Treatment of Norbornen-7-one with Diazomethane.—Norbornen-7-one (5.0 g, 0.046 mole) was treated with an excess of diazomethane. A large amount of bicyclo[2.2.2]oct-2-en-5-one (79.0%) was formed. This product was identified by comparison of the retention time and infrared spectrum with those of an authentic sample. There was very little material formed which had the same retention time as bicyclo[3.2.2]non-6-en-2-one.

Treatment of Bicyclo[2.2.2]octan-2-one with Diazomethane.—Bicyclo[2.2.2]octan-2-one (5.5 g, 0.044 mole) was treated with an excess of diazomethane in the same fashion as bicyclo[3.2.1]-oct-2-en-8-one. Only a trace of new material was formed, which had the same retention time as bicyclo[3.2.2]nonan-2-one.

Cycloheptanone.—Using the apparatus and procedure described by Leonard,[23] 40.4 g (0.200 mole) of dimethyl suberate was converted to cycloheptanone in 58% yield using high-dilution conditions. The reaction time was 3 days. When the reaction was attempted with the dimethyl ester of **4**, starting material was obtained along with a trace of product which gave a positive 2,4-dinitrophenylhydrazine test but which was present in amounts insufficient to characterize.

Registry No.—**2**, 14565-01-6; **3**, 14638-73-4; **10**, 6671-66-5; **11**, 13366-99-9; **12**, 10036-15-4; **14**, 2568-17-4; **15**, 1614-77-3; **17**, 14565-07-2; **18**, 14565-08-3; bicyclo[3.2.2]non-2-yl tosylate, 14565-09-4; **20**, 14565-36-7; **21**, 14565-35-6; **22**, 14565-34-5.

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[23] N. J. Leonard and R. C. Sentz, *J. Am. Chem. Soc.*, **74**, 1704 (1952)

Synthesis of 8α- and 9β-B-Norestrone[1]

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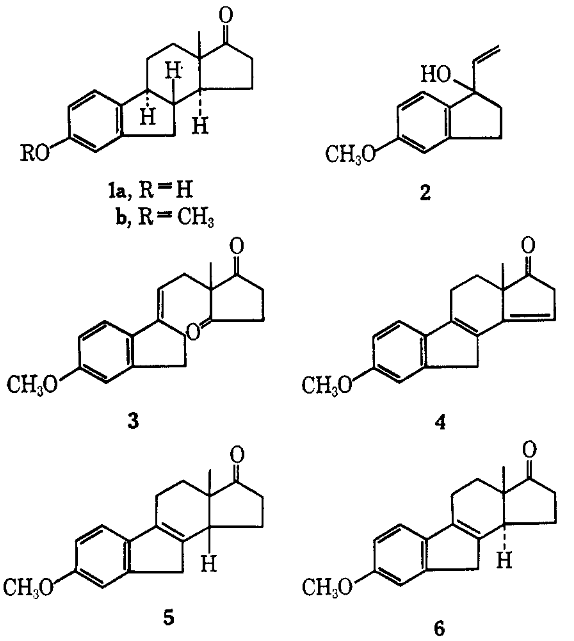
(±)-3-Methoxy-B-norestra-1,3,5(10),8-tetraen-17β-ol (**8a**) was prepared in five steps beginning with 5-methoxyindan-1-one. Metal–ammonia reduction of **8a** followed by chromic acid oxidation gave a mixture of (±)-3-methoxy-B-nor-9β-estra-1,3,5(10)-trien-17-one (**9a**) and (±)-3-methoxy-B-nor-8α-estra-1,3,5(10)-trien-17-one (**10a**), with **9a** as the predominant isomer. Catalytic reduction of **8a** gave a mixture of the same two products with **10a** predominating.

The synthesis of B-norestrone (**1a**) (Chart I) was undertaken as part of our continuing efforts to separate the lipodiatic and feminizing properties of estrone.[3,4] The synthetic approach was based on the recent method developed by Torgov[5] for steroidal total syntheses, which has since been extensively used by several laboratories.[3d,6] 5-Methoxyindan-1-one with vinyl magnesium bromide was readily transformed into allylic alcohol **2** (Chart I). Alkylation of 2-methylcyclopentane-1,3-dione with **2** in the presence of Triton B afforded diketone **3** in 70% over-all yield from the indanone.[7] Warm methanolic hydrochloric acid caused **3** to undergo cyclodehydration and tetracyclic ketone **4** was isolated in 92% yield. Selective reduction of the 14,15 double bond of **4** in the presence of 5% palladium on calcium carbonate afforded a 1:3 mixture (by nmr) of **5** and **6**, respectively, from which the *trans* ketone **6** was isolated in pure form in 25% yield. The configurations at C-14 were assigned on the basis of the shielding effect of the 8,9 double bond on the angular methyl group of **6** compared with that of **5**.[8] The poor yield of **6** was overcome by relying

CHART I



1a, R = H
b, R = CH$_3$

2

3

4

5

6

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[1] Presented in part at the 152nd National Meeting of the American Chemical Society, New York, N. Y., Sept 1966. Taken in part from the Ph.D. dissertation of F. C. Sciavolino, The University of Michigan, Ann Arbor, Mich., 1966.

[2] National Institutes of Health Predoctoral Fellow, 1963–1966. Monsanto Co. Summer Fellow, 1963.

[3] (a) J. H. Burckhalter and J. A. Durden, *J. Org. Chem.*, **25**, 298 (1960); (b) J. H. Burckhalter and H. Watanabe, Abstracts, 142nd National Meeting of the American Chemical Society, Cincinnati, Ohio, Jan 1963, p 14a; (c) J. H. Burckhalter and H. Watanabe, Abstracts, International Symposium on the Chemistry of Natural Products, Kyoto, Japan, April 1964, p 253; (d) H. Watanabe, K. Matsumori, L. W. Rampy, and J. H. Burckhalter, Abstracts, Agricultural Chemical Society, Hokkaido, Japan, July 1964, p 140.

[4] (a) For a review of the subject with leading references, see N. Applezweig, "Steroid Drugs," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, pp 222–230; see also (b) A. H. Goldkamp, W. M. Hoehn, R. A. Mikulec, E. F. Nutting, and D. L. Cook, *J. Med. Chem.*, **8**, 409 (1965); (c) G. C. Buzby, Jr., R. A. Edgren, J. A. Fisher, G. A. Hughes, R. C. Jones, K. Ledig, T. W. Pattison, R. Rees, H. Smith, L. L. Smith, D. M. Teller, and G. R. Wendt, *ibid.*, **7**, 755 (1964); (d) S. Gordon, E. W. Cantrall, W. P. Cekleniak, H. J. Albers, S. Maver, S. M. Stolar, and S. Bernstein, *Steroids*, **4**, 267 (1964); (e) C. H. Robinson, N. F. Bruce, E. P. Oliveto, S. Tolksdorf, M. Steinberg, and P. L. Perlman, *J. Am. Chem. Soc.*, **82**, 5256 (1960); (f) G. P. Muller, W. F. Johns, D. L. Cook, and R. A. Edgren, *ibid.*, **80**, 1769 (1958).

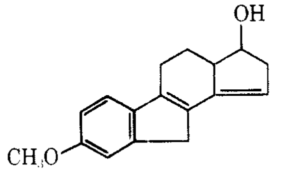
[5] (a) S. N. Ananchenko, V. Ye. Limanov, V. N. Leonov, V. N. Rzheznikov, and I. V. Torgov, *Tetrahedron*, **18**, 1355 (1962); (b) S. N. Ananchenko, C.-O. T'ang, and I. V. Torgov, *Bull. Acad. Sci. USSR, Div. Chem. Sci. Engl. Transl.*, 275 (1962); (c) S. N. Ananchenko, V. N. Leonov, A. V. Platonova, and I. V. Torgov, *Proc. Acad. Sci. USSR, Chem. Sect. Engl. Transl.*, **135**, 1211 (1960).

[6] (a) T. Miki, K. Hiraga, and T. Asako, *Chem. Pharm. Bull.* (Tokyo), **13**, 1285 (1965); (b) G. H. Douglas, J. M. H. Graves, D. Hartley, G. A. Hughes, B. J. McLoughlin, J. Siddall, and H. Smith, *J. Chem. Soc.*, 5072 (1963); (c) T. B. Windholz, J. H. Fried, and A. A. Patchett, *J. Org. Chem.*, **28**, 1092 (1963).

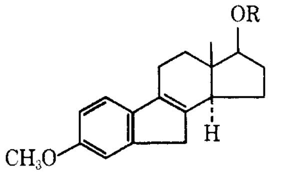
[7] All structures with the exception of **1b** depict racemic mixtures.

[8] J. A. Steele, L. A. Cohen, and E. Mosettig, *J. Am. Chem. Soc.*, **85**, 1134 (1963); (b) J. H. Burckhalter and H. Watanabe, ref 3b and c; (c) W. N. Speckamp, U. K. Pandit, and H. O. Huisman, *Tetrahedron Letters*, 2781 (1966); (d) W. N. Speckamp, H. deKoning, U. K. Pandit, and H. O. Huisman, *Tetrahedron*, **21**, 2517 (1965).

on the directing influence of a 17β-hydroxy group.[6a,9] Thus, reduction of **4** with sodium borohydride in methanol afforded tetracyclic alcohol **7** in 91% yield. Since **7** was the sole product of the reduction and in view of the fact that analogous pentaenones are known to reduce to the 17β alcohols under similar conditions,[6a,10] it was reasonable to assume that **7** had the 17β-OH configuration at C-17. In addition, the nmr spectrum of this material showed the 17α proton as a tripletlike multiplet centered at 246 cps with observed splittings of 8 cps, reminiscent of the 17α proton of testosterone.[11,12] Stereoselective reduction of the 14,15 double bond of **7** in the presence of 5% palladium on charcoal now proceeded smoothly and alcohol **8a** could be consistently obtained in yields of 65–70%. Ketone **6**, whose stereochemistry was assigned previously, was transformed by sodium borohydride into **8a**, thus affording additional support to both the 17β-OH configuration of **7** and the C/D *trans* stereochemistry of **6**.[13,14]



7

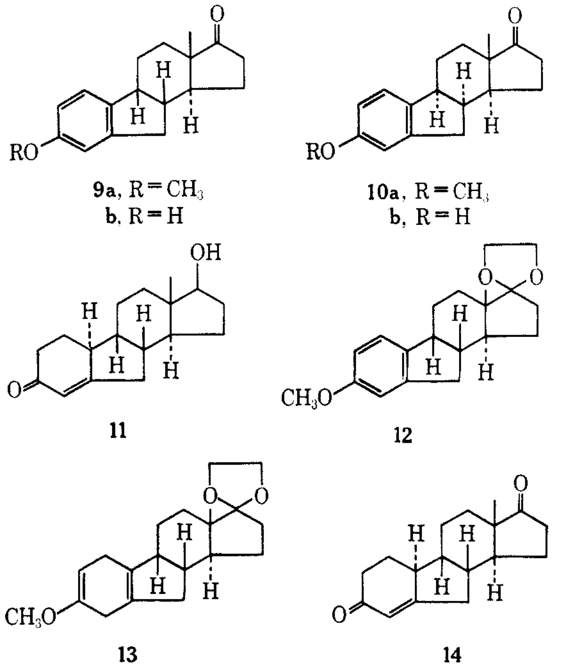


8a, R = H
b, R = CH_3CO

With **8a** in hand, various possibilities for reducing the 8,9 double bond were investigated. Based on previous studies,[6b,15,16] the double bond could be reduced in its present position in a dissolving metal reduction or it could be initially isomerized from the 8,9 to the 9,11 position and then reduced catalytically. When **8a** was allowed to react under a variety of acidic conditions, it was recovered essentially quantitatively, There was no detectable change in its ultraviolet spectrum and the nuclear magnetic resonance (nmr) spectrum showed the presence of no vinylic protons. Similar negative results were observed when isomerization was attempted with ketone **6**.

Lithium–ammonia reduction[17] of **8a**, followed by Jones oxidation,[18] afforded a mixture of two isomeric compounds, tentatively assigned structures **9a** and **10a**, in a ratio of 20:1, respectively (Chart II). When reduction was carried out in the presence of a proton source, ring A and the 8,9 double bond were reduced. Hydrolysis of the material from this reduction in methanolic hydrochloric acid[19] gave α,β-unsaturated ketone **11**. That **11** possesses the same stereochemical relationship at the B/C ring junction as **9a** was shown by converting both substances to **14**. Thus, cyclic ethylene ketal **12** was reduced with lithium in liquid ammonia[19,20] to dihydroketal **13**. Treatment of **13** with refluxing methanolic hydrochloric acid transformed it into diketone **14**. When **11** was treated with 8 *N* chromic acid solution,[18] the diketone obtained was identical with **14**.[21,22]

CHART II



With C/D ring junction fixed as *trans*, four isomers (**1b**, **9a**, **10a**, and **16**) are possible from lithium–ammonia reduction of the 8-dehydro intermediate. Neither **9a** nor **10a** was identical with an authentic sample of B-norestrone methyl ether (**1b**), prepared in another laboratory through partial, unequivocal synthesis.[23] By analogy with catalytic reduction of 8-dehydroestrone methyl ether,[6b,c] the product expected from catalytic hydrogenation of **8a** (followed by oxidation of the alcoholic function) would be **10a**. When **8a** was reduced in the presence of 10% palladium on charcoal followed by Jones oxidation,[18] a mixture in the ratio 1:8 of **9a** and **10a** was obtained. Since **10a** was the major product from the reduction, it was assigned 8α,9α stereochemistry. This assignment is in accord with anticipated α-face attack of the catalyst on the 8,9 double bond of **8a**. In addition, conformational analysis allows the deduction that steroidal ketones with 8α configuration of **10a** would give a 17β alcohol by hydride reduction.[24] Treatment

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[9] D. K. Banerjee, S. Chattejee, C. N. Pillai, and M. V. Bhatt, *J. Am. Chem. Soc.*, **78**, 3769 (1956).

[10] V. M. Rzheznikov, S. N. Ananchenko, and I. V. Torgov, *Bull. Acad. Sci. USSR, Div. Chem. Sci. Engl. Transl.*, 431 (1962).

[11] N. S. Bhacca and D. H. Williams, "Applications of NMR Spectroscopy in Organic Chemistry," Holden Day, Inc., San Francisco, Calif., 1964, p. 78.

[12] It is worth noting that the 17β proton of 17α-hydroxyandrost-4-en-3-one has been reported as a doubletlike multiplet: J. M. H. Graves, G. A. Hughes, T. Y. Jen, and H. Smith, *J. Chem. Soc.*, 5488 (1964).

[13] R. E. Brown, D. M. Lustgarten, R. J. Stanback, and R. I. Meltzer, *J. Org. Chem.*, **31**, 1489 (1966).

[14] L. F. Fieser and M. Fieser, "Steroids," Reinhold Publishing Corp., New York, N. Y., 1959, p 567.

[15] D. Banes and J. Carol, *J. Biol. Chem.*, **204**, 509 (1953).

[16] A. V. Zakharychev, S. N. Ananchenko, and I. V. Torgov, *Steroids*, **4**, 31 (1964).

[17] W. S. Johnson, E. R. Rogier, J. Szmuszkovicz, H. I. Hadler, J. Ackerman, B. K. Bhattacharyya, B. M. Bloom, L. Stalmann, R. A. Clement, B. Bannister, and H. Wynberg, *J. Am. Chem. Soc.*, **78**, 6289 (1956).

[18] (a) C. Djerassi, R. R. Engle, and A. Bowers, *J. Org. Chem.*, **21**, 1547 (1956); (b) K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon, *J. Chem. Soc.*, 39 (1946).

[19] A. L. Wilds and N. A. Nelson, *J. Am. Chem. Soc.*, **75**, 5366 (1953).

[20] J. A. Cella, E. A. Brown, and R. R. Burtner, *J. Org. Chem.*, **24**, 743 (1959).

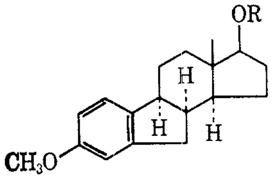
[21] The stereochemistry at C-10 in **11** and **14** was tentatively assigned by analogy with the retrosteroid series.[22]

[22] P. Westerhof and E. H. Reerink, *Rec. Trav. Chim.*, **79**, 1118 (1960), and references therein.

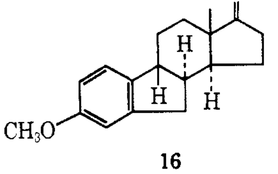
[23] A sample for comparison was kindly supplied to the authors by Dr. J. F. Kerwin through Dr. L. J. Griggs, both of Smith, Kline and French Laboratories.

[24] This consideration stems from the fact that the molecule has a U-shaped conformation with the β face as the concave surface of the U. For an example of this principle using a 3-keto 8α-steroid, see A. J. Birch and G. S. R. Subbarao, *J. Chem. Soc.*, 5139 (1965).

of **10a** with sodium borohydride gave alcohol **15a**, which was characterized as its acetate derivative **15b**. That **15a** has the 17β-OH configuration was established in the following manner. Alcohol **8a**, whose stereochemistry at C-17 was established previously, was reduced catalytically and the crude product was acetylated. An acetate identical with **15b** was isolated from this mixture in 46% yield.[25]



15a, R = H
b, R = CH_3CO



16

Catalytic hydrogenation of 8-dehydroestrone methyl ether proceeds exclusively from the α face.[6b,c] That result is explainable through the presence of the angular methyl group and the C-7β-hydrogen atom which block the β-face approach of the catalyst. However, according to Dreiding models, the C-7 methylene hydrogens of **8a** are oriented away from the 8,9 double bond and render its β face somewhat less hindered than that of 8-dehydroestrone methyl ether. The small amount of **9a** produced during the catalytic reduction of **8a** can thus be explained, assuming that hydrogen added to the double bond in a *cis* manner. In addition, the fourth and remaining structural possibility, 8α,9β isomer **16**, possesses a very severe flagpole interaction between the 9β-hydrogen and the angular methyl group and would not be a thermodynamically favorable product in a metal-ammonia reduction. Therefore, the 8β,9β stereochemistry was assigned to **9a**.[26]

Demethylation of **9a** and **10a** with pyridine hydrochloride[27] afforded phenols **9b** and **10b**.

Experimental Section

Catalytic hydrogenation reactions were carried out at room temperature and atmospheric pressure. Melting points were taken in open capillary tubes by use of a Mel-Temp electric block and are uncorrected. The ultraviolet spectra were determined in ethanol solution by means of a Beckman Model DK-2A ratio recording spectrophotometer. Infrared spectra were obtained with either a Perkin-Elmer Infracord or Model 337 grating spectrophotometer. Nmr spectra were obtained in deuteriochloroform solution with a Varian Associates Model A-60 spectrometer. Chemical shifts were measured with reference to tetramethylsilane as an internal standard. Microanalyses were performed by either Spang Microanalytical Laboratory, Ann Arbor, Mich., or Micro-Tech Laboratories Inc., Skokie, Ill.

(±)-5-Methoxy-1-vinylindan-1-ol (2).—A stirred suspension of 21.6 g (0.90 mole) of magnesium turnings in 400 ml of anhydrous tetrahydrofuran, activated by a crystal of iodine, was warmed to 40° and treated with 129.0 g (1.20 moles) of freshly distilled, dry vinyl bromide in 300 ml of anhydrous tetrahydrofuran under a nitrogen atmosphere. After the addition of *ca.* 50 ml of the vinyl bromide solution, the reaction commenced, the heating source was removed, and the addition rate was adjusted so that gentle refluxing was maintained. When the addition was complete (*ca.* 45 min) the mixture was refluxed for 0.5 hr, cooled to −20°, diluted with 150 ml of anhydrous ether, and treated with a solution of 48.6 g (0.30 mole) of 5-methoxyindan-1-one in 600 ml of anhydrous tetrahydrofuran and 150 ml of dry ether. The suspension was stirred at −20° for 1 hr, at room temperature for 3 hr and at reflux for 2 hr. After having been cooled to 0°, the mixture was hydrolyzed with an ice-cold solution of ammonium chloride, the organic layer was separated, and the aqueous phase was extracted with ether. The combined organic layers were washed with water and saturated sodium chloride solution, then dried over anhydrous sodium sulfate and evaporated *in vacuo*, leaving 59.6 g of crude allylic alcohol (**2**): ν_{max}^{neat} 3550 (OH) and 910 cm^{-1} ($CH{=}CH_2$). This material was used immediately in the preparation of **3**, without purification.

(±)-3-Methoxy-8,14-seco-B-norestra-1,3,5(10),9(11)-tetraene-14,17-dione (3).—Crude 5-methoxy-1-vinylindan-1-ol (**2**) (59.6 g) was dissolved in 300 ml of xylene and 180 ml of *t*-butyl alcohol and 33.6 g (0.3 mole) of 2-methylcyclopentane-1,3-dione was added. After stirring at room temperature for 15 min, 10.8 ml of a 40% methanolic solution of Triton B was added and the mixture was stirred and heated under reflux for 1.5 hr. When the dark brown solution had cooled to room temperature, *ca.* 1000 ml of ether was added and the resulting mixture was stirred for 0.5 hr and filtered. The filtrate was washed successively with 5% potassium hydroxide solution, water, and saturated sodium chloride solution, and dried over anhydrous sodium sulfate. The combined aqueous washings were extracted with ether; the ether was washed with water and saturated sodium chloride solution, and dried over anhydrous sodium sulfate. Evaporation of the organic extracts *in vacuo* afforded 106.8 g of crude semisolid material which was recrystallized once from 500 ml of ethanol to give 53.5 g (first crop), mp 83–86°, and 6.5 g (second crop), mp 80–83°, for a total of 60 g of **3**. Two additional recrystallizations from the same solvent afforded an analytical specimen of **3** as thick tan blades: mp 84–86°; λ_{max} 263 mμ (ε 19,900), 306 mμ (ε 8500); ν_{max}^{KBr} 1750, 1710 (β-diketone), 1650 (trisubstd C=C), 1590, and 1575 cm^{-1} (phenyl nucleus); nmr peaks at δ 7.37–6.61 (3 H multiplet, aromatic protons), 5.53 (1 H multiplet, HC=C), 3.74 (3 H singlet, OCH_3), and 1.13 (3 H singlet, CCH_3).

Anal. Calcd for $C_{18}H_{20}O_3$: C, 76.02; H, 7.09. Found: C, 76.04; H, 7.00.

(±)-3-Methoxy-B-norestra-1,3,5(10),8,14-pentaen-17-one (4).—A solution of 53.5 g (0.19 mole) of (±)-3-methoxy-8,14-seco-B-norestra-1,3,5(10),9(11)-tetraene-14,17-dione (**3**) in 1070 ml of methanol was warmed to 45° and *ca.* 4 ml of concentrated hydrochloric acid was added dropwise until the clear amber solution just became turbid. The heating source was removed and the suspension was stirred at room temperature for 1 hr. After being cooled to 10° in an ice bath, the precipitate was collected by filtration, washed thoroughly with cold methanol, and dried, giving 46 g (92%) of **4**, mp 159–162°. Two recrystallizations from methanol produced an analytical sample of **4** as a light lavender solid: mp 159–160°; λ_{max} 307 mμ (ε 28,400); ν_{max}^{KBr} 1740 (C=O), 1620 (trisubstd C=C), 1600, and 1580 cm^{-1} (phenyl nucleus); nmr peaks at δ 7.10–6.71 (3 H multiplet, aromatic protons), 5.74 (1 H multiplet, HC=C), 3.80 (3 H singlet, OCH_3), and 1.14 (3 H singlet, CCH_3).

Anal. Calcd for $C_{18}H_{18}O_2$: C, 81.17; H, 6.81. Found: C, 81.08; H, 6.89.

(±)-3-Methoxy-B-norestra-1,3,5(10),8-tetraen-17-one (6).—A suspension of 1.0 g of 5% palladium on calcium carbonate in 50 ml of toluene was prereduced in an atmosphere of hydrogen for 1.5 hr. A solution of 2 g (7.7 mmoles) of (±)-3-methoxy-B-norestra-1,3,5(10),8,14-pentaen-17-one (**4**) in 200 ml of toluene was added and the reaction mixture was allowed to consume 1 equiv of hydrogen during 40 min. The catalyst was removed by filtration through Celite 545 and the toluene was evaporated *in vacuo* under nitrogen. The residual tan oil was dissolved in 30 ml of normal hexane, 10 drops of ethyl acetate was added,

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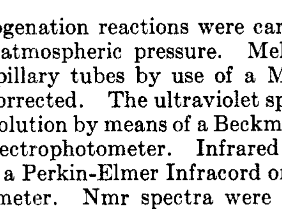
[25] The other product in this mixture is undoubtedly acetate **i**, but no attempt was made to isolate it.



i

[26] Rigorous stereochemical assignments *via* a complete X-ray crystallographic analysis is currently underway in the laboratory of Professor C. E. Nordman of this University.

[27] A. L. Wilds and W. McCormack, *J. Am. Chem. Soc.*, **74**, 2832 (1948).

and the solution was set aside in the icebox for 1 hr. A highly crystalline solid (1.4 g), mp 109–110°, separated and was recrystallized from ethyl acetate to give 800 mg of material, mp 118–120°, with slight previous softening at 115°. The nmr spectrum of this material showed C-18 methyl resonances at δ 0.95 and 0.85 in the ratio of 1:3, respectively. The significance of this observation was discussed in the text. Three additional recrystallizations from methanol gave 500 mg (25%) of **6** as light tan flakes: mp 121–122.5°; λ_{max} 269 mμ (ϵ 17,500); ν_{max}^{KBr} 1730 (C=O), 1600, and 1570 cm^{-1} (phenyl nucleus); nmr peaks at δ 7.13–6.66 (3 H multiplet, aromatic protons), 3.78 (3 H singlet, OCH_3), and 0.83 (3 H singlet, CCH_3).

Anal. Calcd for $C_{18}H_{20}O_2$: C, 80.56; H, 7.51. Found: C, 80.58; H, 7.59.

This transformation can also be effected using 2% palladium on strontium carbonate in toluene in approximately the same yield.

(±)-3-Methoxy-B-norestra-1,3,5(10),8,14-pentaen-17β-ol (7).—A suspension of 40 g (0.15 mole) of (±)-3-methoxy-B-norestra-1,3,5(10),8,14-pentaen-17-one (**4**) in 1500 ml of methanol was cooled in an ice bath and treated with 18.24 g (0.48 mole) of sodium borohydride in one portion. After 20 min, the cooling source was removed and the yellow suspension was stirred at room temperature for an additional 100 min. The ice bath was again set in place and 500 ml of cold water was added. The pH was adjusted to 7 with *ca.* 30 ml of concentrated hydrochloric acid, and an additional 250 ml of cold water was added. The yellow precipiate was collected by filtration, washed with cold aqueous methanol, and dried, giving 37.3 g (91%) of **7**, mp 167–170°, with softening at 166°. One recrystallization from aqueous methanol afforded an analytical specimen of **7** as thin yellow needles: mp 168–169°; λ_{max} 308 mμ (ϵ 29,000); ν_{max}^{Nujol} 3575 (OH), 1600 (trisubstd C=C), 1585, and 1560 cm^{-1} (phenyl nucleus); nmr peaks at δ 7.27–6.73 (3 H multiplet, aromatic protons), 5.41 (1 H triplet, J = 3 cps, HC=C), 4.10 (1 H, approximate triplet, J = 8 cps, 17α-H), 3.81 (3 H singlet, OCH_3), and 1.00 (3 H singlet, CCH_3).

Anal. Calcd for $C_{18}H_{20}O_2$: C, 80.56; H, 7.51. Found: C, 80.48; H, 7.49.

(±)-3-Methoxy-B-norestra-1,3,5(10),8-tetraen-17β-ol (8a). A. From Catalytic Reduction of 7.—A suspension of 200 mg of 5% palladium on charcoal in 50 ml of ethanol was equilibrated in an atmosphere of hydrogen for 25 min. A solution of 538 mg (2 mmoles) of (±)-3-methoxy-B-norestra-1,3,5(10),8,14-pentaen-17β-ol (**7**) in 150 ml of ethanol was added and the reaction mixture was allowed to consume 1 equiv of hydrogen (6 min). The catalyst was removed by filtration through Celite 545 and the ethanol was evaporated under reduced pressure. Two recrystallizations of the residue from aqueous methanol gave 129 mg (24%) of **8a** as large colorless crystals: mp 140–142°, with the evolution of bubbles at the melt; λ_{max} 268 mμ (ϵ 15,000); ν_{max}^{Nujol} 3375 (OH), 1600, and 1570 cm^{-1} (phenyl nucleus); nmr peaks at δ 7.15–6.70 (3 H multiplet, aromatic protons), 3.80 (4 H, singlet overlapping a multiplet, OCH_3 and 17α-H), and 0.75 (3 H singlet, CCH_3). This spectrum also shows a minor peak at δ 0.83, possibly representing the 14β epimer. It constitutes *ca.* 10% of the product and could not be removed through repeated recrystallization.

Anal. Calcd for $C_{18}H_{22}O_2$: C, 79.96; H, 8.20. Found: C, 78.79; H, 8.19.

Apparently this substance solvates quite strongly. It was not uncommon for an aqueous methanolic solution of **8a**, when allowed to stand at room temperature for several hours, to crystallize as three or four extremely large crystals. Powdering the crystals in a mortar and prolonged drying at 0.05 mm over refluxing toluene improved the analysis somewhat.

Anal. Calcd for $C_{18}H_{22}O_2$: C, 79.96; H, 8.20. Found: C, 79.36; H, 8.27.

In larger scale work, ethyl acetate was used as the solvent both for the reaction and to recrystallize the product. Also, reduction of the quantity of catalyst greatly improved the yields. For example, in a typical 3.75-g run, 100 mg of 5% palladium on charcoal was used. Under these conditions, material comparable in purity to that just described could be obtained in yields consistently in the range of 65–70%. The use of milder catalysts such as 5% palladium on calcium carbonate or 2% palladium on strontium carbonate did not improve either the yield or the purity of the product in this transformation.

B. From Hydride Reduction of 6.—A solution of 250 mg (0.93 mmole) of (±)-3-methoxy-B-norestra-1,3,5(10),8-tetraen-17-one (**6**) in 20 ml of methanol was treated with 125 mg (3.29 mmoles) of sodium borohydride in one portion. The colorless solution was stirred at room temperature until the evolution of hydrogen stopped (*ca.* 1 hr). After being cooled to 0° in an ice bath, 20 ml of cold water was added and the resulting suspension was stirred for 15 min. The precipitate was collected by filtration, washed with water, and dried. The crude alcohol (250 mg), mp 130–140°, was recrystallized once from ethyl acetate, affording 148 mg (59%) of **8a**, mp 140–142°, with the evolution of bubbles at the melt. On admixture with a specimen prepared by catalytic reduction of **7**, the mixture melted at 140–142°, also evolving bubbles at the melt. The infrared spectra were the same.

(±)-3-Methoxy-B-norestra-1,3,5(10),8-tetraen-17β-ol Acetate (8b).—A solution of 540 mg (2 mmoles) of (±)-3-methoxy-B-norestra-1,3,5(10),8-tetraen-17β-ol (**8a**) in 5 ml of acetic anhydride and 5 ml of dry pyridine was allowed to stand at room temperature for 24 hr. The clear, faintly yellow solution was poured onto ice and the mixture was extracted with three 25-ml portions of ether. The combined ether extracts were washed successively with water, saturated sodium bicarbonate solution, water, saturated sodium chloride solution, and dried over anhydrous sodium sulfate. Evaporation of the ether *in vacuo* afforded a pale yellow oil which was recrystallized three times from methanol to give 287 mg (46%) of **8b** as small white flakes: mp 109–111°; λ_{max} 267 mμ (ϵ 18,000); ν_{max}^{Nujol} 1720 (C=O), 1600, 1570 (phenyl nucleus), and 1240 cm^{-1} (C–O–CO); nmr peaks at δ 7.13–6.68 (3 H multiplet, aromatic protons), 4.80 (1 H multiplet, 17α-H), 3.78 (3 H singlet, OCH_3), 2.05 (3 H singlet, $OOC\text{-}CH_3$), and 0.77 (3 H singlet, CCH_3).

Anal. Calcd for $C_{20}H_{24}O_3$: C, 76.89; H, 7.74. Found: C, 76.96; H, 7.60.

In an attempt to grow larger crystals of **8b**, a sample was recrystallized from a very dilute solution in methanol. A second crystalline form, mp 88–89°, was obtained. The infrared spectra of both polymorphic forms in chloroform solution were identical.

(±)-3-Methoxy-B-nor-9β-estra-1,3,5(10)-trien-17-one (9a).—A solution of 4.32 g (16 mmoles) of (±)-3-methoxy-B-norestra-1,3,5(10),8-tetraen-17β-ol (**8a**) in 240 ml of anhydrous tetrahydrofuran was placed in a three-necked, 1000-ml flask equipped with two Dewar condensers and a magnetic stirring bar. The flask was charged with 480 ml of liquid ammonia and the clear, colorless solution treated with 560 mg (80.0 mmoles) of lithium wire (*ca.* 1-cm lengths) during 1 min. The deep blue reaction mixture was stirred for an additional 15 min and decomposed by the rapid addition of 2 g of ammonium chloride. The solvents were evaporated in a current of air with the aid of gentle warming on a steam bath. The residue was dissolved in ether and water; the organic layer was separated and washed successively with water, Claisen's alkali, water, and saturated solution of sodium chloride, and dried over anhydrous sodium sulfate. Evaporation of the ether *in vacuo* gave a pale yellow gum which showed two components by thin layer chromatography (tlc) analysis (silica gel G eluted with 50% ethyl acetate in benzene and developed with iodine vapor). The gum was dissolved in 250 ml of alcohol free acetone and titrated with 8 N chromic acid solution until the orange-red color persisted, *ca.* 7.5 ml. Excess chromic acid was destroyed by adding several drops of 2-propanol and cracked ice was added in small portions until precipitation was complete. The precipitate was collected by filtration, washed with water, dried briefly, and recrystallized twice from aqueous ethanol to give 1.6 g (37%) of **9a**, mp 93–95°. An analytical specimen prepared by recrystallization from the same solvent system crystallized as long thin blades: mp 93–95°; λ_{max} 282 mμ (ϵ 2900) and 288 mμ (ϵ 2500); ν_{max}^{KBr} 1725 (C=O), 1600, and 1560 cm^{-1} (phenyl nucleus); nmr peaks at δ 7.13–6.61 (3 H multiplet, aromatic protons), 3.76 (3 H singlet, OCH_3), and 0.91 (3 H singlet, CCH_3).

Anal. Calcd for $C_{18}H_{22}O_2$: C, 79.96; H, 8.20. Found: C, 79.80; H, 8.11.

This compound could not be induced to form a crystalline 2,4-dinitrophenylhydrazone. In subsequent runs this isomer (**9a**) was obtained in yields up to 52%.

The filtrate from the chromic acid oxidation was evaporated to a small volume in a current of air, diluted with water, and extracted with ether. The ether was washed with saturated sodium bicarbonate solution, water, and saturated sodium chloride solution. After being dried over anhydrous sodium sulfate, the solvent was evaporated *in vacuo*, and the gummy residue was chromatographed on 200 g of neutral alumina. Elution with benzene gave, after recrystallization from aqueous ethanol, 300 mg of a crystalline mixture of **9a** and **10a**, mp 83–102°. Further elution with the same solvent afforded, after recrystallization from aqueous ethanol, 65 mg of **10a**, mp 121–122.5°, as fine white needles. On admixture with a sample of **10a** prepared by catalytic hydrogenation, mp 120–122°, the mixture melted at 120–122°.

(±)-3-Hydroxy-B-nor-9β-estra-1,3,5(10)-trien-17-one (9b).—A mixture of 72 mg (0.26 mmole) of (±)-3-methoxy-B-nor-9β-estra-1,3,5(10)-trien-170one (**9a**) and 720 mg of dry pyridine hydrochloride was heated at 205–208° for 40 min in a nitrogen atmosphere. After having cooled to room temperature, the contents of the flask were added to 25 ml of ice-cold water, the precipitate was collected by filtration, washed well with cold water, and then was dissolved in 75 ml of ether. The ether was extracted with three 20-ml portions of 20% sodium hydroxide and the combined basic extracts were cooled in an ice bath and acidified with concentrated hydrochloric acid. The resulting suspension was extracted with three 25-ml portions of ether and the combined ether extracts were washed with 5% sodium bicarbonate solution, water, and saturated solution of sodium chloride, and dried over anhydrous sodium sulfate. Evaporation of the solvent under reduced pressure, followed by one recrystallization from 50% aqueous methanol, gave 28.4 mg (41%) of **9b** as small white flakes: mp 169.5–171.5°; λ_{max} 283 mμ (ϵ 3000); λ_{max}^{base} 244 mμ (ϵ 8500) and 303 mμ (ϵ 3450); ν_{max}^{KBr} 3500 (OH), 1720 (C=O), 1600, and 1575 cm^{-1} (phenyl nucleus).

Anal. Calcd for $C_{17}H_{20}O_2$: C, 79.65; H, 7.86. Found: C, 79.66; H, 7.74.

In larger runs, the melting point of this material was raised to 172.5–174.5°. The **benzoate** of **9b** crystallized from methanol as small colorless needles, mp 153–155°.

Anal. Calcd for $C_{24}H_{24}O_3$: C, 79.97; H, 6.71. Found: C, 80.14; H, 6.73.

(±)-17β-Hydroxy-B,19-dinor-9β,10α-androst-4-en-3-one (11).—A solution of 540 mg (2 mmoles) of (±)-3-methoxy-B-nor-estra-1,3,5(10),8-tetraen-17β-ol (**8a**) in 20 ml of anhydrous tetrahydrofuran, 20 ml of dry ether, and 7 ml of 2-propanol was placed in a three-necked, 300-ml flask equipped with a Dewar condenser and magnetic stirring bar. Liquid ammonia (75 ml) was distilled into the flask and freshly cut sodium metal was added in small portions until the deep blue color persisted. The mixture was stirred for 7 min and decomposed with excess ammonium chloride. The solvents were evaporated in a current of nitrogen and the residue was dissolved in ether and water. The ether layer was separated, washed with water and saturated sodium chloride solution, and dried over anhydrous sodium sulfate. Evaporation of the solvent *in vacuo* afforded a gum which could not be induced to crystallize. The gum showed peaks in the infrared at 1680 and 1650 cm^{-1} (1,4-dihydroanisole system) and no appreciable absorption in the ultraviolet between 220 and 360 mμ. It was dissolved in 25 ml of methanol; the solution was heated to 60° and treated with 15 ml of concentrated hydrochloric acid. After being refluxed for 15 min, the pale yellow solution was cooled to room temperature and diluted with ether and water. The organic phase was separated, washed successively with water, saturated sodium bicarbonate solution, water, and saturated sodium chloride solution, and dried over anhydrous sodium sulfate. Evaporation of the solvent *in vacuo*, followed by two recrystallizations from benzene, afforded 100 mg (19%) of **11** as beige rosettes: mp 196.5–198.5°; λ_{max} 240 mμ (ϵ 15,500); ν_{max}^{KBr} 3500 (OH) and 1625 cm^{-1} (unsaturated C=O); nmr peaks at δ 5.88 (1 H, poorly resolved multiplet, HC=C), 3.65 (1 H, approximate triplet, J = 8 cps, 17α-H), and 0.79 (3 H singlet, CCH_3).

Anal. Calcd for $C_{17}H_{24}O_2$: C, 78.41; H, 9.29. Found: C, 78.48; H, 9.17.

(±)-17,17-Ethylenedioxy-3-methoxy-B-nor-9β-estra-1,3,-5(10)-triene (12).—Ethylene glycol (5 ml) was added to a solution of 353 mg (1.3 mmoles) of (±)-3-methoxy-B-nor-9β-estra-1,3,5(10)-trien-17-one (**9a**) in 100 ml of benzene containing 25 mg of *p*-toluenesulfonic acid monohydrate, and the mixture was stirred and heated under reflux in a system equipped with a Dean–Stark water separator for 24 hr. After being cooled to room temperature, the mixture was extracted with 5% potassium carbonate solution and dried over anhydrous potassium carbonate. The benzene was evaporated *in vacuo* and the residue was recrystallized twice from methanol to give 350 mg (85%) of **12** as small colorless needles: mp 70–72.5°; λ_{max} 282 mμ (ϵ 2720) and 288 mμ (ϵ 2480); ν_{max}^{KBr} 1595 and 1570 cm^{-1} (phenyl nucleus) and devoid of carbonyl absorption; nmr peaks at δ 7.11–6.58 (3 H multiplet, aromatic protons), singlets at 3.78 and 3.75 (7 H, OCH_3CH_2O and OCH_3, respectively), and 0.90 (3 H singlet, CCH_3).

Anal. Calcd for $C_{20}H_{26}O_3$: C, 76.39; H, 8.33. Found: C, 76.38; H, 8.33.

In subsequent work carried out on a larger scale, the melting point of this substance, from ethanol, was raised to 73–74°.

(±)-17,17-Ethylenedioxy-3-methoxy-B-nor-9β-estra-2,5(10)-diene (13). A. From the Wilds–Nelson Procedure.[19]—A solution of 250 mg (0.79 mmole) of (±)-17,17-ethylenedioxy-3-methoxy-B-nor-9β-estra-1,3,5(10)-triene (**12**) in 18 ml of anhydrous ether was placed in a three-necked, 100-ml flask equipped with a Dewar condenser, dropping funnel, and magnetic stirring bar. Liquid ammonia (23 ml) was distilled into the flask and the colorless solution was treated with 250 mg of lithium wire (*ca.* 0.5-cm lengths) during 10 min. The dark blue mixture was stirred for 10 min, then treated dropwise with 5 ml of absolute ethanol over a 10–20-min period. The solvents were evaporated in a current of nitrogen and the residue was dissolved in ether and water. The ether layer was separated, washed with water and saturated sodium chloride solution, and dried over anhydrous sodium sulfate. Evaporation of the solvent *in vacuo* gave 158 mg of crude gummy product which crystallized on scratching. One recrystallization from methanol afforded 125 mg (50%) of **13** as colorless flakes: mp 97–98.5°; λ_{max}, no significant absorption in the region 220–360 mμ; ν_{max}^{KBr} 1695 and 1650 cm^{-1} (1,4-dihydroanisole system); nmr peaks at δ 5.41 (1 H, poorly resolved triplet, HC=C), 3.86 (4 H singlet, OCH_2CH_2O), 3.73 (3 H singlet, OCH_3), and 0.86 (3 H singlet, CCH_3).

Anal. Calcd for $C_{20}H_{28}O_3$: C, 75.91; H, 8.91. Found: C, 75.91; H, 8.98.

B. From the Dryden Procedure.[20]—A solution of 500 mg (1.59 mmoles) of (±)-17,17-ethylenedioxy-3-methoxy-B-nor-9β-estra-1,3,5(10)-triene (**12**) in 7.5 ml of dry *t*-butyl alcohol and 7.5 ml of anhydrous tetrahydrofuran was placed in a three-necked, 100-ml flask equipped with a dewar condenser, dropping funnel, and magnetic stirring bar. Liquid ammonia (30 ml) was distilled into the flask and the colorless solution was treated with 500 mg of lithium wire (*ca.* 0.5-cm lengths) during 30 min. The two-phase system was stirred for 3 hr, after which a solution of 5 ml of absolute ethanol in 10 ml of anhydrous tetrahydrofuran was added dropwise during 30 min. The Dewar condenser was removed and the solvents were evaporated in a current of nitrogen. The residue was dissolved in ether and water, the organic layer was separated, washed with water and saturated sodium chloride solution, and dried over anhydrous sodium sulfate. Evaporation of the ether under vacuum, followed by recrystallization of the residue from methanol, gave 340 mg (first crop), mp 95–98°, and 60 mg (second crop), mp 95–98°, of **13** (80%). A second recrystallization from the same solvent raised the melting point to 98–99°. On admixture with a sample prepared by the Wilds–Nelson procedure, mp 97–98.5°, the mixture melted at 97–98.5°. The infrared spectra were identical.

(±)-B,19-Dinor-9β,10α-androst-4-ene-3,17-dione (14). A. From Hydrolysis of 13.—A solution of 300 mg (0.95 mmole) of (±)-17,17-ethylenedioxy-3-methoxy-B-nor-9β-estra-2,5(10)-diene (**13**) in 25 ml of methanol was heated to reflux and 10 ml of concentrated hydrochloric acid was added in one portion. The clear, colorless solution was maintained at the reflux temperature for 15 min, cooled, and diluted with water and ether. The organic layer was separated, washed successively with water, saturated sodium bicarbonate solution, water, and saturated sodium chloride solution, and dried over anhydrous sodium sulfate. The solvent was evaporated *in vacuo* and the residue was recrystallized once from ethyl acetate to give 115 mg (47%) of **14** as colorless rods: mp 174–176°, λ_{max} 240 mμ (ϵ 15,800), ν_{max}^{KBr} 1725 (saturated C=O) and 1650 cm^{-1} (unsaturated C=O), nmr peaks at δ 5.95 (1 H, poorly resolved multiplet, HC=C) and 0.91 (3 H singlet, CCH_3).

Anal. Calcd for $C_{17}H_{22}O_2$: C, 79.02; H, 8.58. Found: C, 78.89; H, 8.66.

B. From Oxidation of 11.—A solution of 50 mg (0.18 mmole) of (±)-17β-hydroxy-B,19-dinor-9β,10α-androst-4-en-3-one (**11**) in 20 ml of alcohol free acetone was cooled to 0° in a ice bath. Nitrogen was bubbled through the colorless solution while 5 drops of 8 *N* chromic acid solution was added during 3 min. Several drops of 2-propanol was added to destroy the excess oxidant and most of the acetone was evaporated *in vacuo* under nitrogen at 25°. The remaining olive-green suspension was dissolved in ether and water, and the organic layer was separated. It was washed successively with water, saturated sodium bicarbonate solution, water, and saturated sodium chloride solution, and dried over anhydrous sodium sulfate. After evaporating the solvent *in vacuo*, the residue was recrystallized once from ethyl acetate to give 12 mg (first crop), mp 174–176°, and 15 mg (second crop), mp 172–174°, of **14**. A mixture melting point between a sample from the first crop and a specimen of **14** prepared from hydrolysis of **13**, mp 174–176°, showed no depression. The infrared spectra were identical.

(±)-3-Methoxy-B-nor-8α-estra-1,3,5(10)-trien-17-one (10a).—A suspension of 625 mg of 10% palladium on charcoal in 50 ml of methanol–ethyl acetate (1:1) was equilibrated in an atmosphere of hydrogen for 30 min. A solution of 5.0 g (18.5 mmoles) of (±)-3-methoxy-B-norestra-1,3,5(10),8-tetraen-17β-ol (**8a**) in 450 ml of methanol–ethyl acetate (1:1) was added and after consuming 1 equiv of hydrogen during 22 min, the reaction stopped. Stirring was continued for 0.5 hr and no additional hydrogen was taken up. The catalyst was removed by filtration through Celite 545 and the solvents were evaporated *in vacuo*, leaving 5.1 g of colorless oily residue. A second run was conducted exactly as described above and the combined residues (10.1 g) were dissolved in 500 ml of alcohol free acetone and treated dropwise with 8 *N* chromic acid solution until the characteristic orange-red color persisted, *ca.* 16 ml. Excess chromic acid was destroyed through the addition of several drops of 2-propanol and cracked ice was added in small portions until precipitation was complete. The mixture was stirred for 20 min at 0° with cracked ice being added as needed to maintain the temperature. The precipitate was collected by filtration, washed with water and dried, giving 9 g of crude material, mp 98–118°, with previous softening at 79°. One recrystallization from aqueous ethanol gave 6 g (60%) of **10a**, mp 120–122°, with slight previous softening at 116°. The mother liquor from this recrystallization afforded a second isomeric product, *vide infra*. An analytical specimen of **10a** crystallized from aqueous ethanol as thick colorless needles: mp 120–122°; λ_{max} 280 mμ (ϵ 2900) and 287 mμ (ϵ 2500); ν_{max}^{KBr} 1725 (C=O), 1600, and 1570 cm^{-1} (phenyl nucleus); nmr peaks at δ 7.20–6.63 (3 H multiplet, aromatic protons), 3.76 (3 H singlet, OCH_3), and 0.98 (3 H singlet, CCH_3).

Anal. Calcd for $C_{18}H_{22}O_2$: C, 79.96; H, 8.20. Found: C, 80.03; H, 8.29.

The **2,4-dinitrophenylhydrazone** of **10a** crystallized from ethyl acetate as small orange needles, mp 242–244°.

Anal. Calcd for $C_{24}H_{26}N_4O_5$: C, 63.98; H, 5.81; N, 12.43. Found: C, 64.03; H, 5.68; N, 12.54.

The mother liquor from the first recrystallization of the crude oxidized product was concentrated to *ca.* one-half volume in a current of air and allowed to stand at room temperature overnight. The solution deposited 800 mg (8%) of **9a**, mp 92–94°. One recrystallization from aqueous ethanol raised the melting point to 93–95°, undepressed on admixture with a sample of **9a** prepared by the lithium in liquid ammonia method. The infrared and nmr spectra were identical.

On some occasions, the fractional crystallization did not proceed as cleanly as described above and the concentrated mother liquor deposited crystals with a wide melting range. In these cases, the mixture was separated by chromatography on alumina. For example, in a 5-g run carried out exactly as described above, 600 mg of a crystalline mixture of **9a** and **10a**, mp 80–95°, was deposited by the concentrated mother liquor from the first recrystallization of the crude oxidized product. The mixture was chromatographed on 200 g of neutral alumina. Elution with 30% benzene in petroleum ether (bp 30–60°) afforded in the early fractions, after recrystallization from aqueous ethanol, 300 mg of **9a**, mp 93–95°. The middle fractions gave solid material with a wide melting range. Later fractions obtained by continued elution with the same solvent system gave, after recrystallization from aqueous ethanol, 100 mg of **10a**, mp 120–122°.

(±)-3-Hydroxy-B-nor-8α-estra-1,3,5(10)-trien-17-one (10b).—A mixture of 38 mg (0.14 mmole) of (±)-3-methoxy-B-nor-8α-estra-1,3,5(10)-trien-17-one (**10a**) and 400 mg of dry pyridine hydrochloride was allowed to stand at 212° for 40 min in a nitrogen atmosphere. When the reaction mixture had cooled to room temperature, the contents of the flask were transferred with the aid of several drops of ethanol to 20 ml of ice-cold water. The mixture was stirred at room temperature for 20 min and the precipitate was collected by filtration and dried. The crude phenol (28.7 mg) was recrystallized once from methanol to give 18 mg (50%) of **10b** as small colorless needles: mp 265–267° (red melt) with slight charring at 255°; λ_{max} 282 mμ (ϵ 3000); λ_{max}^{base} 240 mμ (ϵ 8450) and 302 mμ (ϵ 3260); ν_{max}^{KBr} 3325 (OH), 1700 (C=O), and 1600 cm^{-1} (phenyl nucleus).

Anal. Calcd for $C_{17}H_{20}O_2$: C, 79.65; H, 7.86. Found: C, 79.72; H, 7.92.

The **benzoate** of **10b** crystallized from methanol–ethyl acetate (2:1) as small colorless flakes, mp 193–198°.

Anal. Calcd for $C_{24}H_{24}O_3$: C, 79.97; H, 6.71. Found: C, 80.10; H, 6.71.

(±)-3-Methoxy-B-nor-8α-estra-1,3,5(10)-trien-17β-ol Acetate (15b). A. From Catalytic Reduction and Acetylation of 8a.—A suspension of 200 mg of 10% palladium on charcoal in 70 ml of methanol was equilibrated in an atmosphere of hydrogen for 30 min. A solution of 383 mg (1.42 mmoles) of (±)-3-methoxy-B-norestra-1,3,5-(10),8-tetraen-17β-ol (**8a**) in 100 ml of methanol was added and the reaction consumed 1.1 equiv of hydrogen during 20 min and stopped. Stirring was continued for 0.5 hr and no additional hydrogen was taken up. Filtration through Celite 545 removed the catalyst and evaporation of the methanol under reduced pressure afforded 425 mg of colorless gum. The gum was dissolved in 7 ml of pyridine and filtered through a small cotton plug. The filtrate was treated with 5 ml of acetic anhydride and allowed to stand at room temperature overnight. The solution was poured into 5% sodium bicarbonate solution, ether was added, and the mixture was stirred for 5 min. The ether layer was separated, washed with water and saturated solution of sodium chloride, and dried over anhydrous sodium sulfate. Removal of the solvent under reduced pressure afforded 255 mg of crude product. One recrystallization from aqueous methanol, followed by a second recrystallization from methanol, gave 207 mg (46%) of **15b** as colorless rods: mp 116–118°, λ_{max} 280 mμ (ϵ 2900) and 287 mμ (ϵ 2500); ν_{max}^{KBr} 1720 (C=O), 1600, 1570 (phenyl nucleus), and 1240 cm^{-1} (C-O-CO).

Anal. Calcd. for $C_{20}H_{26}O_3$: C, 76.39; H, 8.33. Found: C, 76.30; H, 8.27.

B. From Hydride Reduction and Acetylation of 10a.—A solution 300 mg (1.1 mmoles) of (±)-3-methoxy-B-nor-8α-estra-1,3,5(10)-trien-17-one (**10a**) in 35 ml of methanol was treated with 300 mg of sodium borohydride in one portion. The colorless solution was stirred at room temperature for 3 hr, diluted with ice water, the precipitate was collected by filtration and dried at 55° for 3 hr. The crude alcohol (**15a**, 300 mg) precipitated from a variety of solvents as an amorphous solid. This material (**15a**) appeared homogeneous in two tlc systems: silica gel G eluted with 50% ethyl acetate in benzene, R_f 0.59; and alumina G eluted with ethyl acetate, R_f 0.60. The solid was dissolved in 4 ml of acetic anhydride and 1 ml of pyridine and the solution heated under reflux for 1 hr. The solvents were distilled at atmospheric pressure and the residue was crystallized immediately on contact with several drops of water. The crystals were collected by filtration, washed well with cold water, and recrystallized twice from methanol, affording 225 mg (65%) of **15b** as colorless rods, mp 117–118°. This material showed nmr peaks at δ 7.17–6.58 (3 H multiplet, aromatic protons), 4.64 (1 H, approximate triplet, $J = 7$ cps, 17α-H), 3.75 (3 H singlet, OCH_3), 2.01 (3 H singlet, $OOCCH_3$), and 0.90 (3 H singlet, CCH_3). On admixture with a specimen prepared by method A, mp 116–118°, the mixture melted at 116–118°. The infrared spectra were identical.

Hydrolysis of a sample of **15b** in aqueous methanolic potassium carbonate during 20 hr gave back **15a** as the same amorphous solid.

Registry No.—**3**, 14789-51-6; **4**, 14805-08-4; **6**, 14805-09-5; **7**, 14805-10-8; **8a**, 14805-11-9; **8b**, 14805-12-0; **9a**, 14805-13-1; **9b**, 14805-14-2; benzoate of **9b**, 14805-15-3; **10a**, 14805-16-4; 2,4-dinitrophenylhydrazone of **10a**, 14805-17-5; **10b**, 14901-44-1; benzoate of **10b**, 14901-45-2; **11**, 14805-18-6; **12**, 14805-19-7; **13**, 14805-20-0; **14**, 14805-21-1; **15b**, 14805-22-2.