References

(1) M. Terao, K. Karasawa, N. Tanaka, H. Yonehara, and H. Umezawa, *J. Antibiot., Ser. A*, 13, 401 (1960).
(2) M. Bobek and A. Bloch, *J. Med. Chem.*, 15, 164 (1972).
(3) P. T. Berkowitz, T. J. Bardos, and A. Bloch, *ibid.*, 16, 183 (1973).
(4) R. A. Sharma, M. Bobek, and A. Bloch, Abstracts, 164th National Meeting of the American Chemical Society, New York, N. Y., August 1972.
(5) F. L. Muehlmann and A. R. Day, *J. Amer. Chem. Soc.*, 78, 242 (1956).
(6) G. B. Brown and V. S. Weliky, *J. Biol. Chem.*, 204, 1019 (1953).
(7) N. Löfgren and L. Björn, *Acta Chem. Scand.*, 7, 225 (1953).
(8) G. Germain, P. Main, and M. M. Woolfson, *Acta Crystallogr., Sect. A*, 27, 368 (1971).
(9) J. J. Bisele, M. C. Slautterback, and M. Margolis, *Cancer*, 8, 87 (1955).
(10) A. R. I. Munns and P. Tollin, *Acta Crystallogr., Sect. B*, 26, 1101 (1970).
(11) U. Thewalt, C. E. Bugg, and R. E. Marsh, *ibid.*, 26, 1089 (1970).
(12) E. Ochiai, *J. Org Chem.*, 18, 535 (1953).
(13) A. Bloch and C. Coutsogeorgopoulos, *Biochemistry*, 5, 3345 (1966).
(14) A. Bloch and C. Coutsogeorgopoulos, *ibid.*, 10, 4394 (1971).
(15) C. H. Gray and E. L. Tatum, *Proc. Nat. Acad. Sci. U. S.*, 30, 304 (1944).
(16) A. Bloch and G. Dutschman, *Bioeng. Biotechnol.*, 15, 197 (1973).
(17) G. E. Moore, A. A. Sandberg, and K. Ulrich, *J. Nat. Cancer Inst.*, 36, 405 (1966).
(18) T. Spector and D. G. Johns, *J. Biol. Chem.*, 245, 5079 (1970).
(19) M. C. Wang and A. Bloch, *Biochem. Pharmacol.*, 21, 1063 (1972).

Preparation of 17α-Acetoxy-7-oxaprogesterone

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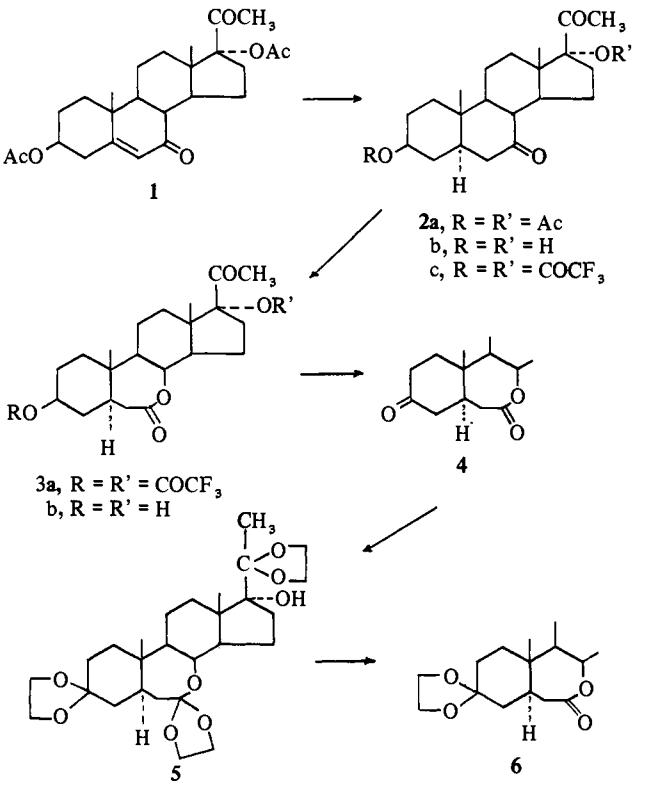
The synthesis of both 17α-acetoxy-7-oxaprogesterone and the corresponding Δ^1 derivative was accomplished. Neither compound exhibited a significant level of progestational or antiprogestational activity.

The steroid nucleus has been modified recently by the insertion of an oxygen atom at various positions. (See ref 1 for leading references.) Perhaps because of altered metabolic pathways, some of these compounds have interesting biological activity.[2-4] Although 7-oxa-5α-androstanes have been prepared,[5] the corresponding 7-oxaprogesterone analogs have not been reported so we prepared several examples of this class of compounds.

Hydrogenation of **1**[6] gave the 5α-dihydro derivative **2a** (for hydrogenation of a steroidal Δ^5-7-ketone to the 5α isomer, see ref 7) which was hydrolyzed to the 3,17-diol **2b**. The diol was then converted to the bistrifluoroacetate derivative **2c** since easily hydrolyzable protecting groups were desired. Baeyer-Villiger oxidation of **2c** with *m*-chloroperbenzoic acid yielded the *B*-homo lactone **3a**. The trifluoroacetate groups were removed very readily with potassium bicarbonate to provide **3b** which was oxidized with chromium trioxide-pyridine to give the ketone **4**. Ketalization of **4** using an extended reaction time to ensure complete reaction of the 20-ketone also caused reaction with the lactone and yielded **5**. (For other examples of this reaction, see ref 8.) The structure of **5** was established by the lack of carbonyl absorption in the infrared spectrum, the molecular ion at *m/e* 495 in the mass spectrum, and its facile hydrolysis by magnesium sulfate[9] in benzene saturated with water to the bisketal lactone **6** (Scheme I).

Treatment of **6** with methyllithium gave the hemiketal **7**, which was not purified but was treated directly with perphthalic acid to yield the Baeyer-Villiger product **8**. Hydrolysis of crude **8** followed by cyclization with *p*-toluenesulfonyl chloride in pyridine[10] provided the 7-oxa steroid **9**. Acid hydrolysis removed the ketal functions to yield **10a**. Acetylation with acetic anhydride-perchloric acid[11] followed by hydrolysis of the 3-enol acetate with sodium bicarbonate gave **10b**. Dehydrogenation with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in refluxing dioxane yielded **11**. Hydrogenation of **11** using the soluble catalyst, tris(triphenylphosphine)chlororhodium,[12] gave the desired enone **12** along with the product of overreduction, the saturated 3-ketone **10a**. This mixture gave a single spot of tlc and could not be separated by crystallization. However, reduction of the mixture with lithium tri-*tert*-butyloxyaluminum hydride followed by oxidation with manganese dioxide gave a mixture of **12** and the saturated 3-alcohol which were readily separated by preparative tlc (Scheme II).

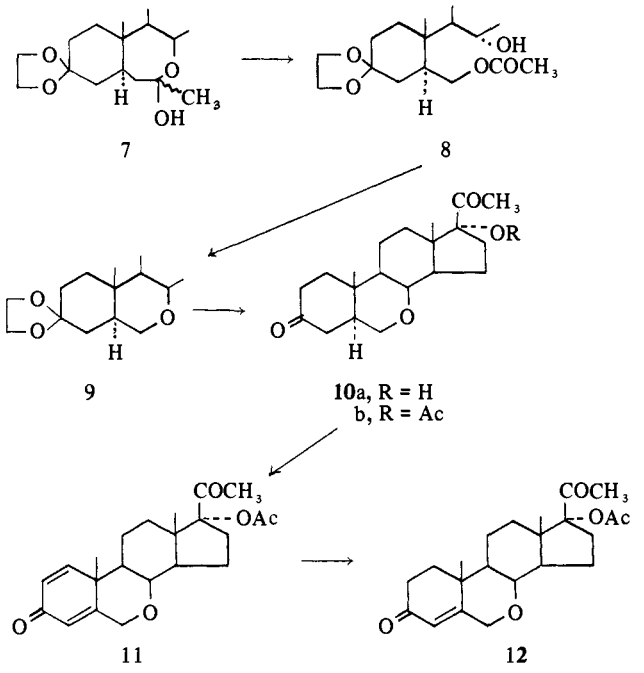
Scheme I



Biological Activity. Compounds **10b**, **11**, and **12** were tested for progestational activity in a modified Clauberg-McPhail assay.[13,14] In this procedure progesterone given subcutaneously at a dose of 40 μg/day produced significant secretory development of the uterine endometrium (+1.5 McPhail index). Compounds **10b**, **11**, and **12** were inactive by both routes of administration at a dose of 400 μg/day.

The three compounds were tested for antiprogestational

Scheme II



activity by a similar method except they were administered concurrently with progesterone at 200 μg/day by separate sc injections. In our laboratories a standard dose of progesterone of 200 μg/day consistently gives a +4 McPhail index. Compounds **10b** and **11** were given at 10 mg/day, while **12** was given at 1 mg/day. All three compounds failed to inhibit the development of the secretory uterine endometrium produced by progesterone.

It is apparent from the above results that incorporation of a 7-oxa function into the progesterone nucleus greatly diminishes primary endocrinological properties. In addition, no antiprogestational activity was observed for these compounds.

Experimental Section

All melting points were taken in glass capillaries and are corrected. Rotations were measured in $CHCl_3$ at 25° at a concentration of about 0.7%; uv spectra are of EtOH solutions, and ir spectra are in $CHCl_3$ solutions. The nmr spectra were determined in $CDCl_3$ (internal Me_4Si) using a Varian A-60 spectrometer. Where analyses are indicated only by symbols of the elements, analytical results obtained for those elements were within ±0.4% of the theoretical values. Unless otherwise stated, extracts were dried over anhydrous $MgSO_4$.

3β,17α-Dihydroxy-5α-pregnane-7,20-dione Diacetate (2a). A solution of 45.73 g of 3β,17α-dihydroxypregn-5-ene-7,20-dione diacetate[3] in 1 l. of EtOAc and 5 ml of C_5H_5N containing 5 g of 10% Pd/C was shaken in H_2 atmosphere at room temperature for 9 hr. The catalyst was removed by filtration through Celite and the filtrate was concentrated *in vacuo* to yield a solid. Two crystallizations from CH_2Cl_2–MeOH gave 28.00 g of **2a**: mp 265–267°; [α]D −63.1°; nmr showed no vinyl hydrogen absorption. *Anal.* ($C_{25}H_{36}O_6$) C, H.

The combined filtrates from the crystallizations were concentrated to dryness *in vacuo*. The resultant solid was dissolved in 600 ml of EtOAc and 2 ml of C_5H_5N containing 3 g of 10% Pd/C and shaken in an H_2 atmosphere at room temperature for 9 hr. Work-up as above gave a solid which was crystallized from CH_2Cl_2–MeOH to give 13.05 g of **2a**.

3β,17α-Dihydroxy-5α-pregnane-7,20-dione (2b). To a solution of 39.6 g of 3β,17α-dihydroxy-5α-pregnane-7,20-dione diacetate (7a) in 600 ml of dioxane and 500 ml of MeOH under an N_2 atmosphere at room temperature was added 450 ml of 1.0 *N* NaOH dropwise over 30 min. After stirring the reaction mixture at 25° for 3.5 hr, 200 ml of 3 *N* HCl was added and most of the solvent was removed *in vacuo*. H_2O was added and the resultant solid was filtered and air-dried to give 30.74 g of crude **2b** which was used directly for the next experiment.

3β,17α-Dihydroxy-5α-pregnane-7,20-dione Bistrifluoroacetate (2c). To 0.700 g of 3β,17α-dihydroxy-5α-pregnane-7,20-dione (**2b**) in 10 ml of anhydrous C_5H_5N cooled in an ice bath was added 0.87 ml of trifluoroacetic anhydride. After stirring for 1 hr at 3°, the yellow solution was added dropwise to 10 ml of concentrated HCl and ice with stirring. The resultant solid was removed by filtration, dissolved in C_6H_6, and passed through a column of 16 g of silica gel. Elution with 200 ml of 5% EtOAc in C_6H_6 and concentration of the eluent *in vacuo* gave a solid. Crystallization from CH_2Cl_2–Et_2O gave 0.753 g of **2c**: mp 194–196°; [α]D −58.6°; ir 1765 and 1710 cm^{-1} *Anal.* ($C_{25}H_{30}F_6O_6$) C, H, F.

3β,17α-Dihydroxy-7a-oxa-5α-*B*-homopregnane-7,20-dione Bistrifluoroacetate (3a). To 0.822 g (1.5 mmol) of 3β,17α-dihydroxy-5α-pregnane-7,20-dione bistrifluoroacetate **2c** in 20 ml of $CHCl_3$ was added 0.609 g (3 mmol) of 87% *m*-chloroperbenzoic acid. After the reaction mixture was left at room temperature for 64 hr, 40 ml of 10% Na_2SO_3 solution was added and stirred for 15 min. The organic layer was separated and washed with 5% $NaHCO_3$ solution, dried, and concentrated *in vacuo*. Crystallization from CH_2Cl_2–Et_2O gave 0.591 g of 3a: mp 210–212°; [α]D −48.4°; ir 1740 and 1690 cm^{-1} (br); nmr δ 4.20 (m, 1, C-8 H). *Anal.* ($C_{25}H_{30}F_6O_7$) C, H, F.

3β,17α-Dihydroxy-7a-oxa-5α-*B*-homopregnane-7,20-dione (3b). To 0.590 g of 3β,17α-dihydroxy-7a-oxa-5α-*B*-homopregnane-7,20-dione bistrifluoroacetate (3a) dissolved in 5 ml of dioxane and 10 ml of MeOH was added 0.64 g of $KHCO_3$ in 4 ml of H_2O. After the reaction mixture was stirred for 40 min, 10 ml of H_2O was added and most of the solvent was removed *in vacuo*. H_2O was added and the crystalline solid was removed by filtration and air-dried to yield 0.331 g of crude 3b, which was used directly in the next experiment.

17α-Hydroxy-7a-oxa-5α-*B*-homopregnane-3,7,20-trione (4). CrO_3 (0.669 g) was added in portions to 1.5 ml of anhydrous C_5H_5N and 50 ml of CH_2Cl_2 with stirring at room temperature. After stirring the above solution for 15 min, 0.331 g of 3β,17α-dihydroxy-7a-oxa-5α-*B*-homopregnane-7,20-dione 3b in 50 ml of CH_2Cl_2 was added and the mixture was stirred for 30 min. The dark solution was washed with H_2O and 1 *N* HCl and dried, and the solution was passed through a column of 2 g of silica gel. Elution with 100 ml of CH_2Cl_2 and then with 100 ml of 30% EtOAc–C_6H_6 and concentration of the combined eluent gave a solid. Crystallization from EtOAc gave 0.179 g of 4: mp 249–252°; [α]D −52.0°; ir (KBr) 1727 and 1692 cm^{-1}; nmr (DMSO-d_6) δ 4.55 (m, 1, C-8 H). *Anal.* ($C_{21}H_{30}O_5$) C, H.

17α-Hydroxy-3,3,7,7,20,20-trisethylenedioxy-7a-oxa-5α-*B*-homopregnane (5). A solution of 0.131 g of 17α-hydroxy-7a-oxa-5α-*B*-homopregnane-3,7,20-trione (4) in 50 ml of anhydrous C_6H_6, 0.4 ml of ethylene glycol, and 5.2 mg of TsOH was stirred and refluxed under a Dean-Stark water separator filled with molecular sieve 4A for 47 hr. The mixture was washed with 5% $NaHCO_3$, dried (Na_2SO_4), and concentrated *in vacuo*. Crystallization from CH_2Cl_2–Et_2O gave 0.118 g of **5**: mp 236–242°; [α]D −39.9°; ir showed no carbonyl absorption; nmr δ 3.89 (m, 12, ethylenedioxy); mass spectrum *m/e* 495. *Anal.* ($C_{27}H_{42}O_8$) C, H.

17α-Hydroxy-3,3,20,20-bisethylenedioxy-7a-oxa-5α-*B*-homopregnan-7-one (6). A solution of 0.130 g of 17α-hydroxy-3,3,7,7,-20,20-trisethylenedioxy-7a-oxa-5α-*B*-homopregnane (**5**) in 100 ml of C_6H_6 saturated with H_2O was stirred at room temperature with 10 g of anhydrous $MgSO_4$ for 2 hr, filtered and concentrated *in vacuo*. Crystallization from CH_2Cl_2–Et_2O–C_6H_{14} gave 75 mg of 6: mp 262–267°; [α]D −40.5°; ir 1720 cm^{-1}; nmr δ 3.89 (m, 8, ethylenedioxy). *Anal.* ($C_{25}H_{38}O_7$) C, H.

17α-Hydroxy-3,3,20,20-bisethylenedioxy-7a-oxa-5α-pregnane (9). To 1.98 g (4.4 mmol) of 17α-hydroxy-3,3,20,20-bisethylenedioxy-7a-oxa-5α-*B*-homopregnan-7-one (**6**) in 150 ml of anhydrous THF at 3° was added over 20 min 13 ml (21 mmol) of 1.6 *M* MeLi in Et_2O under N_2. The bath was removed after 15 min and stirring was continued at room temperature for 1.5 hr. H_2O (25 ml) was added dropwise and most of the solvent was removed *in vacuo*. H_2O was added and the product was extracted with EtOAc, dried, and concentrated *in vacuo* to yield a solid. The crude product 7 was dissolved in 50 ml of $CHCl_3$ and 18 ml of 0.73 *M* monoperphthalic acid in Et_2O was added. The mixture was stirred at room temperature for 1.5 hr and filtered to remove the precipitated phthalic acid; the filtrate was washed with saturated $NaHCO_3$ solution, dried (Na_2SO_4), and concentrated to yield **8** as a solid. This crude product was dissolved in 80 ml of EtOH and 3.5 ml of 10 *N* NaOH was added. The solution was refluxed for 40 hr and then concentrated *in vacuo*. H_2O was added and the product was extracted with CH_2Cl_2, dried, and concentrated to yield a foam (1.78 g). The crude product was dissolved in 20 ml of anhydrous C_5H_5N and treated at room temperature with 2.0 g of TsCl. After stirring at 25° for 4 hr, chipped ice was added slowly to hydrolyze the excess TsCl. Most of the C_5H_5N

was removed at ~1 mm, H_2O was added, and the resultant solid was filtered and washed well with H_2O. The solid was dissolved in CH_2Cl_2, dried, and concentrated *in vacuo* to afford a yellow solid. Crystallization from CH_2Cl_2–Et_2O gave 0.323 g of **9**, mp 198–206°. The filtrate was concentrated to dryness and chromatographed on 25 g of alumina (activity III). Elution with C_6H_6 and with 10% EtOAc–C_6H_6 gave, on crystallization from CH_2Cl_2–Et_2O, 0.241 g of **9**: mp 200–211°; [α]D −1.5°; ir showed no carbonyl absorption; nmr δ 3.90 (m, 8, ethylenedioxy), 3.45 (m, 3, C-6 and C-8 H's). *Anal.* ($C_{24}H_{38}O_6$) C, H.

17α-Hydroxy-7-oxa-5α-pregnane-3,20-dione (10a). Deketalization of **9** (6.68 g) was accomplished by refluxing with 500 ml of 8% H_2SO_4 in 500 ml of dioxane under N_2 for 2.5 hr. The solution was concentrated *in vacuo* to remove the dioxane, H_2O was added, and the product was extracted with CH_2Cl_2. After washing the extract with 5% $NaHCO_3$, it was dried and concentrated to yield a yellow solid. Crystallization from CH_2Cl_2–Et_2O gave 4.01 g of **10a**: mp 249–264°; [α]D +32.9°; ir (KBr) 1700 cm^{-1}; nmr δ 3.46 (m, 3, C-6 and C-8 H's). An additional 1.17 g of **10a** was obtained from the filtrate to give a total yield of 98%. *Anal.* ($C_{20}H_{30}O_4$) C, H.

17α-Hydroxy-7-oxa-5α-pregnane-3,20-dione Acetate (10b). To 1.50 g of **10a** dissolved in 75 ml of anhydrous EtOAc was added 0.03 ml of 70% $HClO_4$ and 15 ml of Ac_2O in 60 ml of EtOAc.[11] After stirring for 7 min at room temperature, the solution was washed with 5% $NaHCO_3$, dried, and concentrated to dryness. The solid mixture of 3-ketone and 3-enol acetate was dissolved in 300 ml of hot MeOH; 15 ml of 1 *M* $NaHCO_3$ was added and refluxed for 30 min. The solvent was removed *in vacuo*, H_2O was added, and the product was extracted with EtOAc. Chromatography of the crude product on 40 g of silica gel and elution with 10% EtOAc–C_6H_6 gave pure **14**. Crystallization of the combined fractions from CH_2Cl_2–Et_2O gave 0.91 g (53% yield) of **10b**: mp 237–244°; [α]D +29.4°; ir 1738 and 1720 cm^{-1}; nmr δ 3.50 (m, 3, C-6 and C-8 H's), 2.03 and 2.07 (s, 3, C-21 Me and C-17 OAc). *Anal.* ($C_{22}H_{32}O_5$) C, H.

17α-Hydroxy-7-oxapregna-1,4-diene-3,20-dione Acetate (11). A solution of 2.32 g (6.16 mmol) of **10b** and 3.92 g (17.25 mmol) of DDQ in 75 ml of anhydrous dioxane containing 15 mg of TsOH was refluxed under N_2 with stirring for 24 hr. An additional 0.136 g (0.6 mmol) of DDQ was added and reflux was continued for 4 hr. CH_2Cl_2 (100 ml) was added and the precipitated solids were removed by filtration. The filtrate was washed with five portions of 3 *N* NaOH and with saturated brine, dried, and concentrated to an oil. Preparative tlc on silica gel served to purify the product which was crystallized from CH_2Cl_2–Et_2O to give 0.71 g of **11**: mp 223–228°; [α]D +30.1°; λ_{max} 240 nm (ε 16,000); ir 1733, 1718, 1670, 1633, and 1610 cm^{-1}; nmr δ 7.04 (d, 1, J = 11 Hz, C-1 H), 6.29 (d of d, $J_{2\text{-}1}$ = 11 Hz, $J_{2\text{-}4}$ = 2 Hz, C-2 H), and 6.15 (broad s, 1, C-4 H). *Anal.* ($C_{22}H_{28}O_5$) C, H. A second crop (0.33 g) was obtained from the filtrate making the total yield 44%.

17α-Hydroxy-7-oxapregn-4-ene-3,20-dione Acetate (12). Reduction of the Δ^1 double bond was achieved by stirring a solution of 1.10 g of **11** and 0.55 g of $[(C_6H_5)_3P]_3RhCl$ in 220 ml of C_6H_6–EtOH (5:1) under an H_2 atmosphere for 3 hr at room temperature.[12] The solvents were removed *in vacuo* and the residue was dissolved in C_6H_6 and passed through a column of 22 g of neutral alumina. Elution with 500 ml of C_6H_6 and concentration of the eluent gave a dark foam. Preparative tlc on silica gel gave material (0.72 g) which was homogeneous by tlc but was shown by nmr analysis to contain the desired compound **12**, contaminated by about 30% of the fully saturated 3-ketone. Attempted purification by recrystallization was unsuccessful. The above mixture (0.72 g) dissolved in 30 ml of anhydrous THF was reduced by dropwise addition to 1.44 g of $LiAlH[OC(CH_3)_3]_3$ in 10 ml of THF over a 30-min period at room temperature. After stirring the reaction mixture for 1.5 hr, 10 ml of Me_2CO was added and the solvent was removed *in vacuo*. $CHCl_3$ was added followed by 10% AcOH to acidify the aqueous layer. The extract was washed with 5% $NaHCO_3$, dried, and concentrated to dryness. The mixture of 3β-hydroxy-Δ^4 and 3β-hydroxy-5α compounds was dissolved in 30 ml of $CHCl_3$, treated with 5 g of activated MnO_2, and stirred at 25° for 1 hr. The mixture was filtered through Celite and the filtrate was concentrated to dryness and purified by preparative tlc on silica gel. The purified product was crystallized from CH_2Cl_2–Et_2O to yield 0.18 g of **12**: mp 190–195°; $[\alpha]^{25}D$ +62.1°; λ_{max} 232 nm (ε 15,800); ir 1735, 1720, 1680, and 1630 cm^{-1}; nmr δ 5.75 (s, 1, C-4 H).

The analytical sample was obtained from EtOAc–C_6H_{14}. It melted at 192–198°, resolidified, and remelted at 207–209°. *Anal.* ($C_{22}H_{30}O_5$) C, H.

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References

(1) L. Tokes in "Steroid Reactions," C. Djerassi, Ed., Holden Day, San Francisco, Calif., 1963, pp 459–502.
(2) S. D. Levine, *J. Med. Chem.*, **8**, 537 (1965).
(3) R. Pappo and C. J. Jung, *Tetrahedron Lett.*, 365 (1962).
(4) H. D. Lennon and F. J. Saunders, *Steroids*, **4**, 689 (1964).
(5) R. W. Guthrie, A. Boris, J. Mullin, F. Mennona, and R. W. Kierstead, *J. Med. Chem.*, **16**, 257 (1973).
(6) C. W. Marshall, R. E. Ray, I. Laos, and B. Riegel, *J. Amer. Chem. Soc.*, **79**, 6303 (1957).
(7) H. J. Ringold, *ibid.*, **82**, 961 (1960).
(8) R. A. LeMahieu and R. W. Kierstead, *Tetrahedron. Lett.*, 511 (1970).
(9) J. J. Brown, R. H. Lenhard, and S. Bernstein, *J. Amer. Chem. Soc.*, **86**, 2183 (1964).
(10) N. J. Doorenbos and M. T. Wu, *J. Org. Chem.*, **26**, 4550 (1961).
(11) B. E. Edwards and P. N. Rao, *ibid.*, **31**, 324 (1966).
(12) C. Djerassi and J. Gutzwiller, *J. Amer. Chem. Soc.*, **88**, 4537 (1966).
(13) R. A. LeMahieu, A. Boris, M. Carson, and R. W. Kierstead, *J. Med. Chem.*, **14**, 629 (1971).
(14) A. Boris and L. DeMartino, *Steroidologia*, **2**, 57 (1971).

19-Norprogestins. Synthesis and Biological Activity of 6-Chloro-16-methylene-17α-hydroxy-19-nor-4,6-pregnadiene-3,20-dione 17-Acetate

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Two chemical syntheses of 6-chloro-16-methylene-17α-hydroxy-19-nor-4,6-pregnadiene-3,20-dione 17-acetate (**1a**), starting respectively from 19-norpregnane and from pregnane substrates, are presented. In rabbits and rats, **1a** is among the most active members of the 16-methylene-17α-acetoxy-20-keto steroid family but superior in neither Clauberg assay nor antiandrogenic activity to its 10-methyl homolog.

The pharmacology and chemistry of 16-alkylideneprogestins have been of interest to us for some time.[1,2] More recently we have been particularly interested in 6-chloro-Δ^6 members of the 16-alkylidene family[3–7] as exemplified by **1b** (Scheme II). With the findings of enhanced progestational activity (compared to the 19-methyl-containing counterpart) for a modified 19-norprogesterone[8] and for 19-norprogesterone,[9] there resulted an interest, which is still continuing, in the synthesis of 19-norprogestins.#

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Relevant to our publications may be cited ref 10–13.