16**, 21727-69-5; **17**, 21727-70-8.

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(13) Prepared by the method of R. E. Beyler, R. M. Moriarity, F. Hoffman, and L. H. Sarett, *J. Amer. Chem. Soc.*, **80**, 1517 (1958).