quaternary bromide salt (0.27 g, 0.001 mole) was treated with an equiv amt of freshly prepared AgCl to furnish 0.23 g of **11**: crystd (EtOH–Et_2O 15:1), mp 223–235°, $[\alpha]^{26}D$ +41.4 (*c* 1.15, EtOH). The nmr spectrum included a signal at 5.35 (2 H, singlet, NCH_2-Ph) and was identical with the spectrum of **8** except for the absence of the *N*-Me resonance at 6.77 (Table I).

(1*S*,4*S*)-*N*,*N*-Dimethyl-2-oxa-5-azoniabicyclo[2.2.1]heptane Chloride (9).—An EtOH soln (4 ml) contg 0.4 g of **5** was mixed with 10 ml of MeI and allowed to stand for 24 hr during which time crystn of product (0.50 g) took place. Two recrystns (ab EtOH) afforded the pure methiodide, mp 292–294° dec. This salt (0.50 g, 0.002 mole) was dissolved in 10 ml of H_2O and treated with 0.35 g (0.0025 mole) of freshly prepared AgCl to give 0.29 g (92%) of product after crystn (EtOH–Et_2O 10:1): mp 292–294° dec; $[\alpha]^{26}D$ +59.0° (*c* 1.1, EtOH). The nmr spectrum included signals at 6.67 and 6.71 (6 H, two singlets, N-$(CH_3)_2$) (Table I). *Anal.* ($C_7H_{14}ClNO$) C, H, N.

(1*S*,4*S*)-*exo*-5-Trideuteriomethyl-*endo*-5-methyl-2-oxa-5-azoniabicyclo[2.2.1]heptane Chloride (12).—An EtOH soln (6 ml) contg 0.6 g of **5** was treated with 1.48 of CD_3Br in a sealed Carius tube for 24 hr. The yield of product (mp 300° dec) which crystd spontaneously from soln was 0.44 g. The Et_2O treated mother liquor yielded an additional 0.07 g of product which had an ir spectrum identical with that of the major fraction of product. The bromide salt (0.40 g, 0.0019 mole) was dissolved in about 10 ml of H_2O and treated with 0.35 g (0.0025 mole) of freshly prepd AgCl to obtain after recrystn (EtOH–Et_2O) 0.27 g (86%) of product, mp 300° dec, $[\alpha]^{26}D$ +58.0° (*c* 1.21, EtOH). The nmr spectrum was identical with that of **9** except that the signal corresponding to exo *N*-Me was of very low intensity (Table I).

(1*S*,4*S*)-*exo*-5-Methyl-*endo*-5-trideuteriomethyl-2-oxa-5-azoniabicyclo[2.2.1]heptane Chloride (13).—An EtOH soln (25 ml) contg 0.25 g of **6** was mixed with 5 ml of MeI and allowed to stand for 24 hr during which time crystn of a product occurred. The crude (0.44 g) was twice crystd (abs EtOH), mp 297° dec. Material obtained from the mother liquor was identical in all respects with the product that crystd. The quaternary iodide salt (0.35 g, 0.0013 mole) was dissolved in 10 ml of distd H_2O and the soln treated with 0.35 g (0.0025 mole) of freshly prepared AgCl. Crystn (EtOH–Et_2O 10:1) afforded 0.21 g (93%) of **13**, mp 300° dec, $[\alpha]^{26}D$ +53.6° (*c* 1.24, EtOH). The nmr spectrum was identical with that of **9** except that the peak corresponding to endo *N*-Me was of very low intensity (Table I).

(1*S*,4*S*)-*N*,*N*-Ditrideuteriomethyl-2-oxa-5-azoniabicyclo[2.2.1]heptane Chloride (14).—An EtOH soln (7 ml) contg 0.7 g of **6** was treated with 1.20 g of CD_3Br in a Carius tube as described for the prepn of **12**. The crude product (0.74 g) was crystd (abs EtOH), mp 297° dec. The bromide salt (0.40 g, 0.0019 mole) was treated with AgCl as previously described to obtain 0.29 g of **14**: crystn (EtOH–EtOAc); mp 300° dec; $[\alpha]^{26}D$ +56.1° (*c* 1.04, EtOH). The nmr spectrum was identical with those of **9**, **12**, and **13** except for the absence of *N*-Me resonances.

Pharmacological Testing.—Testing was carried out with isolated guinea pig ileum obtained from freshly sacrificed animals (av wt, 300 g). Pieces of ileum were sutured at each end through the mesenteric side of the organ. The intestinal strips were suspended in a thermostated muscle bath (37.5°) contg 16 ml of modified Tyrode soln,[20] through which was bubbled a continuous flow of Carbogen (95/5). Recording of muscle contractions were made with a lightly loaded (*ca.* 500 mg) isotonic lever attached to a C. F. Palmer Super 10 recording drum and stand. In studies with antagonists, drugs were allowed to remain in contact with the ileum for 1 min prior to the introduction of an agonist. Ileum strips were rinsed 3 times between administration of doses of agonist compounds.

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Synthesis of Some 6-Chloro-3,7-dihydroxy-Δ⁵-pregnene Derivatives

R. A. LEMAHIEU,* A. BORIS, M. CARSON, AND R. W. KIERSTEAD

Chemical Research Department, Hoffmann-La Roche Inc., Nutley, New Jersey 07110

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The progestational activities and syntheses of the 6-chloro-3,7-dihydroxy-Δ⁵-pregnene derivatives **4a,b,c,d**, and **5** as well as their 16-methylene analogs are reported. Several of these compounds exhibited high progestational activity when tested in the rabbit.

It is well known that cholesterol is converted into 3β-hydroxycholest-5-en-7-one, cholest-5-ene-3β,7β-diol, and the corresponding 7α-hydroxy isomer by different fractions of rat liver homogenate.[1] Cholest-5-ene-3β,7α-diol is also converted by these homogenates into 7α-hydroxycholest-4-en-3-one[2] probably *via* the intermediate formation of a 3-keto-Δ⁵-steroid. If 3-hydroxy-Δ⁵-pregnenes are metabolized in this manner, dehydration of the resultant 7-hydroxy metabolite would lead to the 4,6-dien-3-one system. The high activity of such progesterone derivatives, incorporating the 6-chloro-4,6-diene system, is well known.[3] It is also reported that various 3-hydroxy-Δ⁵-pregnenes have the same activity as the corresponding Δ⁴-3-ketones.[4] We therefore felt it to be of interest to prepare some Δ⁵-pregnenes incorporating the 6-chloro-3,7-dihydroxy system.

Chlorination of 3β,17α-diacetoxypreg-5-ene-7,20-dione[5] (**1**) followed by dehydrochlorination with pyridine gave an inseparable mixture of **2** and the 8-Cl impurity **3** (Scheme I). Purification was accomplished by treatment of the mixture with Zn in HOAc which converted **3** into **2**. Reduction of **2** with $LiAl(t\text{-}BuO)_3H$ gave the desired 7-OH isomers **4a** and **5** in 53 and 7% yield, respectively, after column chromatography.

The stereochemistry at C-7 in **4a** and **5** was assigned on the basis of the nmr spectra. In **4a** the C-7 H appeared as a broad signal at δ 3.92 (half-band width ~11 Hz), which is consistent with axial–axial coupling with the C-8 H.[6] The broadening of the signal is prob-

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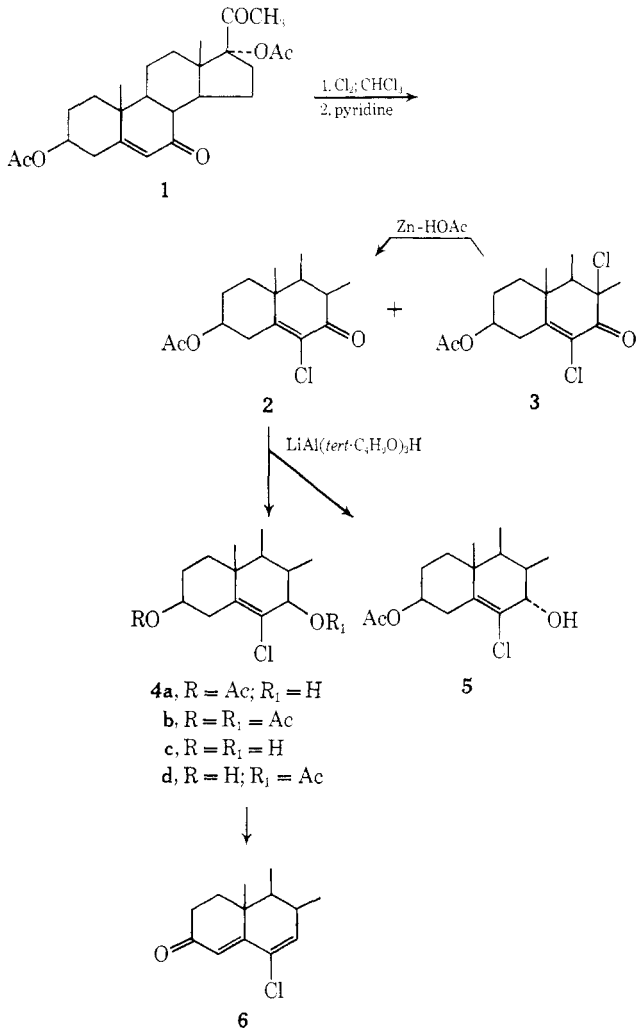
Scheme I

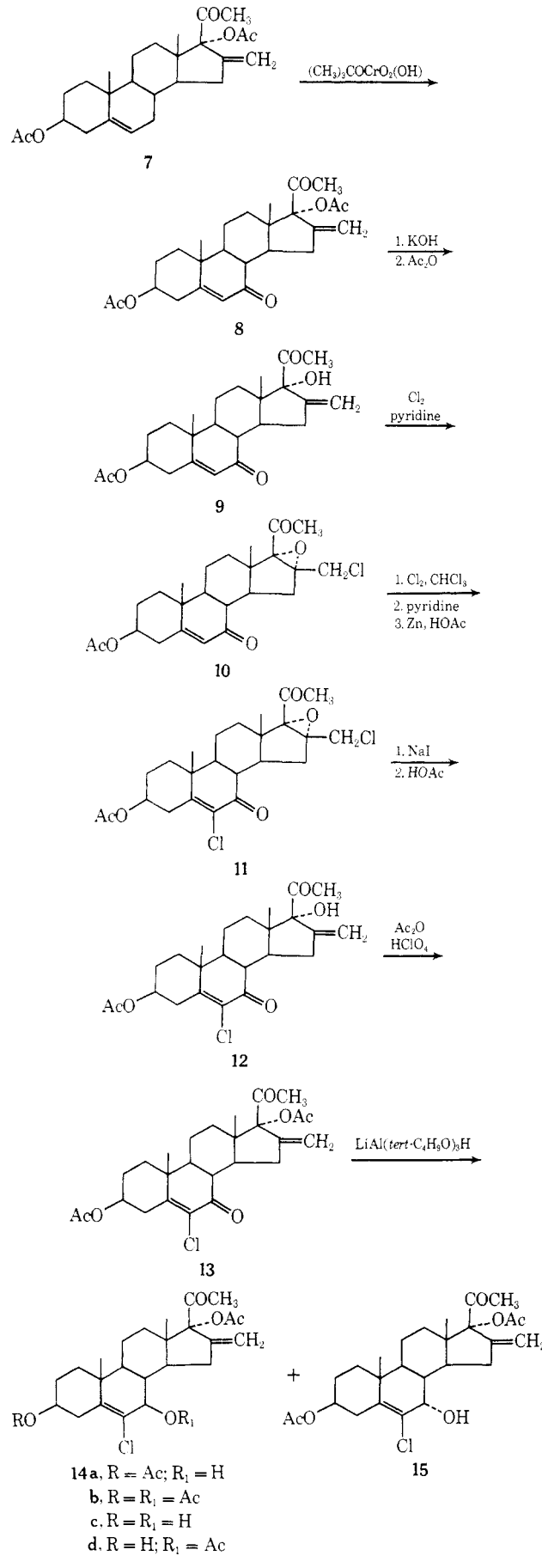


ably due to coupling of the C-7 H to the OH proton as well as homoallylic coupling with the C-4 methylene hydrogens. In **5** the C-7 H appeared as a broad signal at δ 3.94 (half-band width ~7 Hz) which indicates an equatorial–axial coupling with the C-8 proton.[6]

Acetylation of **4a** gave diacetate **4b** and hydrolysis of **4a** afforded diol **4c**. Selective hydrolysis of **4b** with base gave the 3β-hydroxy-7β-acetate **4d**. Oxidation of **4d** with Jones reagent yielded the 6-chloro-4,6-diene **6** by elimination of HOAc from the intermediate Δ^5-3-one.

The progestational potentiating effect of the 16-methylene group in the 6-chloro-4,6-dien-3-one series has been described.[7] We therefore prepared some 16-methylene analogs in the present series of compounds. Oxidation of **7** with *tert*-butyl chromate[5] gave the 7-ketone **8** (Scheme II). Selective chlorination of the 5,6-double bond of **8** was impossible since Cl_2 preferentially added to the 16-CH_2 group. Hydrolysis of **8** with base followed by selective acetylation of the C-3 OH afforded **9**. Treatment of **9** with Cl_2 in the presence of pyridine gave the 16,17-epoxy-16-chloromethyl compound **10**. Chlorination of the 5,6-double bond followed by dehydrochlorination with pyridine and reduction of the 8-chloro impurity with Zn in HOAc yielded **11**. Reductive removal of the protecting group with NaI and HOAc proceeded quantitatively to the 16-methylene-

Scheme II



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17-hydroxy compound **12** which was acetylated with Ac_2O in the presence of $HClO_4$[8] to give **13**. Reduction of the 7-ketone with $LiAl(t\text{-}BuO)_3H$ afforded the 7β- and 7α-OH isomers **14a** and **15** which were separated in 33 and 35% yield, respectively, by careful column chromatography.

The stereochemistry at C-7 of **14a** and **15** was assigned on the basis of the nmr spectra. In **14a** the C-7 H was observed as a broad signal at δ 3.86 (half-bandwidth ~11 Hz) indicating axial–axial coupling with the C-8 H. In **15** the C-7 proton appeared as a broad band at δ 3.87 (half-bandwidth ~6.5 Hz), which is consistent with equatorial–axial coupling with the C-8 proton. Reduction of **13** with $NaB(OMe)_3H$ gave a much greater proportion of the 7β-OH isomer **14a**, although under these conditions some elimination of the 3-acetate occurred. Acetylation of **14a** gave diacetate **14b** and hydrolysis of **14a** gave diol **14c**. Selective hydrolysis of **14b** yielded the 3β-hydroxy 7β-acetate **14d**.

Biological Activity.—The compounds were tested for progestational activity in a modified Clauberg–McPhail assay. Immature, New Zealand white rabbits (600–800 g) were primed with 0.5 μg/day sc of estradiol benzoate in sesame oil for 5 consecutive days. The compounds were dissolved or suspended in sesame oil and administered for 5 consecutive days following estrogen priming. All compounds were tested at dosages of 1, 2, 4, 10, 20, 40, 100, 200, and 400 μg/day both sc and orally with 4–6 rabbits per group. Uterine sections were examined histologically for progestational activity beginning with the highest dosage group and progressing stepwise toward the lowest dosage level. The minimum dosages showing significant secretory development of the uterine endometrium (at least +1 on the McPhail scale) are listed in Table I. Minimum effective doses for 17α-hydroxyprogesterone acetate and for chlormadinone acetate (**6**) are given for comparison purposes. The usual progestational potentiating effect of the 16-CH_2 group was not observed in the 7-hydroxy series.

TABLE I

Compound	Minimum effective dose (μg day) sc	po
17α-Hydroxyprogesterone acetate	4–10	200–400
6	1–2	1–2
2	20–40	20–40
4a	1–2	1–2
4b	4–10	400
4c	2–4	2–4
4d	4–10	4–10
5	4–10	4–10
14a	2–4	2–4
14b	10–20	4–10
14c	10–20	2–4
14d	4–10	4–10
15	20–40	20–40

Experimental Section[9]

6-Chloro-3β,17α-dihydroxypregn-5-ene-7,20-dione Diacetate (2).—To 30.00 g (0.07 mole) of 3β,17α-dihydroxypregn-5-ene-7,20-dione diacetate (**1**)[5] in 200 ml of $CHCl_3$ (filtered through silica gel to remove EtOH), cooled to 5°, was added 89.5 ml (0.77 mole) of a 0.86 *M* soln of Cl_2 in CCl_4 in one portion. The reaction mixt was left at 5° for 16 hr and then at 25° for 2.5 hr. After washing with 5% $NaHCO_3$, the soln was dried ($MgSO_4$) and concd *in vacuo* to an oil. The crude product was dissolved in 250 ml of pyridine and left at room temp for 20 hr. The pyridine was removed at 1 mm (bath temp <25°), 300 ml of Et_2O–CH_2Cl_2 (2:1) was added, and the ext was washed with 1 *N* HCl, 5% $NaHCO_3$, and H_2O and dried ($MgSO_4$). Concn *in vacuo* gave an oil which was taken up in 1 l. of AcOH and stirred for 2 hr at 25° with 15 g of Zn dust. The Zn was removed by filtration and washed with AcOH and the filtrate was concd at 1 mm (bath temp <25°). H_2O was added and the amorphous solid was extd with CH_2Cl_2. The ext was washed with 5% $NaHCO_3$ and dried ($MgSO_4$). Concn *in vacuo* yielded an oil which was crystd twice from CH_2Cl_2–Et_2O to give 17.59 g (54%) of **2**: mp 227–228.5°; λ_{max} 249 mμ (ϵ 11,400); $[\alpha]D$ −144°. *Anal.* ($C_{25}H_{33}ClO_6$) C, H.

6-Chloro-3β,7β,17α-trihydroxypregn-5-en-20-one 3,17-Diacetate and 6-Chloro-3β,7α,17α-trihydroxypregn-5-en-20-one 3,17-Diacetate (4a and 5).—A soln of 5.1 g (0.11 mole) of **2** in 50 ml of anhyd THF was added dropwise under N_2 to 8.4 g (0.033 mole) of $LiAlH(O\text{-}tert\text{-}Bu)_3$ in 80 ml of anhyd THF with stirring over 20 min at 25°. The reaction mixt was stirred at 25° for 2.5 hr and cooled to 0° and 10 ml of Me_2CO was added dropwise followed by 20 ml of H_2O. The mixt was concd to a small vol at reduced pressure, 250 ml of $CHCl_3$ was added followed by 150 ml of H_2O and 100 ml of AcOH. The org layer was sepd and the aq layer extd with $CHCl_3$. The combined ext was washed carefully with 5% $NaHCO_3$, dried ($MgSO_4$), and concd at reduced pressure. Crystn of the crude product from CH_2Cl_2–Et_2O yielded 1.9 g (38%) of **4a**: mp 211.5–214°; $[\alpha]D$ −43.9°. *Anal.* ($C_{25}H_{35}ClO_6$) C, H.

The filtrate from the first crystn was chromatographed on 75 g of silica gel. Elution with 5% EtOAc–C_6H_6 gave several fractions contg pure **4a** (by tlc assay). Crystn of these combined fractions from CH_2Cl_2–Et_2O gave 0.6 g of **4a**, mp 212–214°. Continued elution with 5% EtOAc–C_6H_6 and then with 10% EtOAc–C_6H_6 gave several fractions contg pure **5** (by tlc). These fractions were combined and crystd from CH_2Cl_2–C_6H_{14} to give 0.57 g (11%) of **5**, mp 210–214°. Recrystn from CH_2Cl_2–C_6H_{14} gave the anal. sample: mp 211–215.5°; $[\alpha]D$ −97.9°. *Anal.* ($C_{25}H_{35}ClO_6$) C, H.

6-Chloro-3β,7β,17α-trihydroxypregn-5-en-20-one Triacetate (4b).—Acetylation of 0.500 g of **4a** was accomplished by treatment with 5 ml of redistd Ac_2O and 5 ml of anhyd pyridine at 25° for 20 hr. The soln was concd to dryness at ~1 mm (bath temperature <35°). Xylene was added and concd again to remove traces of Ac_2O. Two crystns of the crude product from CH_2Cl_2–Et_2O gave 0.322 g (60%) of **4b**: mp 242–245°; $[\alpha]D$ −9.7°. *Anal.* ($C_{27}H_{37}ClO_7$) C, H.

6-Chloro-3β,17β,7α-trihydroxypregn-5-en-20-one (4c).—To a soln of 0.500 g (1.07 mmoles) of **4a** in 25 ml of MeOH was added 1.2 ml (1.18 mmoles) of 1.0 *N* NaOH dropwise over 10 min. After stirring at 25° for 70 min, 0.25 ml of AcOH was added and the solvent was removed *in vacuo*. H_2O was added and the product was extd with CH_2Cl_2. The ext was dried ($MgSO_4$) and concd to a foam. Crystn from MeOH gave 0.295 g (65%) of **4c**: mp 259.5–261°; $[\alpha]D$ −28.9°. *Anal.* ($C_{23}H_{33}ClO_5$) C, H.

6-Chloro-3β,7β,17α-trihydroxypregn-5-en-20-one 7,17-Diacetate (4d).—Partial hydrol of 0.200 g (0.39 mmole) of **4b** in 50 ml of MeOH was accomplished by treatment with 0.43 ml (0.43 mmole) of 1.0 *N* NaOH. After stirring at 25° for 4 hr, 0.2 ml of AcOH was added and the solvent was removed *in vacuo*. H_2O was added and the product was extd with CH_2Cl_2. The ext was dried ($MgSO_4$), concd, and crystd from CH_2Cl_2–Et_2O to yield 0.125 g (68%) of **4d**: mp 244.5–246.5°; $[\alpha]D$ +6.2°. *Anal.* ($C_{25}H_{35}ClO_6$) C, H.

Oxidation of 4d.—Jones reagent (0.06 ml) was added to 0.100 g of **4d** in 12 ml of Me_2CO (distd from $KMnO_4$) with stirring at 3°. A stream of N_2 was bubbled through the soln before and during the reaction. After stirring at 3° for 5 min, 1 ml of MeOH was added and most of the solvent was removed *in vacuo*. H_2O was added and the product was extd with EtOAc. The ext was dried ($MgSO_4$) and concd to an oil. Prep tlc on silica gel served to sep the product from some residual **4d**. Crystn from CH_2Cl_2–Et_2O gave 23 mg (27%) of **6**: mp 206–210°; λ_{max} 284

(8) B. E. Edwards and P. N. Rao, *J. Org. Chem.*, **31**, 324 (1966).

(9) All melting points were taken in glass capillaries and are corrected. Rotations are in $CHCl_3$ at 25° at a concn of about 0.7%; uv spectra are of EtOH solns, and ir spectra are in $CHCl_3$ solns. The nmr spectra were detd using a Varian A-60 spectrometer in $CDCl_3$ (Me_4Si). Where anal. are indicated only by symbols of the elements, anal. results obtained for those elements were within ±0.3% of the theoretical values.

mμ (ε 21,200). The mixture melting point with authentic **6** exhibited no depression.

3β,17α-Dihydroxy-16-methylenepregn-5-ene-7,20-dione Diacetate (8).—A *tert*-butyl chromate soln was prepd by adding 226 g (2.26 moles) of anhyd CrO_3 in 220 ml of H_2O dropwise at 25° to 570 ml (6.2 moles) of *tert*-BuOH. After the addn, the soln was stirred for 15 min at 25° and then extd with two 1.2-l. portions of CCl_4. The ext was washed with 1.2 l. of H_2O, dried (Na_2SO_4), and concd to ~600 ml *in vacuo*. The soln was dild to 1.2 l. with CCl_4 and 315 ml of AcOH and 90 ml of Ac_2O were added. This soln was then added dropwise over 90 min to 90.4 g (0.21 mole) of **7** in 400 ml of CCl_4, 210 ml of AcOH, and 60 ml of Ac_2O which was being stirred and heated at 65°. The reaction mixt was stirred at 65° for 16 hr and filtered through a Celite pad and the filtrate was added dropwise over 45 min to 4 l. of 10% oxalic acid soln which was stirred and cooled at 3°. After stirring for 30 min at 25°, the org layer was washed with two 1-l. portions of H_2O, three 1-l. portions of 5% $NaHCO_3$, and finally with H_2O. The ext was dried ($MgSO_4$) and concd *in vacuo* to yield a yellow solid. Two crystns from CH_2Cl_2–Et_2O gave 38.0 g of **8**: mp 174–176°; λ_{max} 236 mμ (ε 14,100); $[\alpha]D$ −242.6°. A second crop of 4.6 g, mp 175–178° was obtained from the mother liquor after two crystns. The total yield is thus 46%. The anal. sample, mp 185.5–188.5°, was obtained after 2 recrystns from CH_2Cl_2–Et_2O. *Anal.* ($C_{26}H_{34}O_6$) C, H.

3β,17α-Dihydroxy-16-methylenepregn-5-ene-7,20-dione 3-Acetate (9).—Hydrol of 42.50 g (0.096 mole) of **8** in 2.1 l. of MeOH under N_2 at 25° was accomplished by adding 36.7 g (0.67 mole) of KOH dissolved in 40 ml of H_2O. After stirring at 25° for 5 hr, the solid which crystd was removed by filtration. The filtrate was concd to 500 ml *in vacuo* and dild with H_2O and the resultant solid was filtered. The combined solids were air dried to yield 27.7 g of the 3,17-diol. The crude product was dissolved in 250 ml of pyridine and 250 ml of Ac_2O and left at 25° for 4.5 hr. Concn to dryness at ~1 mm and 30° gave a tan solid which was crystd from CH_2Cl_2–Et_2O to yield 19.85 g (52%) of **9**: mp 227–229°; λ_{max} 235 mμ (ε 14,950); $[\alpha]D$ −190.6°. The anal. sample, mp 233.5–238°, was obtained after two recrystns from CH_2Cl_2–Et_2O. *Anal.* ($C_{24}H_{32}O_5$) C, H.

16β-Chloromethyl-16α,17α-epoxy-3β-hydroxypregn-5-ene-7,20-dione Acetate (10).—To a soln of 5.0 g (0.012 mole) of **9** in 100 ml of anhyd C_6H_6, 35 ml of $CHCl_3$, and 3 ml of pyridine was added with stirring at 10° in one portion 17.4 ml (0.86 *M*, 0.015 mole) of Cl_2 in CCl_4. After stirring at 10° for 30 min, the reaction mixt was washed with two 50-ml portions of 3 *N* HCl and with three 50-ml portions of 5% $NaHCO_3$. The org layer was dried ($MgSO_4$) and concd *in vacuo* to yield a foam. Crystn from CH_2Cl_2–Et_2O gave 3.7 g (69%) of **10**: mp 155–157.5°; λ_{max} 235 mμ (ε 14,390); $[\alpha]D$ −69.1°. The anal. sample, mp 178–180°, was obtained after 2 recrystns from CH_2Cl_2–MeOH. *Anal.* ($C_{24}H_{31}ClO_5$) C, H.

6-Chloro-16β-chloromethyl-16α,17α-epoxy-3β-hydroxypregn-5-ene-7,20-dione Acetate (11).—Crude **10** (23.1 g, 0.05 mole) in 200 ml of $CHCl_3$ at 3° was treated with 49 ml (1.36 *M*, 0.066 mole) of a soln of Cl_2 in CCl_4. The reaction mixt was kept at 3° for 17 hr, washed with 5% $NaHCO_3$, dried ($MgSO_4$), and concd *in vacuo*. Crystn from CH_2Cl_2–Et_2O gave 11.8 g, mp 212–213°, of the 5,6-dichloro compd. A second crop of 2.3 g was obtained from the filtrate. The total yield is thus 54%. The 5,6-dichloro compd (16.56 g) was added to 600 ml of pyridine and stirred for 17 hr at 25°. Removal of the pyridine at ~1 mm and below 30° gave a brown solid which was dissolved in EtOAc and washed once with H_2O, twice with 3 *N* HCl and once with 5% $NaHCO_3$. Concn *in vacuo* gave a yellow solid which was dissolved in 500 ml of AcOH and stirred at 25° with 16 g of Zn dust for 1 hr to reduce any 8-chloro impurity. The Zn was removed by filtration and the filtrate was concd at ~1 mm below 30°. The product was dissolved in Et_2O–CH_2Cl_2 (2:1) and the extract was washed once with 5% $NaHCO_3$, dried ($MgSO_4$), and concd *in vacuo* to yield a solid. Crystn from CH_2Cl_2–Et_2O gave 8.9 g of **11**: mp 227.5–230°, λ_{max} 251 mμ (ε 11,200); $[\alpha]D$ −63.8°. A second crop of 1.9 g was obtained from the filtrate and the total yield is thus 70%. The anal. sample, mp 231–233.5°, was obtained after two recrystns from CH_2Cl_2–Et_2O. *Anal.* ($C_{24}H_{30}Cl_2O_5$) C, H.

6-Chloro-3β,17α-dihydroxy-16-methylenepregn-5-ene-7,20-dione 3-Acetate (12).—A soln of 10.78 g (0.023 mole) of **11** in 650 ml of Me_2CO and 108 g of NaI was stirred and refluxed for 8.5 hr. HOAc (25 ml) was added and reflux was continued for 3 hr. Most of the solvent was removed *in vacuo* and H_2O was added and the product was extd with CH_2Cl_2. The ext was washed with 0.1 *N* $Na_2S_2O_3$, with 5% $NaHCO_3$, dried ($MgSO_4$), and concd to a yellow solid. Crystn from CH_2Cl_2–Et_2O gave 8.94 g of **12**: mp 201–204°; λ_{max} 253 mμ (ε 11,960). A second crop of 0.99 g, mp 200–202.5°, was obtained from the filtrate making the total yield 99%. The anal. sample, mp 196–200°, was obtained by sublimation at 185° (0.1 mm). *Anal.* ($C_{24}H_{31}ClO_5$) C, H.

6-Chloro-3β,17α-dihydroxy-16-methylenepregn-5-ene-7,20-dione Diacetate (13).—Ac_2O (96 ml) and 1 ml of 72% $HClO_4$ in 400 ml of anhyd EtOAc was added to 4.0 g of **12** in 200 ml of EtOAc. After stirring at 25° for 10 min, the soln was washed with 3 portions of satd $NaHCO_3$, dried ($MgSO_4$), and concd *in vacuo* (finally at ~1 mm) to yield a yellow solid. Crystn from CH_2Cl_2–Et_2O gave 3.3 g (74%) of **13**: mp 254–255°; λ_{max} 253 mμ (ε 12,100); $[\alpha]D$ −240.3°. The anal. sample, mp 257–259°, was obtained after 2 recrystns from CH_2Cl_2–Et_2O. *Anal.* ($C_{26}H_{33}ClO_6$) C, H.

6-Chloro-3β,7β,17α-trihydroxy-16-methylenepregn-5-en-20-one 3,17-Diacetate (14a) and **6-Chloro-3β,7α,17α-trihydroxy-16-methylenepregn-5-en-20-one 3,17-Diacetate (15).** To LiAl(*tert*-BuO)$_3$H (2.4 g, 9.4 mmoles) in 20 ml of anhyd THF under N_2 at 25° was added with stirring over 20 min 1.50 g (3.1 mmoles) of **13** in 40 ml of anhyd THF. After stirring at 25° for 5 hr, the reaction mixt was cooled at 3° during the addn of 30 ml of Me_2CO and 10 ml of H_2O. Most of the solvent was removed *in vacuo* and 75 ml of $CHCl_3$ was added followed by 80 ml of 50% aq AcOH. The organic layer was washed with 3 portions of 5% $NaHCO_3$, dried ($MgSO_4$), and concd *in vacuo*. The crude product was chromatographed on 70 g of silica gel. Elution with 4% EtOAc–C_6H_6 gave several fractions containing pure **14a** (by tlc). These fractions were combined and crystd from CH_2Cl_2–C_6H_{14} to yield 0.49 g (33%) of **14a**: mp 209.5–212.5°; $[\alpha]D$ −142.5°. Recrystn from EtOAc–C_6H_{14} gave the anal. sample, mp 212–214°. *Anal.* ($C_{26}H_{35}ClO_6$) C, H.

Elution with 5% EtOAc–C_6H_6 then gave several fractions containing pure **15** (by tlc). These fractions were combined and crystd from EtOAc–C_6H_{14} to give 0.53 g (35%) of **15**: mp 187.5–188.5°; $[\alpha]D$ −196.4°. Recrystn from EtOAc–C_6H_{14} gave the anal. sample, mp 187.5–189°. *Anal.* ($C_{26}H_{35}ClO_6$) C, H.

6-Chloro-3β,7β,17α-trihydroxy-16-methylenepregn-5-en-20-one Triacetate (14b).—Acetylation of 0.600 g of **14a** was accomplished by treatment with 6.0 ml of pyridine and 6.0 ml of Ac_2O at 25° for 18 hr. The soln was concd to dryness at 1 mm (bath temp <30°) and the resultant solid was crystd from EtOAc to yield 0.523 g (80%) of 14b: mp 235–238°; $[\alpha]D$ −96.4°. Recrystn from EtOAc furnished the anal. sample, mp 236–238°. *Anal.* ($C_{28}H_{37}ClO_7$) C, H.

6-Chloro-3β,7β,17α-trihydroxy-16-methylenepregn-5-en-20-one (14c).—To 0.300 g (0.63 mmole) of **14b** dissolved in 15 ml of MeOH at 25° was added 0.69 ml (0.69 mmole) of 1.0 *N* NaOH. After stirring at 25° for 2 hr, 0.25 ml of AcOH was added and the solvent was removed *in vacuo*. H_2O was added and the product was extd with CH_2Cl_2. The ext was dried ($MgSO_4$) and concd to a foam. Crystn from EtOAc gave 0.220 g (80%) of **14c**: mp 212–221°; $[\alpha]D$ −117.2°. Recrystn from EtOAc gave the anal. sample, mp 223–224.5°. *Anal.* ($C_{24}H_{33}ClO_5$) C, H.

6-Chloro-3β,7β,17α-trihydroxy-16-methylenepregn-5-en-20-one 7,17-Diacetate (14d).—To 0.324 g (0.62 mmole) of **14b** in 65 ml of MeOH at 25° was added 0.69 ml (0.69 mmole) of 1.0 *N* NaOH. The soln was left at 25° for 4 hr, 0.25 ml of AcOH was added, and the solvent was removed *in vacuo* to yield a solid. Crystn from EtOAc gave 0.143 g (48%) of **14d**: mp 228–232°; $[\alpha]D$ −86.6°. *Anal.* ($C_{26}H_{35}ClO_6$) C, H.

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