Stereoelectronically Controlled, Thallium(III)-Mediated C-19 Degradation of 19-Hydroxy Steroids. An Expedient Route to Estrone and its Congeners via 19-Nor-10β-hydroxy Intermediates†

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Estrone (**8b**) has been synthesized in four steps from 3β-acetoxy-19-hydroxyandrost-5-en-17-one (**2b**), readily available from an industrial precursor. A key feature of the strategy is a stereoelectronically controlled, Tl(III)-mediated degradation (**2b** → **5b**). Oppenauer oxidation of diol **6b**, resulting from saponification of the acetate **5b**, afforded the unsaturated 10β-hydroxy ketone **7b**, acid treatment of which induced aromatization affording **8b**. An alternative route including dehydration (**5b** → **9b**) followed by Oppenauer oxidation (**10b** → **8b**) gave comparable results. This strategy has first been developed with the aid of cholestane model compounds (**2a** → **5a**) and then successfully applied to the synthesis of analogues in the cholestane, androstane, and pregnane series to produce the corresponding 19-nor-10β-hydroxy derivatives **7a–d** and A-aromatic steroids **8a–d**.

Introduction

Steroids with an aromatic A-ring, namely estrone (**8b**) and estradiol (**8c**), are imporant hormones that control the menstruation cycle of female mammals.[1] Extensive labeling studies have shown that biosynthesis of estrone and its congeners proceeds via the initial C-19 functionalization followed by aromatization.[2]

All sources for industrial synthesis of steroids (namely diosgenin, sitosterol, and cholesterol) also contain the 10β-methyl group (C-19), as in **1**. Hence, any partial synthesis starting from this chiral pool[1,3] must encompass demethylation at some stage, thus mimicking the strategy employed by Nature. However, the removal of C-19 is an elaborate process.[3] Consequently, total syntheses[4] can compete successfully, in particular the recent enantioselective approaches,[4b–d] which have succeeded those of the early days, that required tedious resolution of synthetic racemates.[5]

We now wish to rekindle interest in the partial synthetic approach by presenting an expedient route toward A-aromatic steroids starting with abundant, natural C-19 precursors, namely cholesterol and its androstane and pregnane congeners. The synthesis has first been developed using the cholestane models and then applied in the androstane and pregnane series. Furthermore, this synthetic approach brings about 19-nor-10β-hydroxy steroids that might serve as precursors in a search for inhibitors of enzymes such as placental aromatase[6] or 5α-reductase[7] that are often responsible for metabolic disorders.[8]

Results and Discussion

Functionalization of C-19 (**1** → **2a**), an initial synthetic step required for removing this carbon,[3,9] was developed in the 1960s as an efficient and reliable, three-step procedure affording up to ca. 50% overall yield of 19-hydroxy 5-unsaturated derivatives.[3,9,10]

Recently, we have discovered a unique, stereoelectronically controlled reaction that converts the 5-unsaturated 19-hydroxy derivative **2a** directly into 19-nor-10β-alcohol **5a** in ca. 80% yield (Scheme 1).[11] This reaction presumably commences by the Tl(III) electrophilic attack at the

† Dedicated to Dr. John A. Edwards on the occasion of his retirement from Syntex Research.

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(2) (a) Cole, P. A.; Robinson, C. H. *J. Am. Chem. Soc.* **1991**, *113*, 8130 and refs cited therein. (b) Caspi, E.; Dharmaratne, H. R. W.; Roitman, E.; Shackleton, C. *J. Chem. Soc., Perkin Trans. 1* **1993**, 1191. (c) Dharmaratne, H. R. W.; Kilgore, J. L.; Roitman, E.; Shackleton, C.; Caspi, E. *J. Chem. Soc., Perkin Trans. 1* **1993**, 1529.

(3) (a) Fried, J.; Edwards, J. A. *Organic Reactions in Steroid Chemistry*; Van Nostrand: New York, 1972. (b) For a review, see: Windholz, T. B.; Windholz, M. *Angew. Chem., Int. Ed. Engl.* **1964**, *3*, 353.

(4) (a) Taub, D. In *The Total Synthesis of Natural Products*; ApSimon, J.; Ed.; J. Wiley: New York, 1973; Vol. 2, p 641. (b) Corey, E. J.; Cheng, X.-M. *The Logic of Chemical Synthesis*; J. Wiley: New York, 1989; pp 23 and 385. Recent total syntheses: (c) Taber, D. F.; Raman, K.; Gaul, M. D. *J. Org. Chem.* **1987**, *52*, 28. (d) Groth, U.; Köhler, T.; Taapken, T. *Tetrahedron* **1991**, *47*, 7583. (e) Takano, S.; Moriya, M.; Ogasawara, K. *Tetrahedron Lett.* **1992**, *33*, 1909.

(5) On the other hand, 3β-acetoxy-19-hydroxycholest-5-ene (**2a**) can be transformed into estrone (**8b**) in one step in 72% yield by CSD-10 microorganisms. This route probably represents the most economic technology for estrone synthesis: Sih, C. J.; Lee, S. S.; Tsong, Y. Y.; Wang, K. C.; Chang, F. N. *J. Am. Chem. Soc.* **1965**, *87*, 2765.

(6) For recent inhibitors of human placental aromatase, see, e.g.: (a) Wright, J. N.; Calder, M. R.; Akhtar, M. *J. Chem. Soc., Chem. Commun.* **1985**, 1733. (b) Shih, M.-J.; Carrell, M. H.; Carrell, H. L.; Lee Wright, C.; O'Neal Johnston, J.; Robinson, C. H. *J. Chem. Soc., Chem. Commun.* **1987**, 213. (c) Childers, W. E.; Robinson, C. H. *J. Chem. Soc., Chem. Commun.* **1987**, 320. (d) Bednarski, P. J.; Nelson, S. D. *J. Med. Chem.* **1989**, *32*, 203. (e) Wright, J. N.; Van Leersum, P. T.; Chamberlin, S. G.; Akhtar, M. *J. Chem. Soc., Perkin Trans. 1* **1989**, 1647. (f) Njar, V. C. O.; Safi, E.; Silverton, J. V.; Robinson, C. H. *J. Chem. Soc., Perkin Trans. 1* **1993**, 1161.

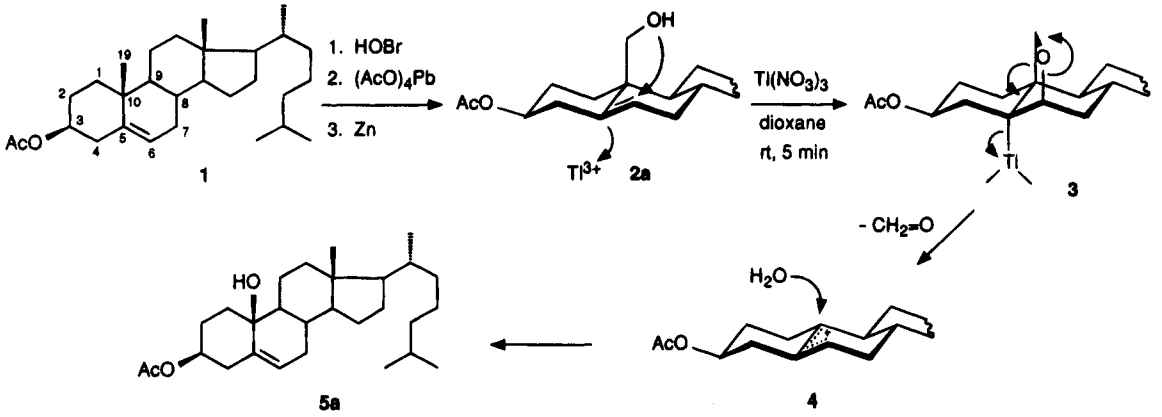
(7) For recent inhibitors of human 5α-reductase, see, e.g.: (a) Rasmusson, G. H.; Reynolds, G. F.; Utne, T.; Jobson, R. B.; Primka, R. L.; Berman, C.; Brooks, J. R. *J. Med. Chem.* **1984**, *27*, 1690. (b) Weintraub, P. M.; Blohm, T. R.; Laughlin, M. *J. Med. Chem.* **1985**, *28*, 831. (c) Rasmusson, G. H.; Reynolds, G. F.; Steinberg, N. G.; Walton, E.; Patel, G. F.; Liang, T.; Cascieri, M. A.; Cheug, A. H.; Brooks, J. R.; Berman, C. *J. Med. Chem.* **1986**, *29*, 2298. (d) Cooke, G.; Robaire, B. *J. Steroid Biochem.* **1986**, *24*, 877. (e) Brown, L.; Lyall, W. J. S.; Suckling, C. J.; Suckling, K. E. *J. Chem. Soc., Perkin Trans. 1* **1987**, 595. (f) Pack, T. G.; Bruner, K. *J. Chem. Soc., Chem. Commun.* **1987**, 1233. (g) Brandt, M.; Levy, M. A. *Biochemistry* **1989**, *28*, 140. (h) Cole, P. A.; Robinson, C. H. *J. Med. Chem.* **1990**, *33*, 2933. (i) Audia, J. E.; Lawthorn, D. E.; Deeter, J. B. *Tetrahedron Lett.* **1993**, *34*, 7001. (j) Haffner, C. *Tetrahedron Lett.* **1994**, *35*, 1349.

(8) For other, recently developed steroidal inhibitors of enzymes, see, e.g.: (a) Hu, Y.; Covey, D. F. *J. Chem. Soc., Perkin Trans. 1* **1993**, 417. (b) Howarth, N. M.; Purohit, A.; Reed, M. J.; Potter, B. V. L. *J. Med. Chem.* **1994**, *37*, 219.

(9) (a) For a review on functionalization, see: Kalvoda, J.; Heusler, K. *Synthesis* **1971**, 501. (b) For a recent application of this method in the synthesis of strophanthidin, see: Kočovský, P.; Stieborová, I. *Tetrahedron Lett.* **1989**, *30*, 4295.

0022-3263/94/1959-5439$04.50/0

Scheme 1

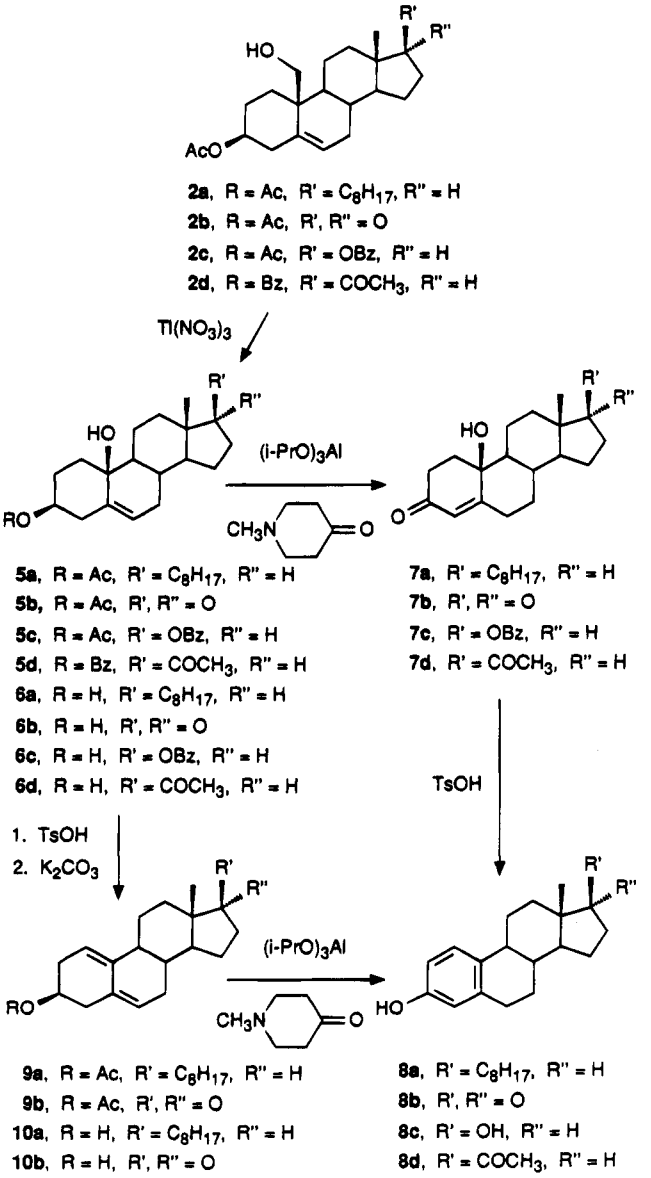


double bond of **2a**, followed by the 5(O)^n-*endo-Trig* ring closure[12] to generate the short-lived thalliated heterocycle **3**.[13] The organothallium intermediate **3** then undergoes a spontaneous, stereoelectronically controlled fragmentation, producing formaldehyde and the allylic cation **4**. Quenching of the latter cation with water plants an axial hydroxy group at C-10 (**4** → **5a**).[15]

Dehydration of **5a** by means of *p*-toluenesulfonic acid (Scheme 2) turned out to be regioselective and afforded the known[17a,19] 1(10)-unsaturated derivative **9a** (98%); its 9,10-isomer has not been detected. The acetoxy group in **9a** was saponified and the resulting alcohol **10a** (96%) was oxidized using modified[20] Oppenauer conditions to afford the expected, known[21] aromatic steroid **8a** in 82% isolated yield.

A more speculative alternative route to **8a** has also been explored and found to be equally good if not better. The diol monoacetate **5a**, resulting from the fragmentation reaction, was first saponified to give the diol **6a** (93%), which, on the modified[20] Oppenauer oxidation, furnished **7a** in 86% isolated yield. The latter compound

Scheme 2



was, rather surprisingly, stable enough to survive the relatively harsh conditions of Oppenauer oxidation (i.e. reflux in toluene for several hours). A rapid workup with ice-cold aqueous 1% H_2SO_4 or HCl (to wash out the basic components) was found to be tolerated by the sensitive functionality of **7a**. In contrast, treatment of **7a** with TsOH at room temperature overnight resulted in a

(10) A new, recently developed methodology employing a stoichiometric amount of $(C_5Me_5)Ru^+$ does not require the initial C-19 functionalization: (a) Urbanos, F.; Fernandez-Baeza, J.; Chaudret, B. *J. Chem. Soc., Chem. Commun.* **1991**, 1739. (b) Halcrow, M. A.; Urbanos, F.; Chaudret, B. *Organometallics* **1993**, *12*, 955. (c) Urbanos, F.; Halcrow, M. A.; Fernandez-Baeza, J.; Dahan, F.; Labroue, D.; Chaudret, B. *J. Am. Chem. Soc.* **1993**, *115*, 3484.

(11) (a) Kočovský, P.; Langer, V.; Gogoll, A. *J. Chem. Soc., Chem. Commun.* **1990**, 1026. (b) Kočovský, P.; Pour, M. *J. Org. Chem.* **1990**, *55*, 5580.

(12) For notation, see: Kočovský, P.; Stieborová, I. *J. Chem. Soc., Perkin Trans. 1* **1987**, 1969.

(13) The corresponding reaction of **2a** with the isoelectronic Hg^{2+} gives a stable organomercurial analogous to **3**, i.e. the 5α-(bromomercurio)-6β,19-epoxide.[11b,14]

(14) (a) Kočovský, P. *Organometallics* **1993**, *12*, 1969. (b) Welzel, P.; Holtmeier, W.; Wessling, B. *Liebigs Ann. Chem.* **1978**, 1327.

(15) Reaction of **2** with $(AcO)_4Pb$ gives an allylic isomer of **5** in much lower yield and on prolonged time and is believed to proceed *via* a radical mechanism.[16] Low-yielding photochemical degradations[17] and decarboxylation (of 10β-CO_2H)[18] have also been reported.

(16) (a) Guida, A.; Mousseron-Canet, M. *Bull. Soc. Chim. Fr.* **1971**, 1098. (b) Kaufman, M.; Morand, P.; Samad, S. A. *J. Org. Chem.* **1972**, *37*, 1067.

(17) (a) Watanabe, Y.; Mizuhara, Y. *J. Chem. Soc., Chem. Commun.* **1973**, 752. (b) Moriarty, R. M.; Paaren, H. E. *J. Org. Chem.* **1981**, *46*, 970.

(18) Sunthankar, S. V.; Telang, D. V. *Tetrahedron Lett.* **1969**, 2113.

(19) Mastalerz, H.; Morand, P. *J. Chem. Soc., Perkin Trans. 1* **1981**, 154.

(20) (a) Keana, J. F. W.; Reich, R. *Synth. Commun.* **1972**, *2*, 323. (b) Kirk, D. N.; Rajagopalan, M. S.; Varley, M. J. *J. Chem. Soc., Perkin Trans. 1* **1983**, 2225.

(21) (a) Romo, J.; Rosenkranz, G.; Djerassi, C. *J. Org. Chem.* **1950**, *15*, 1289. (b) Cambie, R. C.; Carlisle, V. F.; Manning, T. D. R. *J. Chem. Soc. (C)* **1969**, 1240. (c) Lack, R. E.; Ridley, A. B. *J. Chem. Soc. (C)* **1970**, 1437. (d) Inhoffen, H. H. Ger. Patent 889,442, 1953; *Chem. Abstr.* **1953**, *60*, 10740g.

quantitative aromatization of the A-ring to give the desired estrone-type steroid **8a** in 90% isolated yield. Alternatively, refluxing of **7a** with a base as weak as $KHCO_3$ for 10 min in $MeOH-H_2O$ also produced **8a**, essentially in quantitative yield.

Being encouraged by these model experiments, we have applied this strategy to the synthesis of estrone (**8b**). The 19-hydroxyandrostane derivative **2b**, required for the synthesis, is available through the C-19 functionalization[3,22] (as described in Scheme 1). To our delight, the C-19 removal proceeded sufficiently well despite the presence of an unprotected keto group[23] in position 17 and the desired 19-nor derivative **5b** (Scheme 2) was obtained in acceptable yield (69%); TLC analysis revealed few byproducts.[24]

Having thus accomplished the crucial step, we have explored the two synthetic routes to estrone, initially applied in the cholestane series. The monoacetate **5b** was first saponified to give the diol **6b** (97%), which, on the modified[20] Oppenauer oxidation, furnished ketone **7b** in 78% isolated yield.[25,29] Treatment of **7b** with TsOH at room temperature overnight resulted in a quantitative aromatization of the A-ring to give estrone (**8b**) in 96% yield.[30]

In an alternative approach, **5b** was dehydrated to afford the known[19] diene **9b** (78%) regioselectively. Alcohol **10b**, obtained from the latter acetate (96%), readily afforded estrone (**8b**; 77%) on Oppenauer[20] oxidation, which occurred with concomitant aromatization.

Estradiol (**8c**) was synthesized from the androstane derivative **2c** via the Tl(III)-mediated degradation (**2c** → **5c**; 58%), followed by selective hydrolysis with $KHCO_3$ (**5c** → **6c**; 93%) and Oppenauer[20] oxidation (81%). The resulting ketone **7c** was then treated with KOH to induce saponification and dehydration with concomitant aromatization to yield estradiol (**8c**; 68%).

Finally, in the pregnane series, the synthetic approach was identical to the latter one, giving 19-nor-10β-hydroxy enone **7d**, conversion of which to **8d** was accomplished under acidic conditions (TsOH).

These results demonstrate that removing the 10β-methyl group in all four series (**2** → **5**) can readily be accomplished in reasonable yields. The resulting 19-nor-10β-hydroxy derivatives **5** can be converted into A-aromatic steroids via two routes: (a) Oppenauer oxidation followed by dehydration of the 10β-hydroxy enone with concomitant aromatization (**6** → **7** → **8**) or (b) regioselective dehydration of 10β-alcohol (**5** → **9**) followed by Oppenauer oxidation (**10** → **8**). These two approaches work with similar efficiency; however, the former is more versatile as it provides an opportunity for synthesizing 10β-hydroxy analogues of sexual hormones (**7**).

Conclusion

Starting with C-19 steroids **2a** – **2d**, we have designed a novel, expedient route to 19-nor-10β-alcohols **5a** – **5d**, which can readily be converted into A-aromatic steroids. Synthesis of estrone (**8b**), estradiol (**8c**) and their pregnane (**8d**) and cholestane (**8a**) analogues has been accomplished using this approach. One of the synthetic strategies proceeds via 19-nor-10β-hydroxy-4-en-3-ones **7a** – **7d**, which may be of use in developing inhibitors of enzymes involved in steroid biosynthesis.[31,32,35]

Experimental Section

General Methods. Melting points were determined on a Kofler block and are uncorrected. The optical rotations were measured in $CHCl_3$ with a Perkin-Elmer 141 polarimeter at 22 °C with an error of $<\pm1°$. The NMR spectra were recorded for $CDCl_3$ solutions at 25 °C on a Bruker AM 300 spectrometer. Chemical shifts were indirectly referenced to TMS *via* the solvent signals (7.26 ppm for ^1H, and 77.0 ppm for ^{13}C). The IR spectra were recorded in $CHCl_3$ on a Perkin-Elmer 621 instrument. All reactions were carried out under nitrogen. Standard workup of an ethereal solution means washing with 5% HCl (aqueous), water, and 5% $KHCO_3$ (aqueous) and drying with $MgSO_4$. Petroleum ether refers to the fraction boiling in the range 40–60 °C. The identity of samples prepared by different routes was checked by TLC and IR and NMR spectra. Yields are given for isolated product showing one spot on a chromatographic plate and no impurities detectable in the NMR spectrum.

3β-Acetoxy-10β-hydroxy-19-norandrost-5-ene-17-one (5b). To a solution of **2b** (300 mg; 0.87 mmol) in dioxane (4 mL) was successively added water (0.2 mL), 10% aqueous

(22) Morand, P.; Williamson, D. G.; Layne, D. S.; Lompa-Krzymien, L.; Salvador, J. *Biochemistry* **1975**, *14*, 635.

(23) For reactions of ketones with Tl(III), see: McKillop, A.; Taylor, E. C. In *Comprehensive Organometallic Chemistry*: Wilkinson, G.; Stone, F. G. A.; Abel, E. W., Eds.; Pergamon: Oxford, 1982; Vol. VII, Chapter 47.

(24) For a preliminary account of this work, see: Kočovský, P.; Baines, R. S. *Tetrahedron Lett.* **1993**, *38*, 6139.

(25) The hydroxy enone **7b** has been prepared previously by several independent methods: (1) A catalytic oxidation (O_2/Pt) of 3β,5,10β-trihydroxy-19-nor-5β-androstan-17-one, which in turn was obtained by degradation of strophanthidin.[26] (2) A microbial hydroxylation of 19-nor-androst-4-ene-3,17-dione using *Rhizopus arrhizus*.[27] (3) Patent literature[28] describes osmylation of the 3-oxo-5(10)-ene followed by treatment with mild alkali which, presumably, produced both **7b** and its 10α-epimer. From the data reported (mp 198–201 °C), it can be assumed that the product actually isolated by the authors was **7b**.

(26) Wartburg, A. von *Helv. Chim. Acta* **1963**, *46*, 591.

(27) Holland, H. L.; Diakow, P. R. P. *Can. J. Chem.* **1978**, *56*, 694.

(28) Pedersen, R. L.; Babcock, J. C. U.S. Patent 2,806,862, 1957; *Chem. Abstr.* **1958**, *52*, 10225e.

(29) Interestingly, the mass spectrum of **7b** shows the M^+ ion as a base peak (100%), whereas the abundance of the expected $(M - H_2O)^+$ ion reaches only 60%.[27] Hence, **7b** is not as unstable as one may predict.

(30) Estrone (**8b**) has previously been prepared from **7b** using rather harsh conditions, namely by bubbling gaseous HCl through the MeOH solution of **7b**.[26] For related work, see: (a) Neeman, M.; Mukai, T.; O'Grodnick, J. S.; Rendall, A. L. *J. Chem. Soc., Perkin Trans. 1* **1972**, 2300. (b) Neeman, M.; O'Grodnick, J. S.; Morgan, K. *J. Chem. Soc., Perkin Trans. 1* **1972**, 2302. (c) Neeman, M.; O'Grodnick, J. S. *Can. J. Chem.* **1974**, *52*, 2941. (d) Gardi, R.; Perdali, C.; Ercoli, A. *Gazz. Chim. Ital.* **1963**, *93*, 1503. (e) Kirdani, R. Y.; Layne, D. S. *J. Med. Chem.* **1964**, *7*, 592.

(31) For various biological tests of 19-nor-10β-hydroxy steroids, see, e.g.: (a) Bonne, C.; Raynaud, J. P. *Biochemie* **1973**, *55*, 227. (b) Weintraub, H.; Vincent, F.; Baulieu, E. E.; Alfsen, A. *Biochemistry* **1977**, *16*, 5045. (c) Pons, M.; Michel, F.; Descomps, B.; Crastes de Paulet, A. *Eur. J. Biochem.* **1978**, *84*, 257. (d) Petrow, V.; Padilla, G. M. *Prostate* **1986**, *9*, 169. (e) Kuehn-Velten, N.; Meyer, I.; Staib, W. *J. Steroid Biochem.* **1989**, *33*, 33. (f) Peters, R. H.; Crowe, D. F.; Avery, M. A.; Chong, W. K. M.; Tanabe, M. *J. Med. Chem.* **1989**, *32*, 1642.

(32) Some data[33] suggested that the last step in estrone biosynthesis may take place via 10β-alcohol **7**; however, this mechanism has been ruled out by further labeling experiments[34] so that the formation of **7** in human placenta is now believed to be an artifact.

(33) Watanabe, Y.; Ishimura, Y. *J. Am. Chem. Soc.* **1989**, *111*, 8047.

(34) (a) Caspi, E.; Dharmaratne, H. R. W.; Shackleton, C. *J. Chem. Soc., Chem. Commun.* **1989**, 1699. (b) Akhtar, M.; Calder, M. C.; Corina, D. L.; Wright, J. N. *Biochem. J.* **1982**, *201*, 569. (c) Covey, D. F.; Hood, W. F.; Beusen, D. D.; Carrell, H. L. *Biochemistry* **1984**, *23*, 5398.

(35) Alternatively, **7b** can be obtained from 19-nortestosterone or estrone by microbial hydroxylation: (a) De Flives, J.; van der Waard, W. F.; Miss, W. J.; Szpilfogel, S. A. *Rec. Trav. Chim.* **1963**, *82*, 129; *Chem. Abstr.*, **1964**, *61*, 7654. (b) Kondo, E.; Mitsugi, T. Japan Patent 20,089, 1966; *Chem. Abstr.* **1967**, *67*, 10389f. (c) Browne, J. W.; Denny, W. A.; Jones, E. R. H.; Meakins, G. D.; Yasu, M.; Pendelbury, A.; Pragnell, J. *J. Chem. Soc., Perkin Trans. 1* **1973**, 1493. (d) Faver, J.; Marchand, J.; Winternitz, F. *Bull. Soc. Chim. Fr.* **1977**, 310. (e) Shankar, V. N.; Row, T. N. G.; Madyastha, K. M. *J. Chem. Soc., Perkin Trans. 1* **1993**, 2233. For related work, see: (f) Maumy, M.; Rigaudy, J. *Bull. Soc. Chim. Fr.* **1976**, 2021.

perchloric acid (0.02 mL), and thallium nitrate trihydrate (500 mg; 1.13 mmol) and the mixture was stirred at rt for 15 min.[36] The mixture was then diluted with ether and filtered and the filtrate was worked up. The crude product was purified by flash chromatography on silica gel (12 g) with a petroleum ether–ether–acetone mixture (87:10:3), which eluted lipophilic impurities, and then with the 84:10:6 mixture to give **5b** (199 mg; 69%): mp 163–164 °C (ether–petroleum ether); $[\alpha]_D$ −11° (*c* 2.3); ^{1}H NMR δ 0.93 (s, 3 H, 18-H), 2.07 (s, 3 H, CH_3CO_2), 4.68 (m, *W* = 32 Hz, 1 H, 3α-H), 5.64 (br d, *J* = 5.4 Hz, 1 H, 6-H); ^{13}C NMR δ 13.45 (q, C-18), 19.45 (t), 21.37 (q, CH_3CO), 21.86 (t), 26.97 (t), 30.46 (t), 30.96 (t), 31.75 (d), 34.80 (t), 35.77 (t), 37.40 (t), 47.45 (s, C-13), 49.09 (d), 50.74 (d), 69.13 (s, C-10), 72.78 (d, C-3), 125.25 (d, C-6), 136.88 (s, C-5), 170.51 (s, CH_3CO), 220.71 (s, C-17). Anal. Calcd for $C_{20}H_{28}O_4$: C, 72.26; H, 8.49. Found: C, 72.04; H, 8.61.

19-Norandrost-5-ene-3β,10β,17β-triol 3-Acetate 17-Benzoate (5c). To a solution of **2c**[37] (500 mg; 1.11 mmol) in dioxane (5 mL) was successively added water (0.2 mL), 10% aqueous perchloric acid (0.05 mL), and thallium nitrate trihydrate (740 mg; 1.66 mmol) and the mixture was stirred at rt for 15 min. The mixture was then diluted with ether and filtered and the filtrate was worked up. The crude product was purified by flash chromatography on silica gel (15 g) with a petroleum ether–ether–acetone mixture (88:10:2), which eluted lipophilic impurities, and then with the 85:10:5 mixture to give **5c** (281 mg; 58%) as an amorphous foam: $[\alpha]_D$ −27° (*c* 2.8); ^{1}H NMR δ 1.01 (s, 3 H, 18-H), 2.08 (s, 3 H, CH_3CO_2), 4.70 (m, *W* = 32.3 Hz, 1 H, 3α-H), 4.90 (dd, *J* = 9.0 and 7.7 Hz, 1 H, 17α-H), 5.63 (br d, *J* = 5.6 Hz, 1 H, 6-H), 7.47 (m, *W* = 16.4 Hz, 2 H, arom *o*-H), 7.59 (m, *W* = 17.5 Hz, 1 H, arom, *p*-H), 8.07 (m, *W* = 11.5 Hz, 2 H, arom *m*-H); ^{13}C NMR δ 12.05 (q), 19.72 (t), 21.39 (q), 23.69 (t), 27.00 (t), 27.70 (t), 31.16 (t), 32.02 (d), 34.79 (t), 36.37 (t), 37.42 (t), 42.77 (s), 48.92 (d), 50.13 (d), 69.15 (s), 72.90 (d), 83.07 (d), 125.59 (d), 128.26 (d), 129.46 (d), 130.61 (s), 132.73 (d), 136.75 (s), 166.46 (s), 170.51 (s). Anal. Calcd for $C_{27}H_{34}O_5$: C, 73.95; H, 7.81. Found: C, 74.23; H, 7.52.

3β-(Benzoyloxy)-10β-hydroxy-19-norpregn-5-en-20-one (5d). To a solution of **2d**[38] (450 mg; 1.03 mmol) in dioxane (10 mL) was successively added water (0.5 mL), 10% aqueous perchloric acid (0.1 mL), and thallium nitrate trihydrate (700 mg; 1.58 mmol) and the mixture was stirred at rt for for 30 min. The mixture was then diluted with ether and filtered and the filtrate was worked up. The crude product was purified by flash chromatography on silica gel (15 g) with a petroleum ether–ether–acetone mixture (86:10:4), which eluted lipophilic impurities, and then with the 83:10:7 mixture to give **5d** (270 mg; 62%): mp 184–185 °C (aqueous acetone); $[\alpha]_D$ +28° (*c* 2.9); ^{1}H NMR δ 0.69 (s, 3 H, 18-H), 2.17 (s, 3 H, 21-H), 4.95 (m, *W* = 32 Hz, 1 H, 3α-H), 5.64 (br d, *J* = 5.6 Hz, 1 H, 6-H), 7.46 (m, *W* = 15 Hz, 2 H, arom *o*-H), 7.58 (m, *W* = 16 Hz, 1 H, arom *p*-H), 8.06 (m, *W* = 17.5 Hz, 2 H, arom *m*-H); ^{13}C NMR δ 13.10 (q), 20.21 (t), 22.81 (t), 24.44 (t), 27.10 (t), 31.47 (t), 31.52 (q), 32.08 (d), 34.78 (t), 37.48 (t), 38.33 (t), 43.92 (s), 48.83 (d), 55.85 (d), 63.57 (d), 69.09 (s), 73.49 (d), 125.76 (d), 128.22 (2 × d), 129.48 (2 × d), 132.76 (d), 136.69 (s), 165.95 (s). Anal. Calcd for $C_{27}H_{34}O_4$: C, 76.74; H, 8.11. Found: C, 76.40; H, 8.37.

19-Norcholest-5-ene-3β,10β-diol (6a). A mixture of the acetate **5a**[11] (478 mg) and potassium carbonate (225 mg) in methanol (18 mL) and water (3 mL) was stirred at rt overnight. The mixture was then diluted with ether and water and washed with water and dried with Na_2SO_4 and evaporated to give diol **6a** (400 mg; 93%): mp 131–133 °C (acetone); $[\alpha]_D$ −7° (*c* 1.3); ^{1}H NMR δ 0.58 (s, 3 H, 18-H), 3.55 (m, *W* = 32 Hz, 1 H, 3α-H), 5.54 (m, *W*/2 = 10 Hz, 1 H, 5-H). Anal. Calcd for $C_{26}H_{44}O_2$: C, 80.35; H, 11.41. Found: C, 80.03; H, 11.76.

3β,10β-Dihydroxy-19-norandrost-5-en-17-one (6b). The acetate **5b** (160 mg; 0.48 mmol) in methanol (10 mL) was treated with potassium hydroxide (100 mg) at rt for 3 h. The mixture was then concentrated in vacuo at ≤ 30 °C to about 1/5, the residue was diluted with ether and water and the ethereal phase was worked up to afford oily **6b** (136 mg; 97%): $[\alpha]_D$ −6° (*c* 2.0); ^{1}H NMR δ 0.91 (s, 3 H, 18-H), 3.58 (m, *W* = 30.5 Hz, 1 H, 3α-H), 5.58 (br d, *J* = 5.3 Hz, 1 H, 6-H); ^{13}C NMR δ 13.65 (q, C-18), 19.37 (t), 21.48 (t), 29.77 (t), 30.35 (t), 30.98 (t), 31.63 (d), 34.88 (t), 35.47 (t), 36.46 (t), 47.35 (s, C-13), 49.39 (d), 51.48 (d), 68.91 (s, C-10), 70.23 (d, C-3), 124.19 (d, C-6), 137.71 (s, C-5), 219.75 (s, C=O). Anal. Calcd for $C_{18}H_{26}O_3$: C, 73.93; H, 9.65. Found: C, 73.68; H, 9.92.

19-Norandrost-5-ene-3β,10β,17β-triol 17-Monobenzoate (6c). The diester **5c** (250 mg; 0.57 mmol) was dissolved in a mixture of benzene (10 mL) and methanol (20 mL) by heating, and then a solution of potassium hydrogen carbonate (400 mg) in a mixture of water (6 mL) and methanol (5 mL) was added and the mixture was heated at 40 °C for 52 h while monitored by TLC. The mixture was then concentrated in vacuo at ≤30 °C to ca. 1/5 and then diluted with ether and water, and the ethereal phase was worked up to give pure **6c** (210 mg; 93%): mp 164–165 °C (acetone–petroleum ether); $[\alpha]_D$ −23° (*c* 2.0); ^{1}H NMR (90 MHz) δ 1.03 (s, 3 H, 18-H), 3.55 (m, *W* = 32 Hz, 1 H, 3α-H), 4.90 (dd, *J* = 9.0 and 7.5 Hz, 1 H, 17α-H), 5.53 (br d, *J* = 5.5 Hz, 1 H, 6-H), 7.27–7.58 (m, 3 H, arom *o*-H and *p*-H), 7.92–8.08 (m, 2 H, arom *m*-H). Anal. Calcd for $C_{25}H_{32}O_4$: C, 75.73; H, 8.13. Found: C, 75.51; H, 8.38.

3β,10β-Dihydroxy-19-norpregn-5-en-20-one (6d). A mixture of benzoate **5d** (200 mg; 0.47 mmol) and potassium hydroxide (200 mg) in methanol (8 mL), acetone (2 mL), and water (0.5 mL) was refluxed for 30 min. The mixture was then concentrated in vacuo to about 1/5, the residue was diluted with ether and water, and the ethereal phase was worked up to afford oily **6d** (145 mg; 98%): $[\alpha]_D$ +26° (*c* 2.0); ^{1}H NMR (90 MHz) δ 0.68 (s, 3 H, 18-H), 2.15 (s, 3 H, 21-H), 3.53 (m, *W* = 32 Hz, 1 H, 3α-H), 5.54 (br d, *J* = 5.5 Hz, 1 H, 6-H). Anal. Calcd for $C_{20}H_{30}O_3$: C, 75.43; H, 9.50. Found: C, 75.07; H, 9.74.

10β-Hydroxy-19-norcholest-4-en-3-one (7a). From a mixture of **6a** (250 mg) and 1-methyl-4-piperidone (10 mL) in toluene (30 mL) was distilled off ca. 3 mL. A solution of aluminum isopropoxide (400 mg) in toluene (1 mL) was then added and the mixture was refluxed for 5 h. After cooling, the mixture was diluted with ether, washed successively with ice-cold 1% aqueous H_2SO_4 (4 times), water, 5% aqueous $KHCO_3$ (3 times), and water, and dried with Na_2SO_4. The solvent was evaporated, and the crude product was dissolved in a mixture of benzene and ether and filtered through a pad of silica gel to give pure **7a** (215 mg; 86%): mp 126–129 °C (EtOH); $[\alpha]_D$ +26° (*c* 2.0); ^{1}H NMR δ 0.73 (s, 3 H, 18-H), 5.76 (d, *J* = 1.2 Hz, 1 H, 4-H); ^{13}C NMR δ 11.91 (q), 18.64 (q), 20.38 (t), 22.56 (q), 22.81 (q), 23.81 (t), 24.22 (t), 28.00 (d), 28.19 (t), 31.79 (t), 32.11 (t), 33.66 (2 × t); 35.25 (d), 35.71 (d), 36.11 (t), 39.33 (t), 39.48 (t), 42.41 (s), 52.91 (d), 55.49 (d), 56.11 (d), 70.26 (s), 124.51 (d), 164.86 (s), 199.45 (s); IR 1668 ν(C=O), 3455 and 3583 ν(OH) cm^{-1}; UV 234 nm (ϵ = 10000). Anal. Calcd for $C_{26}H_{42}O_2$: C, 80.77; H, 10.95. Found: C, 80.49; H, 11.28.

10β-Hydroxy-19-norandrost-4-ene-3,17-dione (7b). From a mixture of **6b** (100 mg; 0.35 mmol) and 1-methyl-4-piperidone (1 mL) in toluene (10 mL) was distilled of ca. 2 mL. Solid aluminum isopropoxide (300 mg) was then added and the mixture was refluxed for 4 h. After cooling, the mixture was diluted with ether, washed successively with ice-cold 1% aqueous HCl (4 times), water, 5% aqueous $KHCO_3$ (3 times), and water, and dried with Na_2SO_4. The solvent was evaporated and the crude product was flash-chromatographed on silica gel (5 g) with a petroleum ether–ether–acetone mixture (80:10:10) which eluted lipophilic impurities and then with the 70:15:15 mixture to give **7b** (78 mg; 78%): mp 199–201 °C (lit.[26] gives 198–211 °C or 197–207 °C; lit.[27] gives 197–199 °C); ^{1}H NMR δ 0.99 (s, 3 H, 18-H), 5.84 (d, *J* = 1.9 Hz, 4-H); ^{13}C NMR δ 13.57 (q), 19.56 (t), 21.66 (t), 30.39 (t), 30.86 (t),

(36) Unlike with the **2a** → **5a** trans-formation, TLC analysis failed to monitor the progress of this reaction (and also of the **2c** → **5c** and **2d** → **5d** conversions); the starting material and the product exhibited the same mobility in several solvent mixtures. The only way to detect the completion of the reaction by TLC was to spray the plates with $SbCl_3/CHCl_3$ or diluted H_2SO_4 (cherry-red color for the starting material and turquoise/greenish for the product).

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31.60 (t), 33.45 (t), 33.60 (t), 34.68 (d), 35.60 (t), 47.42 (s), 50.29 (d), 52.40 (d), 70.17 (s), 124.79 (d), 163.46 (s), 199.21 (s), 220.23 (s).

10β-Hydroxy-17β-(benzoyloxy)-19-norandrost-4-en-3-one (7c). From a mixture of **6c** (150 mg; 0.38 mmol) and 1-methyl-4-piperidone (1.5 mL) in toluene (15 mL) was distilled off ca. 3 mL. Solid aluminum isopropoxide (400 mg; 1.96 mmol) was then added and the mixture was refluxed for 5 h. After cooling, the mixture was diluted with ether, washed successively with ice-cold 1% aqueous HCl (4 times), water, 5% aqueous $KHCO_3$ (3 times), and water, and dried with Na_2SO_4. The solvent was evaporated and the crude product was flash-chromatographed on silica gel (5 g) with a petroleum ether–ether–acetone mixture (80:10:10) to give **7c** (97 mg; 81%): mp 209–211 °C (petroleum ether–ether–acetone); ^1H NMR δ 1.05 (s, 3 H, 18-H), 4.90 (dd, J = 9.1 and 7.7 Hz, 1 H, 17α-H), 5.82 (d, J = 1.7 Hz, 1 H, 4-H), 7.48 (m, W = 15.8 Hz, 2 H, arom o-H), 7.60 (m, W = 17.5 Hz, 1 H, p-H), 8.08 (m, W = 9.7 Hz, 2 H, arom m-H); ^{13}C NMR δ 12.23 (q), 19.95 (t), 23.64 (t), 27.66 (t), 31.24 (t), 31.92 (t), 33.61 (t), 33.71 (t), 35.07 (d), 36.44 (t), 42.93 (s), 49.90 (d), 52.48 (d), 70.27 (s), 82.91 (d), 124.73 (d), 128.29 (d), 129.46 (d), 130.53 (s), 132.80 (d), 164.18 (s), 166.46 (s), 199.05 (s). Anal. Calcd for $C_{25}H_{30}O_4$: C, 76.11; H, 7.66. Found, C, 75.88; H, 7.91.

10β-Hydroxy-19-norpregn-4-ene-3,20-dione (7d). From a mixture of **6d** (100 mg; 0.31 mmol) and 1-methyl-4-piperidone (1 mL) in toluene (10 mL) was distilled off ca. 2 mL. Solid aluminum isopropoxide (300 mg; 1.47 mmol) was then added and the mixture was refluxed for 4 h. After cooling, the mixture was diluted with ether, washed successively with 1% aqueous ice-cold HCl (four times), water, 5% aqueous $KHCO_3$ (three times), and water, and dried with Na_2SO_4. The solvent was evaporated and the crude product was flash-chromatographed on silica gel (5 g) with a petroleum ether–ether–acetone mixture (80:10:10) which eluted lipophilic impurities and then with the 75:10:15 mixture to give **7d** (82 mg; 83%): mp 199–202 °C (acetone); ^1H NMR δ 0.72 (s, 3 H, 18-H), 2.16 (s, 3 H, 21-H), 5.80 (d, J = 1.9 Hz, 1 H, 4-H); ^{13}C NMR δ 13.27 (q), 20.36 (t), 22.85 (t), 24.39 (t), 31.45 (q), 31.62 (t), 31.94 (t), 33.61 (t), 33.66 (t), 35.14 (d), 38.36 (t), 43.96 (s), 52.41 (d), 55.58 (d), 63.48 (d), 70.10 (s), 124.64 (d), 164.32 (s), 199.12 (s), 209.34 (s). Anal. Calcd for $C_{20}H_{28}O_3$: C, 75.91; H, 8.92. Found: C, 75.71; H, 9.13.

19-Norcholesta-1,3,5(10)-trien-3-ol (8a). (A) From 7a: A mixture of **7a** (14 mg) and p-toluenesulfonic acid (10 mg) in ether (5 mL) was stirred at rt overnight. The mixture was then diluted with ether, washed with water, 5% aqueous $KHCO_3$, and water, dried with Na_2SO_4, and the solvent was evaporated to afford pure **8a** (12 mg: 90%): mp 114–116 °C (hexane) (lit.[21b,c] gives 113–115 °C); ^1H NMR δ 0.61 (s, 3 H, 18-H), 6.43 (d, J = 2.6 Hz, 1 H, 4-H), 6.49 (dd, J = 8.4 and 2.6 Hz, 1 H, 2-H), 7.02 (d, J = 8.4 Hz, 1 H, 1-H); ^{13}C NMR δ 12.00 (q), 18.69 (q), 22.57 (q), 22.83 (q), 23.83 (t), 23.94 (t), 26.79 (t), 27.66 (t), 28.02 (d), 28.30 (t), 29.72 (t), 35.81 (d), 36.18 (t), 38.78 (d), 39.53 (t), 39.95 (t), 42.78 (s), 43.71 (d), 55.42 (d), 56.36 (d), 112.58 (d), 115.20 (d), 126.37 (d), 132.88 (s), 138.22 (s), 153.29 (s); IR 3360 and 3578 ν(OH) cm^{-1}.

(B) From 10a: Diene **10a** (160 mg) was oxidized with 1-methyl-4-piperidone (3 mL) and aluminum isopropoxide (400 mg) in toluene (30 mL) as given in the previous experiments (**7a–d**). After workup, the crude product was chromatographed on silica (10 g) using an petroleum ether–ether mixture (3:2) as eluent to yield **8a** (130 mg; 82%) identical with the product obtained above: mp 114–116 °C.

3-Hydroxyestra-1,3,5(10)-trien-17-one (8b). (A) From 7b: The enone **7b** (50 mg; 0.17 mmol) in ether (10 mL) was treated with p-toluenesulfonic acid (10 mg) at rt overnight. The mixture was then diluted with ether, washed with 5% $KHCO_3$ (aqueous) and water, and dried with Na_2SO_4, and the solvent was evaporated in vacuo to give pure **8b** (45 mg; 96%), identical with an authentic sample obtained from Steraloids: mp 261–263 °C (Merck Index gives 254–256 °C; Aldrich Catalogue gives 258–260 °C; Steraloids Catalogue gives 263–265 °C); mixed melting point with an authentic sample showed no depression.

(B) From 10b: From a mixture of **10b** (30 mg; 0.11 mmol) and 1-methyl-4-piperidone (1 mL) in toluene (10 mL) was distilled off ca. 2 mL. Solid aluminum isopropoxide (100 mg) was then added and the mixture was refluxed for 4 h. After cooling, the mixture was diluted with ether, washed successively with 5% HCl (four times), water, 5% aqueous $KHCO_3$ (three times), and water, and dried with Na_2SO_4. The solvent was evaporated and the crude product was flash-chromatographed on silica gel (3 g) with a petroleum ether–ether–acetone mixture (70:15:15) to give **8b** (23 mg; 77%) identical with the product obtained under A: mp 259–261 °C.

Estra-1,3,5(10)-triene-3,17β-diol (8c). A mixture of benzoate **7c** (80 mg; 0.20 mmol) and potassium hydroxide (100 mg) in methanol (10 mL) was refluxed for 1 h. The mixture was then concentrated by evaporating in vacuo to ca 1/4 and diluted with ether, and the ethereal solution was worked up. The crude product was chromatographed on silica gel using a dichloromethane–acetone mixture (80:20) to afford **8c** (37 mg; 68%): mp 176–178 °C (Steraloids Catalogue gives 176–177 °C; Aldrich Catalogue gives 178–179 °C); $[\alpha]_D$ +77° (c 2.0; dioxane) (Steraloids and Aldrich Catalogues give +80°) identical with an authentic sample purchased from Steraloids (mixed melting point showed no depression).

3-Hydroxy-19-norpregna-1,3,5(10)-trien-20-one (8d). The enone **7d** (60 mg; 0.19 mmol) in ether (10 mL) was treated with p-toluenesulfonic acid (10 mg) at rt overnight. The mixture was then diluted with ether, washed with 5% $KHCO_3$ (aqueous) and water, and dried with Na_2SO_4. The solvent was evaporated in vacuo to give pure **8d** (52 mg; 92%): mp 244–247 °C (lit.[39] gives 238–240 °C to 248–250 °C); $[\alpha]_D$ +156° (c 2.0) (lit.[39] gives $[\alpha]_D$ +150° to +164°); ^1H NMR δ 0.60 (s, 3 H, 18-H), 2.18 (s, 3 H, 21-H), 6.42 (d, J = 2.6 Hz, 1 H, 4-H), 6.48 (dd, J = 8.4 and 2.6 Hz, 1 H, 2-H), 7.99 (d, J = 8.4 Hz, 1 H, 1-H).

19-Norcholesta-1(10),5-dien-3β-yl Acetate (9a). A mixture of **5a** (343 mg) and p-toluenesulfonic acid (10 mg) in chloroform (8 mL) was stirred at 50 °C for 15 min. The mixture was then diluted with ether, washed with water, 5% aqueous $KHCO_3$, and water, and dried with Na_2SO_4, and the solvent was evaporated to afford pure **9a** (322 mg; 98%): mp 72–74 °C (methanol, ether) (lit.[17a,19] gives 74–76 °C); ^1H NMR δ 0.68 (s, 3 H, 18-H), 4.98 (m, W = 22.8 Hz, 1 H, 3α-H), 5.67 (br s, 1 H, 1-H), 5.48 (brd, J = 4.8 Hz, 6-H); ^{13}C NMR δ 11.88 (q), 18.69 (q), 21.46 (q), 22.55 (q), 22.81 (q), 23.80 (t), 23.87 (t), 24.53 (t), 28.00 (d), 28.26 (t), 31.37 (t), 31.56 (t), 35.75 (d), 35.84 (t), 36.16 (t), 37.91 (d), 39.40 (t), 39.50 (t), 42.52 (d), 42.58 (s), 56.13 (d), 56.27 (d), 69.52 (d), 115.22 (d), 124.55 (d), 130.74 (s), 138.36 (s), 170.78 (s); IR 1739 ν(C=O) cm^{-1}; UV λ 236 nm (ε 25500) (lit.[17a] gives λ 240 nm).

3β-Acetoxy-19-norandrosta-1(10),5-dien-17-one (9b). To a solution of **5b** (89 mg; 0.27 mmol) in chloroform (4 mL) was added p-toluenesulfonic acid (10 mg) and the mixture was stirred at rt for 12 h. The mixture was then diluted with ether and the resulting solution was washed successively with water, 5% aqueous $KHCO_3$, and water and dried with $MgSO_4$. The solvent was evaporated and the crude product (81 mg) was crystallized from ether to give pure **9b** (66 mg; 78%): mp 111–113 °C (lit.[19,28] gives 115 °C from C_6H_6/Et_2O); $[\alpha]_D$ −12° (c 1.7); IR (CH_2Cl_2) 1728, 1735 sh ν(C=O) cm^{-1}; ^1H NMR δ 0.90 (s, 3 H, 18-H), 2.04 (s, 3 H, CH_3CO), 5.01 (m, W = 22.5 Hz, 1 H, 3α-H), 5.41 (br s, 1 H, 1-H), 5.51 (br d, J = 5.6 Hz, 1 H, 6-H); ^{13}C NMR δ 13.67 (q), 21.45 (q), 21.57 (t), 23.74 (t), 30.40 (t), 31.09 (t), 31.36 (t), 35.79 (t), 35.86 (t), 37.36 (d), 42.64 (d), 47.76 (s), 51.25 (d), 69.28 (d), 116.13 (d), 123.67 (d), 131.08 (s), 137.41 (s), 170.76 (s), 220.70 (s).

19-Norcholesta-1(10),5-dien-3β-ol (10a). A mixture of **9a** (150 mg) and potassium carbonate (100 mg) in methanol (9 mL), dioxane (1 mL), and water (1 mL) was stirred at rt

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overnight. The mixture was then diluted with ether and water and washed with water and dried with Na_2SO_4 and evaporated to give pure **10a** (130 mg; 96%): $[\alpha]_D$ −21° (*c* 0.5); ^{1}H NMR δ 0.67 (s, 3 H, 18-H), 4.02 (m, W = 18.2 Hz, 1 H, 3α-H), 5.35 (br s, 1 H, 1-H), 5.53 (d, J = 4.6 Hz, 1 H, 6-H); ^{13}C NMR δ 11.88 (q), 18.70 (q), 22.57 (q), 22.82 (q) 23.80 (t), 23.84 (t), 24.52 (t), 28.00 (d), 28.26 (t), 31.71 (t), 34.78 (t), 35.75 (d), 36.17 (t), 38.14 (d), 39.13 (t), 39.39 (t), 39.51 (t), 42.49 (d), 42.58 (s), 56.15 (d), 56.39 (d), 66.05 (d), 115.29 (d), 125.68 (d), 130.31 (s), 138.14 (s). Anal. Calcd for $C_{26}H_{42}O$: C, 84.26; H, 11.42. Found: C, 83.92; H, 11.60.

3β-Hydroxy-19-norandrosta-1(10),5-dien-17-one (10b). A solution of acetate **9b** (60 mg; 0.19 mmol) in methanol (5 mL) was treated with KOH (100 mg) at 50 °C for 10 min. The mixture was then concentrated by evaporation in vacuo to ca. 2 mL and diluted with ether and water and worked up. The crude product was dissolved in a mixture of benzene and ether and filtered through a pad of silica gel to give pure alcohol **10b** (49 mg; 96%): $[\alpha]_D$ −5° (*c* 1.4); ^{1}H NMR δ 0.91 (s, 3 H, 18-H), 4.09 (m, W = 18.0 Hz, 1 H, 3α-H), 5.42 (br s, 1 H, 1-H), 5.60 (br d, J = 5.2 Hz, 1 H, 6-H); ^{13}C NMR δ 13.52 (q), 21.40 (t), 23.56 (t), 30.41 (t), 30.92 (t), 34.65 (t), 35.70 (t), 37.43 (d), 36.93 (t), 42.45 (d), 47.65 (s), 51.22 (d), 65.73 (d), 116.02 (d), 124.67 (d), 130.50 (s), 137.06 (s), 220.66 (s). Anal. Calcd for $C_{18}H_{24}O_2$: C, 79.37; H, 8.88. Found: C, 79.05; H, 9.14.

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