# Synthesis of the C/D/E and A/B Rings of Xestobergsterol-(A)

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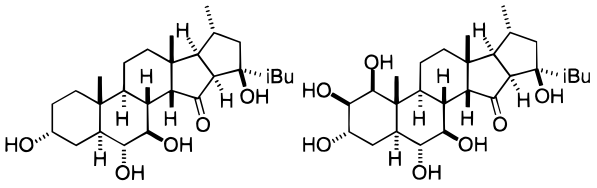
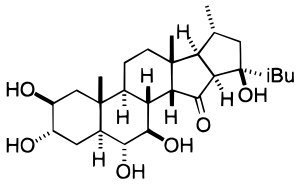
The A/B and the C/D/E rings of the xestobergsterol skeleton have been stereoselectively synthesized starting with testosterone and epiandrosterone, respectively. A deconjugative ketalization of the A-ring enone of testosterone provided a handle for functionalization of the B-ring. A stereoselective aldol condensation was used to incorporate the E-ring.

Marine sponges have been a rich source of new types of steroids, typified by unique side-chain structures and unusual functionalization. Recently, isolation of steroids in a novel class, the xestobergsterols, has been reported,[1] and these compounds showed strong pharmacological properties. Our interest in the xestobergsterol steroids was stimulated by their potent biological activity and the challenging C/D/E ring system.

Xestobergsterol-(A), **1**, and xestobergsterol-(B), **2**, are unique pentacyclic steroids with unusual cis fused C/D ring junctions. They were isolated in 1992 from the crude extract of the Okinawan sponge *Xestospongia bergquistia* Fromont.[1] In 1995, xestobergsterol-(C), **3**, was isolated from the extracts of the Okinawan marine sponge *Ircinia* sp.[2] The structures were elucidated using primarily NMR spectroscopic techniques. In 1995, reexamination of the NMR spectroscopic data of xestobergsterol-(A), **1**, and xestobergsterol-(B), **2**, by Kobayashi et al. resulted in a revision of the configuration at C-23 and of the conformation of the C-ring in both **1** and **2**.[2] Xestobergsterol-(A), **1**, and xestobergsterol-(C), **3**, exhibit cytotoxicity against



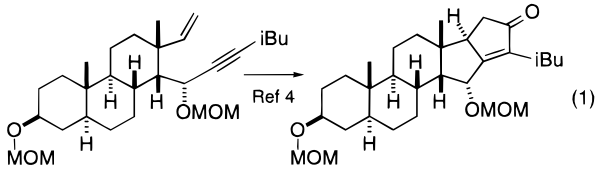
Xestobergsterol-(A), **1** Xestobergsterol-(B), **2**



Xestobergsterol-(C), **3**

L-1210 murine leukemia cells with $IC_{50}$ values of 4.0 $\mu$g/mL and 4.1 $\mu$g/mL, respectively.[2] Additionally, xestobergsterol-(A), **1**, and xestobergsterol-(B), **2**, have been shown to strongly inhibit histamine release from rat peritoneal mast cells induced by anti-IgE in a dose-dependent manner.

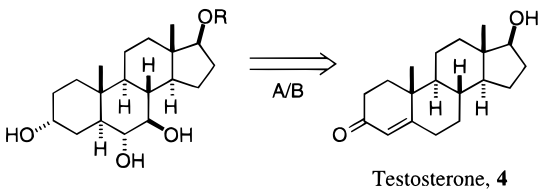
We have recently reported a synthesis of the C/D/E skeleton of the xestobergsterols using an intramolecular Pauson−Khand reaction (eq 1).[3,4] Unfortunately, the key



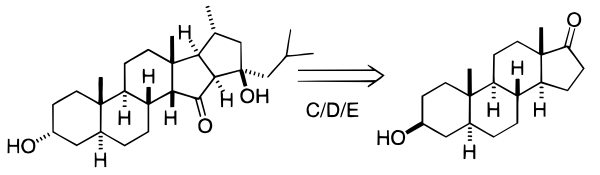
(1)

cycloaddition step provided the pentacyclic steroid skeleton in only modest yield. This prompted us to pursue an alternate route to the C/D/E portion of the skeleton. In addition, we have now successfully synthesized the A/B rings of xestobergsterol-(A). During the course of our work, Jung and co-workers reported a synthesis of 7-deoxyxestobergsterol-(A) from stigmasterol using a ring closing aldol to form the E-ring and a Breslow remote functionalization reaction as key transformations.[5]

Our approach to the synthesis of the xestobergsterols begins with a functionalization of commercially available tetracyclic steroids. Testosterone, **4**, and epiandrosterone, **5**, proved to be suitable starting materials because they provided not only a rapid entry into a substantial portion of the carbon framework but also a source of the necessary chirality.



Testosterone, **4**



Epiandrosterone, **5**

Our original plan for the stereoselective synthesis of the C/D/E portion of **1** is outlined in Scheme 1. We

(1) Shoji, N.; Umeyama, A.; Shin, K.; Takeda, K.; Arihara, S. *J. Org. Chem.* **1992**, *57*, 2996.
(2) Kobayashi, J.; Shinonaga, H.; Shigemori, H. *J. Nat. Prod.* **1995**, *58*, 312.
(3) Krafft, M. E.; Chirico X. *Tetrahedron Lett.* **1994**, *35*, 4511.
(4) Krafft, M. E.; Shao, B.; Dasse, O. A *Tetrahedron* **1998**, *54*, 7033−7044.
(5) Jung, M. E.; Johnson, T. W. *J. Am. Chem. Soc.* **1997**, *119*, 12412.

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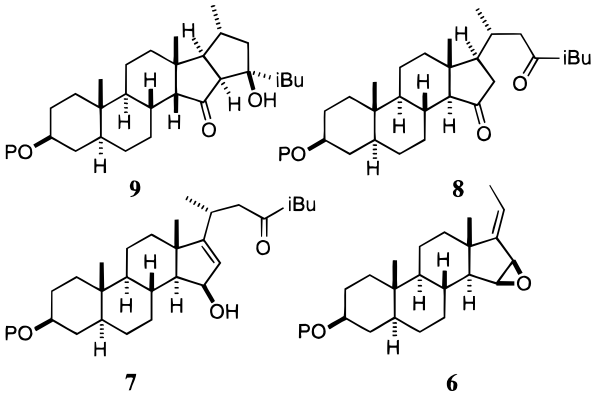
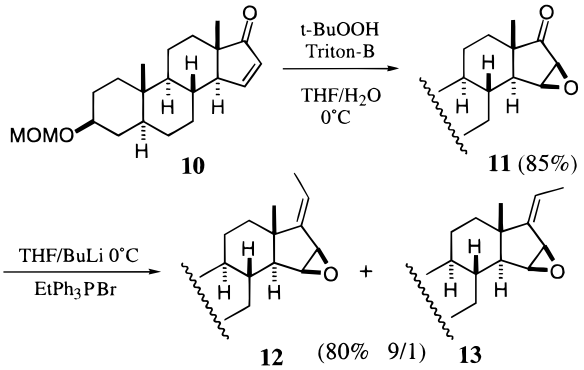
**Scheme 1**

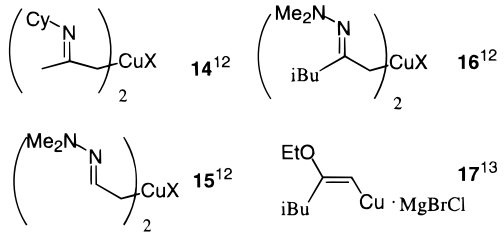



envisioned that we could introduce the side-chain, which would be used to close the last ring, via a 1,4-nucleophilic addition of a properly functionalized cuprate to alkylidene epoxide **6**, readily synthesized from epiandrosterone **5**, to give rise to keto-alcohol **7** (Scheme 1). Further hydrogenation of the $\Delta^{16}$-steroid from the α-face, giving **8** with the proper stereochemistry at C-17, oxidation and aldol ring closure with concomitant C-14 epimerization would then lead to the fully functionalized C/D/E ring system of the xestobergsterols, i.e., **9**.

Epoxidation of enone **10**[4,6] on the *β*-face using *tert*-butyl hydroperoxide in THF/$H_2O$ at 0 °C provided epoxyketone **11** in 85% yield (Scheme 2). Wittig olefination at 0 °C

**Scheme 2**



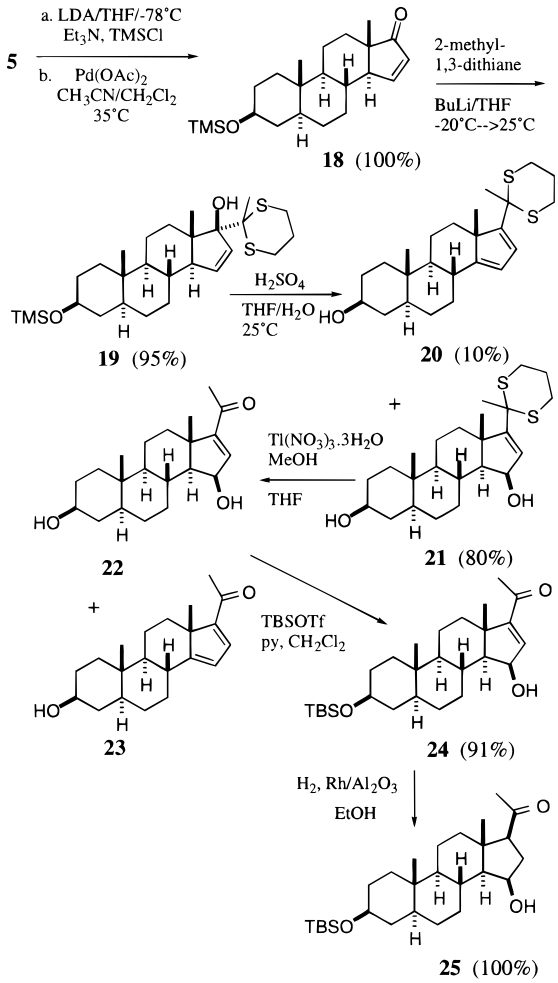




provided a 9/1 mixture of desired epoxyalkene **12** and isomer **13** in 80% yield. Although most reports on similar steroids cite formation of the *E*-isomer only, we still detected the *Z*-isomer under identical reaction conditions.[7−10]

Our plan was then to introduce a functionalized side-chain by 1,4-cuprate addition to alkylidene epoxide **12** from the less sterically demanding α-face.[9−11] However, all attempts to stereo- and regioselectively introduce a side chain moiety using cuprates **14**−**17** or allyl or vinyl cuprates failed and only mixtures of 1,2- and 1,4-addition adducts were obtained.

We turned our attention to an alternate approach for the introduction of the side chain (Scheme 3). Addition

**Scheme 3**




of 2-lithio-2-methyl-1,3-dithiane to enone **18**, obtained in quantitative yield from epiandrosterone **5** via a Pd-mediated trimethylsilyl enol ether oxidation, proceeded smoothly (95% yield) at room temperature from the less-hindered α-face.[14] The resulting tertiary alcohol **19** was then subjected to reaction with aqueous sulfuric acid in

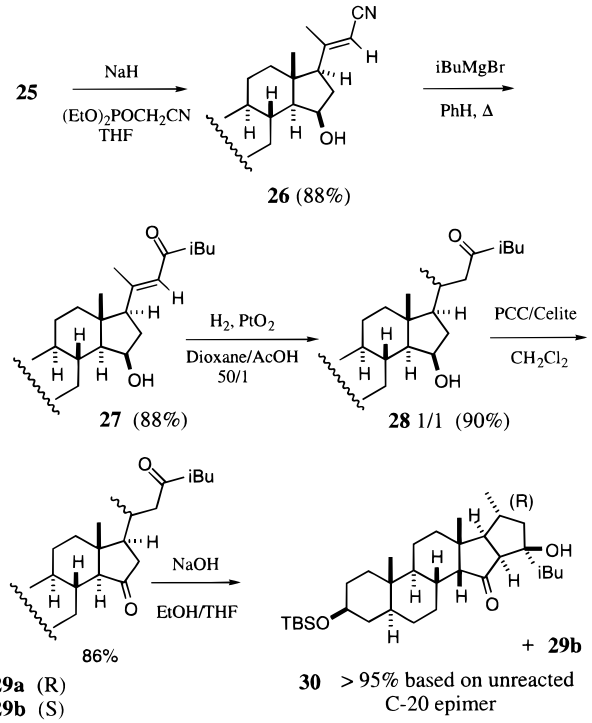
(6) Ito, Y.; Hirao, T.; Saegusa, T. *J. Org. Chem.* **1978**, *43*, 1011.
(7) Moon, S.; Stuhmiller, L. M.; Chadha, R. J.; McMorris, T. C. *Tetrahedron* **1990**, *46*, 2287.
(8) Takahashi, T.; Ootake, A.; Tsuji, J.; Tachibana, K. *Tetrahedron* **1985**, *41*, 5747.
(9) Marino, J. P.; Abe, H. *J. Am. Chem. Soc.* **1981**, *103*, 2907.
(10) Liu, D.; Stuhmiller, L. M.; McMorris, T. C. *J. Chem. Soc., Perkin Trans. 1* **1988,** 2161.
(11) Normant, J. F.; Alexakis, A.; Cahiez, G. *Synthesis* **1978**, 528.
(12) Corey, E. J.; Enders, D.; Bock, M. G. *Tetrahedron Lett.* **1976**, *17*, 7. Corey, E. J.; Enders, D. *Tetrahedron Lett.* **1976**, *17*, 3. Corey, E. J.; Enders, D. *Tetrahedron Lett.* **1976**, *17*, 11. Yamamoto, K.; Iijima, M.; Ogimura, Y. *Tetrahedron Lett.* **1982**, *23*, 3711.
(13) Gardette, M.; Alexakis, A.; Normant, J. F. *Tetrahedron* **1985**, *41*, 5887. Germon, C.; Alexakis, A.; Normant, J. F. *Synthesis* **1984**, 43. Normant, J. F.; Cahiez, G.; Alexakis, A.; Villieras, J. *Bull. Soc. Chim. Fr.* **1977**, 693. Foulon, J. P.; Commercon-Bourgain, M.; Normant, J. F. *Tetrahedron* **1986**, *42*, 1389. Normant, J. F.; Alexakis, A. *Synthesis* **1981,** 841. Normant, J. F.; Cahiez, G.; Bourgain, M.; Chuit, C.; Villieras, J. *Bull. Soc. Chim. Fr.* **1974**, 1656. Lipshutz, B. H.; Sengupta, S. *Org. React.* **1992**, *41*, 135.
(14) Corey, E. J.; Crouse, D. *J. Org. Chem.* **1968**, *33*, 298. Corey, E. J.; Erickson, B. W. *J. Org. Chem.* **1971**, *36*, 3553. Jones, J. B.; Grayshan, R. *Can. J. Chem.*, **1972**, *50*, 1414.

THF to provide rearranged C-15 hydroxylated pregnane derivative **21** in 80% yield along with diene **20** (10% yield). The hydrolysis was best performed with 300 mol % of sulfuric acid. An increase in acid concentration resulted in extensive diene formation. It is not clear whether diene **20** arises directly from tertiary alcohol **19** or from alcohol **21**. The stereochemistry at C-15 was determined by a combination of $^1$H NMR DQCOSY and NOESY experiments. The substitution reaction leading to alcohol **21** can occur by either a syn $S_N2'$ or $S_N1$ pathways. The high stereoselectivity of an addition would tend to point toward a syn-$S_N2'$ pathway;[15] however, it is known that the addition of alcohols to the C-15 enone position results in the stereoselective formation of 15$\beta$-ethers.[16]

Deprotection of the masked ketone proved to be challenging. Attempts to hydrolyze dithiane **21** using MeI/THF/water[17] resulted in extensive formation of dienone **23**, presumably due to HI-catalyzed hydrolysis. Addition of solid bicarbonate resulted in only a small amount of dithiane cleavage and mostly recovered starting material. Enone **22** was obtained in 40% yield along with other products when the thioketal was cleaved by reaction with $NCS/AgNO_3/THF/CH_3CN/H_2O$[18,19] or iodine/ether/sodium bicarbonate.[20] Deprotection with thallium nitrate in MeOH/THF proved to be suitable conditions and provided dihydroxyenone **22** in satisfactory yield (62%).[21,22] Selective protection of the 3$\beta$-hydroxyl group with *tert*-butyldimethylsilyl trifluoromethanesulfonate in pyridine/methylene chloride at −78 °C provided hydroxyenone **24** in 91% yield.[23] Further hydrogenation (1 atm $H_2$, ambient temp, EtOH) from the more accessible α-face using rhodium/alumina as a catalyst provided hydroxyenone **25** in quantitative yield.[8,24,25] The stereochemistry at C-17 was determined by a combination of $^1$H NMR DQCOSY and NOESY experiments. Attempts to carry out the hydrogenation with other catalysts such as Pd/C or $PtO_2$ resulted in extensive hydrogenolysis of the allylic 15$\beta$-alcohol. We did not observe any hydrogenolysis when the rhodium/alumina catalyst was used. At this point, we have now introduced the correct functionalization at C-15, set the stereochemistry at C-17, and can use the C-20 ketone as a handle for elaboration of the side-chain.

Wittig olefination of hydroxyketone **25** provided nitrile **26** in 88% yield (Scheme 4). Addition of isobutylmagnesium chloride to nitrile **26** in refluxing benzene gave enone **27** in 88% yield.[26] Hydrogenation of **27** in 50/1 mixture of dioxane and acetic acid provided a 1/1 mixture of C-20 epimers **28** in 90% yield. The lack of selectivity in the alkene hydrogenation is presumably due to a small energy difference between rotamers around the C-17/C-20 bond which reveals both alkene faces for reduction.

**Scheme 4**




Further oxidation of the C-15 alcohol with PCC in methylene chloride gave a 1:1 mixture of diones **29a** and **29b**, epimeric at the C-20 methyl group (86% yield).[27,28] Examination of a molecular model for the aldol reaction revealed that, in the case of the C-20 nonnatural epimer **29b**, a very severe 1,3-C-13 methyl to C-20-methyl interaction on the concave face of the bicyclo[3.3.0]octane ring system would develop in the transition state. For natural epimer **29a**, the C-20 methyl group is placed on the convex face of the bicyclo[3.3.0]octane therefore eliminating the significant steric interaction (Figure 1).

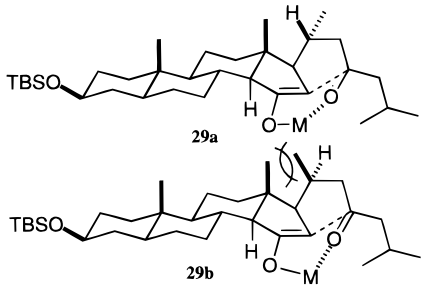



**Figure 1.**

As we expected, treatment of a mixture of diketones **29a/29b** with aqueous sodium hydroxide in methanol at room temperature provided the desired aldol product **30** along with unreacted **29b**.[29] The reaction was quantitative based on unreacted starting material. The stereochemistry of aldol product **30** was confirmed by a combination of $^1$H NMR DQCOSY and NOESY experiments (Figure 2, Table 1).

Even though we had successfully synthesized the fully functionalized C/D/E ring system of the xestobergsterol

(15) Magid, R. M. *Tetrahedron* **1979**, *36*, 1901.
(16) Kelly, R. W.; Sykes, P. J. *J. Chem. Soc. (C)* **1968**, 416.
(17) Takano, S.; Hatakeyama, M.; Ogasawasa, H. *J. Chem Soc., Chem. Commun.* **1977**, 68.
(18) Corey, E. J.; Erickson, B. W. *J. Org. Chem.* **1971**, *36*, 3553.
(19) Rama Rao, A. V.; Venkatswamy, G.; Javeed, S. M.; Deshpande, V. H.; Rao, B. R. *J. Org. Chem.* **1983**, *48*, 1552.
(20) Chattopadhyaya, J. B.; Rama Rao, A. V. *Tetrahedron Lett.* **1973**, *14*, 3735.
(21) Lipshutz. B. H.; Moretti, R.; Crow, R. *Tetrahedron Lett.* **1989**, *30*, 15.
(22) Smith, R. A.; Hannah, D. *J. Synth. Commun.* **1979**, *9*, 301.
(23) Askin, D.; Angst, D.; Danishefsky, S. *J. Org. Chem.* **1987**, *52*, 622.
(24) Joannou, G. E.; Reeder, A. Y. *Steroids* **1996**, *61*, 82.
(25) Joannou, G. E.; Reeder, A. Y. *Steroids* **1996**, *61*, 74.
(26) Canonne, P.; Foscolos, S.; Lemay, F. *Tetrahedron Lett.* **1980**, 155.
(27) Corey, E. J.; Bock, M. G. *Tetrahedron Lett.* **1975**, 2643.
(28) Corey, E. J.; Suggs, J. W. *Tetrahedron Lett.* **1975**, *40*, 2554.
(29) Heathcock, C. H. in *Comprehensive Organic Synthesis*; Trost, B. M., kEd.; Pergamon: Oxford, 1991; Vol. 2, p 133.

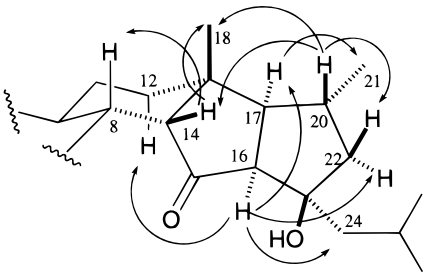


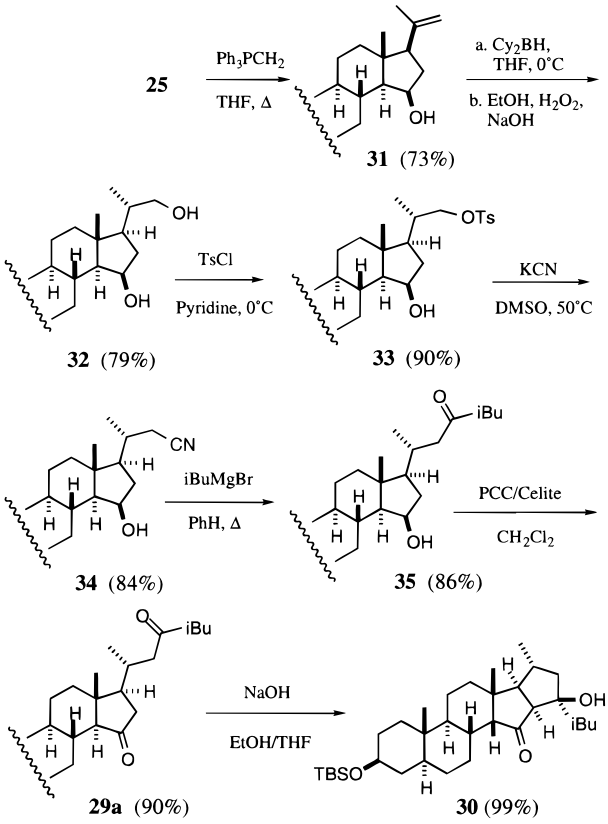

**Figure 2.**

**Table 1. $^1$H NMR NOE Enhancements for 30**

| irradiation | NOE (%) |
|---|---|
| 16α-H | 17α-H, 24-H (6) |
| | 12α-H (4) |
| 20*β*-H | 14*β*-H (5) |
| | 22*β*-H (3) |
| 14*β*-H | 18-H (2) |
| | 8*β*-H (4) |
| 17α-H | 16α-H, 12α-H, 21-H (3) |

steroids, the lack of stereocontrol during the hydrogenation step was not satisfying. Our approach was therefore modified in order to introduce the C-20 stereogenic center with total stereocontrol. Wittig olefination of hydroxy ketone **25** provided hydroxy alkene **31** in 73% yield (Scheme 5). Hydroboration with dicyclohexyl borane in THF at 0 °C followed by borane oxidation provided only one isomer, diol **32** (79% yield).[30−33]

**Scheme 5**



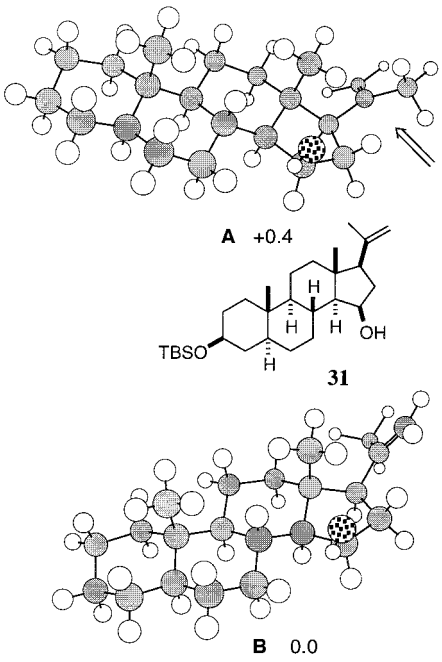




**Figure 3.** Side-chain conformers of alkene **31**.

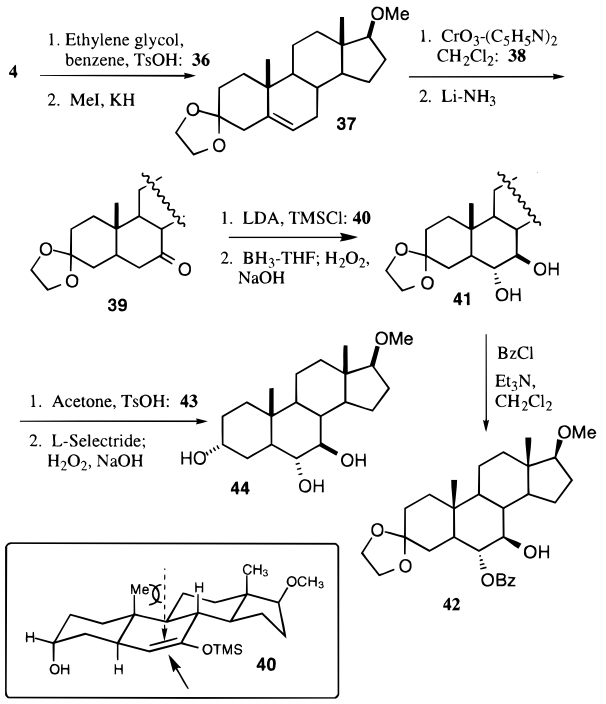
The stereochemical outcome of the reaction can be explained in terms of steric hindrance to approach of the borane. MM2 calculations [Molecular Mechanics, Version 4.0, CAChe system, Oxford Molecular group] indicated the presence of two favored conformers whose energy differs by 0.4 kcal (Figure 3). In **A**, the *si* face is blocked by C-18 and C-12. However, the *re* face is relatively unhindered toward approach of the bulky borane. In conformer **B**, the *re* face is blocked by C-18, and approach of the reagent to the *si* face will be hindered by C-16. Thus, the observed stereochemical outcome for the conversion of **31** to **32** is most readily rationalized by the approach of the borane to the *re* face of conformer **A**. Selective tosylation of the primary alcohol in pyridine (90% yield) followed by displacement with potassium cyanide in DMSO provided the desired nitrile **34** in 84% yield.[34]

Addition of isobutylmagnesium chloride in refluxing benzene provided ketone **35** after imine hydrolysis on silica gel (86%). PCC oxidation provided diketone **29a** which was cyclized with concomitant C-14 epimerization to hydroxy ketone **30** in quantitative yield. The C-20 stereocenter, derived from the hydroboration, was therefore confirmed by successful cyclization. We therefore have effectively synthesized the C/D/E ring system of the xestobergsterol steroids with complete stereocontrol.

With the C/D/E rings in place, we turned our attention to incorporating the alcohols at C-3, C-6, and C-7 in xestobergsterol-A by transformation of testosterone, **4**. Deconjugative ketalization of testosterone,[35] gave the corresponding *β*,*γ*-deconjugated ketal alcohol **36** in 85% yield (Scheme 6). Subsequent protection using KH/MeI provided methyl ether **37** in 95% yield. Allylic oxidation

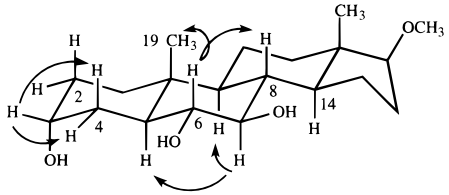
(30) Midland, M. M.; Kwon, Y. C. *J. Am. Chem. Soc.* **1983**, *105*, 5725.
(31) Midland, M. M.; Kwon, Y. C. *Tetrahedron Lett.* **1984**, *25*, 5981.
(32) Midland, M. M.; Kwon, Y. C. *Tetrahedron Lett.* **1985**, *26*, 5017.
(33) Stoilov, I.; Kolaczkowska, E.; Watt, D. S.; St. Pyrek, J.; Carlson, R. M. K.; Fago, F. J.; Maldowan, J. M. *J. Org. Chem.* **1993**, *58*, 3444.
(34) Konno, K.; Ojima, K.; Hayashi, T.; Takayama, H. *Chem. Pharm. Bull.* **1992**, *40*, 1120.
(35) Nitz, T. J.; Paquette, L. A. *Tetrahedron Lett.* **1984**, *25*, 3047. Choe, Y. S.; Katzenellenbogen, J. A. *Steroids* **1995**, *60*, 414. Corey, E. J.; Ohno, M.; Mitra, R. B.; Vatakencherry, P. A. *J. Am. Chem. Soc.* **1964**, *86*, 478.

**Scheme 6**




of **37** with Collins reagent,[36] followed by lithium−ammonia reduction of the resulting enone **38** resulted in the formation of ketone **39** in 76% overall yield. Ketone **39** was then converted into the corresponding trimethylsilyl enol ether **40** by reaction with LDA and TMSCl. Hydroboration of **40** with $BH_3$−THF complex gave the desired diol **41** in 65% yield from **39**. The stereochemical outcome of the enol ether hydroboration can be explained by approach of the reagent from the α-face via a boatlike conformation of the transition state to avoid 1,3 diaxial interactions between the incoming boron reagent and the C-10 methyl group. This explanation is in accord with the stereochemical outcome of enolate alkylations in six-membered rings.[37] The stereochemistry was confirmed by $^1$H NOE experiments on mono benzoate **42**, which was obtained by selective benzylation of **41** with benzyl chloride in the presence of triethylamine.

With the B ring completely functionalized, modification of the A ring was straightforward. Deprotection of ketal **41** with acetone and a catalytic amount of *p*-TsOH provided the keto diol **43** which was reduced using L-Selectride[38] to give triol **44**. The relative stereochemistry of **44** was determined by difference $^1$H NOE experiments and coupling constants. The coupling constants of equatorial H3 (dddd, $J$ = 2.9, 2.9, 2.9, 2.9 Hz), axial H6 (dd, $J$ = 11.2, 8.6 Hz), and axial H7 (dd, $J$ = 9.9, 8.6 Hz) determined the α-(C3 and C6) and β-(C7) oriented hydroxyl groups. The NOE between H3 and both α-H4 and β-H4 also supports the axial hydroxyl group at the C-3 position. The NOE between H6 and β-H4, H8 and 19-$CH_3$, confirmed the C6 configuration. The NOE observed between $H_7$ and H5, H9 and H14, indicated a β-hydroxyl group at the C7 position.



**44** - partial NOE data

In summary, we have now successfully, in separate compounds, synthesized both ends of the xestobergsterol skeleton. By taking advantage of the rigidity of the steroid skeleton we were able to carry out the aldol ring closure[5] and C-14 epimerization stereoselectively. Further studies toward achieving the total synthesis of **1** are currently in progress.

## Experimental Section

Tetrahydrofuran (THF) and diethyl ether ($Et_2O$) were distilled from potassium−benzophenone ketyl prior to each use. Methylene chloride ($CH_2Cl_2$) and pyridine were distilled from calcium hydride. Hexane, chloroform ($CHCl_3$), methanol (MeOH), and ethyl acetate (EtOAc) were distilled prior to use. Toluene was distilled from sodium metal prior to use. All reactions were performed under an atmosphere of nitrogen. Chromatography refers to flash chromatography as reported by Still.[39] All protons were assigned using $^1$H NMR decoupling and NOE experiments.

**3β-(Methoxymethoxy)-5α-androst-15-en-17-one (10).** To a solution of $^i$$Pr_2NH$ (5 mL, 36 mmol) in THF (84 mL) cooled to −78 °C was added a solution of BuLi in hexanes (22.8 mL, 36 mmol). The mixture was stirred at −78 °C for 15 min. A solution of 3β-(methoxymethoxy)-5α-androstan-17-one (6 g, 18 mmol) in THF (18 mL) was added dropwise over a 30-min period, and the reaction mixture was stirred at −78 °C for an additional 15 min. Then, $NEt_3$ (7.5 mL, 54 mmol) and TMSCl (3.4 mL, 24.3 mmol) were added. The mixture was warmed to rt and stirred for an additional 25 min and then quenched with saturated $NaHCO_3$. The aqueous layer was extracted twice with EtOAc, and the combined organic layers were dried over $MgSO_4$ and condensed under vacuum. The crude enol ether was then dissolved in $CH_2Cl_2$ (15 mL) and $CH_3CN$ (75 mL). Palladium acetate (4.4 g, 19 mmol) was added in one portion. The reaction mixture was stirred for 2 h at rt. It was filtered twice through silica gel pads (3/1 hexane EtOAc). Purification of the residue by flash chromatography on silica gel (3/1 hexane EtOAc) gave **10** as white needles (5.72 g, 96%). 500-MHz $^1$H NMR: δ 0.80 (m, 1H, H-9α), 0.89 (s, 3H, H-19), 1.00 (ddd, $J$ = 3.9, 13.8, 13.8, 1H, H-1α), 1.06 (m, 3H, H-18), 1.10 (m, 1H, H-7α), 1.18 (m, 1H, H-5α), 1.32 (m, 1H, H-6β), 1.35 (m, 2H, H-4β, H-6α), 1.47 (m, 1H, H-2β), 1.49 (m, 1H, H-11β), 1.50 (m, 1H, H-12α), 1.65 (m, 1H, H-4α), 1.70 (m, 1H, H-11α), 1.71 (m, 1H, H-1β), 1.78 (m, 1H, H-8β), 1.85 (m, 1H, H-12β), 1.86 (m, 1H, H-2α), 1.99 (dddd, $J$ = 12.8, 3.9, 3.9, 3.9, 1H, H-7β), 2.27 (ddd, $J$ = 11.4, 2.3, 2.3, 1H, H-14α), 3.37 (s, 3H, $CH_3O$), 3.51 (dddd, $J$ = 5, 5, 11.2, 11.2, 1H, H-3α), 4.67 (bs, 2H, $OCH_2O$), 6.01 (dd, $J$ = 3, 6, 1H, H-16), 7.50 (ddd, $J$ = 1, 3, 6, 1H, H-15). 75-MHz $^{13}$C NMR: δ 12.06, 20.03, 20.45, 28.18, 28.48, 29.09, 30.67, 32.31, 35.11, 35.92, 36.63, 45.10, 51.03, 55.01, 55.80, 56.92, 76.15, 94.70, 131.95, 158.61, 213.46. IR ($cm^{-1}$): 2909, 1696. Mass spectrum *m/e* (PCI:isobutane): 333 ($M^+ + 1$, 100). Anal. Calcd for $C_{21}H_{32}O_3 \cdot 0.4H_2O$: C, 74.26; H, 9.61. Found: C, 74.27; H, 9.58. Mp (°C): 56−58. $[\alpha]^{25}_D$ −52 ($c$ = 17.4, $CHCl_3$).

**3β-(Methoxymethoxy)-5α-androstan-17-one.** To a solution of 3β-hydroxy-5α-androstan-17-one (20 g, 66.8 mmol) and $^i$$Pr_2NEt$ (23.2 mL, 133.6 mmol) in $CH_2Cl_2$ (330 mL) cooled to 0 °C was added methoxymethyl chloride (7.6 mL, 100.2 mmol). The solution was kept at 0 °C and stirred for 1 h. It was then allowed to warm to rt and stir overnight. The mixture was

(36) Kato, M.; Kurihara, H.; Yoshikoshi, A. *J. Chem. Soc., Perkin Trans. 1* **1979**, 2740.

(37) Evans, D. in *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic: Orlando, 1984; Chapter 1, Vol. 3.

(38) Brown, H. C.; Krishnamurthy, S. *J. Am. Chem. Soc.* **1972**, *94*, 7159.

(39) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923

then diluted with $CH_2Cl_2$ and washed with water, 10% HCl, saturated $NaHCO_3$, and brine. The organic layer was then dried over anhydrous $MgSO_4$ and condensed to give a white solid. Purification by flash chromatography on silica gel (3/1 hexane/EtOAc) gave 3*β*-(methoxymethoxy)-5α-androstan-17-one as white needles (22.1 g, 99%). 500-MHz $^1$H NMR: *δ* 0.69 (dd, *J* = 3.9, 11.4, 11.4, 1H, H-9α), 0.84 (s, 3H, H-19), 0.86 (s, 3H, H-18), 0.94 (m, 1H, H-1α), 0.98 (m, 1H, H-7α), 1.12 (m, 1H, H-5α), 1.20−1.38 (m, 3H, H-6α, H-6*β*, H-12), 1.26 (m, 1H, H-14α), 1.32 (m, 1H, H-11*β*), 1.34 (m, 1H, H-4*β*), 1.45 (m, 1H, H-2*β*), 1.49 (m, 1H, H-15α), 1.55 (m, 1H, H-8*β*), 1.62−1.69 (m, 1H, H-12), 1.64 (m, 1H, H-4α), 1.65 (m, 1H, H-11α), 1.74 (ddd, *J* = 13.3, 3.4, 3.4, 1H, H-1*β*), 1.80 (m, 1H, H-7*β*), 1.87 (m, 1H, H-2α), 1.92 (m, 1H, H-15*β*), 2.05 (ddd, *J* = 9.1, 9.1, 19.1, 1H, H-16α), 2.43 (ddd, *J* = 1, 9.1, 19.1, 1H, H-16*β*), 3.50 (dddd, *J* = 4.9, 4.9, 11.1, 11.1, 1H, H-3α), 3.36 (s, 3H, $CH_3O$), 4.67 (bs, 2H, $OCH_2O$). 75-MHz $^{13}$C NMR: *δ* 12.00, 13.60, 20.29, 21.58, 28.33, 28.51, 30.77, 31.46, 34.98, 35.13, 35.68, 36.87, 44.86, 47.66, 51.41, 54.49, 55.02, 76.21, 94.68, 221.50. IR (cm$^{-1}$): 2925, 1721. Mass spectrum *m/e* (PCI: isobutane): 335 ($M^+$ + 1), 303 ($M^+$ − 31), 273 ($M^+$ − 61, 100). Anal. Calcd for $C_{21}H_{34}O_3$: C, 75.41; H, 10.25. Found: C, 75.25, H, 10.15. Mp (°C): 95−96. [α]$^{25}_D$ +46 (*c* = 29.4, $CHCl_3$).

**3*β*-((Trimethylsilyl)oxy)-5α-androst-15-en-17-one (18).** To a solution of $^iPr_2NH$ (2.95 mL, 21 mmol) in THF (29 mL) cooled to −78 °C was added a solution of BuLi in hexanes (13.2 mL, 21 mmol). The mixture was stirred at −78 °C for 15 min. A solution of 3*β*-hydroxy-5α-androstan-17-one (2.1 g, 7 mmol) in THF (7 mL) was added dropwise over a 30-min period, and the reaction mixture was stirred at −78 °C for an additional 15 min. Then, $NEt_3$ (3.9 mL, 28 mmol) and TMSCl (2.7 mL, 19 mmol) were added. The mixture was warmed to rt, stirred for an additional 25 min, and then quenched with saturated $NaHCO_3$. The aqueous layer was extracted twice with EtOAc, and the combined organic layers were dried over $MgSO_4$ and condensed under vacuum. The crude enol ether was then dissolved in $CH_2Cl_2$ (30 mL) and $CH_3CN$ (10 mL). Palladium acetate (1.73 g, 7.4 mmol) was added in one portion. The reaction mixture was stirred for 3 h at 35−40 °C (water bath). It was filtered twice through silica gel pads (3/1 hexane EtOAc). Purification of the residue by flash chromatography on silica gel (3/1 hexane EtOAc) gave **18** as white needles (2.39 g, 95%). 500-MHz $^1$H NMR: *δ* 0.11 (s, 9H, $(CH_3)_3SiO$), 0.77 (m, 1H, H-9α), 0.86 (s, 3H, H-19), 0.97 (ddd, *J* = 4.1, 13.1, 13.1, 1H, H-1α), 1.05 (s, 3H, H-18), 1.08 (m, 1H, H-7α), 1.15 (m, 1H, H-5α), 1.32 (m, 1H, H-6*β*), 1.36 (m, 2H, H-6α, H-4*β*), 1.47 (m, 2H, H-4α, H-2*β*), 1.48 (m, 1H, H-11*β*), 1.49 (m, 1H, H-12α), 1.67 (m, 1H, H-1*β*), 1.70 (m, 1H, H-2α), 1.71 (m, 1H, H-11α), 1.77 (dddd, *J* = 3.9, 11.5, 11.5, 11.5, 1H, H-8*β*), 1.85 (m, 1H, H-12*β*), 1.97 (dddd, *J* = 3.7, 12.6, 12.6, 12.6, 1H, H-7*β*), 2.26 (ddd, *J* = 11.5, 3, 3, 1H, H-14α), 3.55 (dddd, *J* = 4.8, 4.8, 11, 11, 1H, H-3α), 6.00 (dd, *J* = 3, 6, 1H, H-16), 7.50 (dd, *J* = 1, 6, 1H, H-15). 75-MHz $^{13}$C NMR: *δ* 0.01 (3C), 12.13, 20.01, 20.52, 28.09, 29.00, 30.66, 31.57, 32.20, 35.73, 36.70, 38.28, 45.15, 51.05, 55.72, 56.87, 71.57, 131.77, 158.82, 213.63. IR (cm$^{-1}$): 2935, 2862, 1703. Mass spectrum *m/e* (PCI:isobutane): 361 ($M^+$ + 1, 100). Anal. Calcd for $C_{22}H_{36}O_2Si$: C, 73.28; H, 10.06. Found: C, 73.43; H, 10.00. Mp (°C): 107−108. [α]$^{25}_D$ −51 (*c* = 1, $CHCl_3$).

**3*β*-((Trimethylsilyl)oxy)-20,20-(trimethylenedithio)-5α-pregn-15-en-17*β*-ol (19).** To a solution of 2-methyl-1,3-dithiane (1.72 mL, 15.26 mmol) in THF (30 mL) cooled to −20 °C was added a solution of BuLi in hexanes (9.82 mL, 15.26 mmol). The mixture was stirred at −20 °C for 1.5 h. A solution of **18** (5.39 g, 14.97 mmol) in THF (35 mL) was then added dropwise, and the reaction was allowed to warm to rt and stir for 20 h. The mixture was then quenched with a saturated solution of $NH_4Cl$. The aqueous layer was extracted with EtOAc, and the combined organic layers were dried over $MgSO_4$ and condensed under vacuum. Purification of the residue by flash chromatography on silica gel (12/1 hexane EtOAc) gave **19** as a white solid (7.03 g, 95%). 500-MHz $^1$H NMR: *δ* 0.10 (s, 9H), 0.63−0.75 (m, 1H), 0.81 (s, 3H), 0.86−1.00 (m, 2H), 1.01 (s, 3H), 1.05−1.12 (m, 1H), 1.22−1.50 (m, 7H), 1.52 (bs, 1H), 1.58−1.70 (m, 4H), 1.83−1.94 (m, 3H), 1.96−2.03 (m, 1H), 2.00 (s, 3H), 2.72−2.89 (m, 2H), 2.92−3.08 (m, 2H), 3.53 (dddd, *J* = 5.5, 5.5, 10.5, 10.5, 1H), 5.80 (bs, 1H), 6.11 (d, *J* = 5.5, 1H). 75-MHz $^{13}$C NMR: *δ* 0.03 (3C), 12.09, 18.13, 21.13, 26.21, 28.37, 31.62, 31.86, 33.25, 33.54, 35.55, 36.75, 38.36, 45.09, 53.87, 54.58, 57.69, 71.79, 91.73, 134.86. IR (cm$^{-1}$): 2934, 2859, 1453. Mass spectrum *m/e* (PCI: isobutane): 496 ($M^+$ + 1), 477 ($M^+$ − 18), 361 ($M^+$ − 134, 100). Anal. Calcd for $C_{27}H_{46}O_2SiS_2$: C, 65.53; H, 9.37. Found: C, 65.64; H, 9.31. Mp (°C): 154−155. [α]$^{25}_D$ −74 (*c* = 1, $CHCl_3$).

**20,20-(Trimethylenedithio)-5α-pregn-16-ene-3*β*,15*β*-diol (21).** To a solution of **19** (1.46 g, 2.95 mmol) in THF (80 mL) was added an aqueous solution of 0.45% $H_2SO_4$ (70 mL). The mixture was stirred at rt for 6 days. Concentrated sulfuric acid (0.16 mL) was then added dropwise and the mixture was stirred at rt for another 3 days. After neutralizing with 2, N NaOH, most of the solvent was removed under vacuum. The residue was dissolved in $CHCl_3$, and the aqueous layer was extracted several times. The combined organic layers were dried over $MgSO_4$ and condensed under vacuum. Purification of the residue by flash chromatography on silica gel (1/1 hexane EtOAc) afforded **21** as a white solid (1 g, 80%). 500-MHz $^1$H NMR: *δ* 0.77 (ddd, *J* = 4.8, 11.4, 11.4, 1H, H-9α), 0.88 (s, 3H, H-19), 0.98 (ddd, *J* = 3.8, 13.4, 13.4, 1H, H-1α), 1.06 (dddd, *J* = 5.7, 11.8, 11.8, 11.8, 1H, H-7α), 1.15 (m, 1H, H-5α), 1.25−1.36 (m, 2H, H-6α, H-6*β*), 1.31 (m, 1H, H-4*β*), 1.37 (dd, *J* = 5, 11.4, 1H, H-14α), 1.41 (m, 1H, H-11*β*), 1.42 (s, 3H, H-18), 1.43 (m, 1H, H-2*β*), 1.56 (m, 1H, H-12α), 1.58 (m, 1H, H-4α), 1.60 (m, 1H, H-11α), 1.72 (ddd, *J* = 3.8, 13.4, 13.4, 1H, H-1*β*), 1.79 (s, 3H, H-21), 1.83 (m, 1H, H-2α), 1.86 (m, 1H, H-8*β*), 1.96 (dddd, *J* = 3.7, 3.7, 3.7, 11.8, 1H, H-7*β*), 1.97 (m, 2H, $SCH_2CH_2$-$CH_2S$), 2.16 (m, 1H, H-12*β*), 2.78−2.90 (m, 4H, $SCH_2$-$CH_2CH_2S$), 3.60 (dddd, *J* = 4.8, 4.8, 11.1, 11.1, 1H, H-3α), 4.48 (dd, *J* = 3.5, 5, 1H, H-15α), 6.26 (d, *J* = 3.5, 1H, H-16). 75-MHz $^{13}$C NMR: *δ* 12.00, 20.72, 24.50, 24.66, 27.64, 28.27, 28.33, 29.58, 30.60, 31.01, 31.20, 35.51, 36.55, 36.65, 37.87, 44.98, 48.66, 50.21, 54.66, 60.59, 71.05, 72.03, 131.79, 161.82. IR (cm$^{-1}$): 3455, 2934, 2860. Mass spectrum *m/e* (PCI: isobutane): 405 ($M^+$ − 90, 100), 315 ($M^+$ − 180). Mp (°C): 165−168. [α]$^{25}_D$ −72 (*c* = 1, $CHCl_3$).

**3*β*,15*β*-Dihydroxy-5α-pregn-16-en-20-one (22).** To a solution of **21** (2.04 g, 4.83 mmol) in MeOH (63 mL) and THF (16 mL) was added rapidly a solution of thallium nitrate trihydrate (9.67 mmol, 4.29 g) in MeOH (16 mL). The reaction mixture was stirred for 10 min at rt, diluted with water, and extracted with $CHCl_3$. After concentration in vacuo, the residue was subjected to flash chromatography (silica gel; 9/1 $CH_2Cl_2$/acetone) to give **22** (990 mg, 62%). 500-MHz $^1$H NMR: *δ* 0.79 (ddd, *J* = 4.5, 10.2, 12.4, 1H, H-9α), 0.88 (s, 3H, H-19), 0.99 (ddd, *J* = 3.8, 13.4, 13.4, 1H, H-1α), 1.11 (dddd, *J* = 5.7, 11.8, 11.8, 11.8, 1H, H-7α), 1.16 (m, 1H, H-5α), 1.23 (m, 1H, H-12α), 1.23 (s, 3H, H-18), 1.28 (dd, *J* = 5.4, 12.1, 1H, H-14α), 1.3−1.4 (m, 1H, H-6α), 1.32 (m, 1H, H-4*β*), 1.38 (m, 1H, H-6*β*), 1.42 (m, 1H, H-2*β*), 1.46 (m, 1H, H-11*β*), 1.59 (m, 1H, H-4α), 1.61 (m, 1H, H-11α), 1.72 (ddd, *J* = 13.4, 3.5, 3.5, 1H, H-1*β*), 1.82 (m, 1H, H-2α), 1.84 (m, 1H, H-8*β*), 1.96 (dddd, *J* = 11.8, 3.3, 3.3, 3.3, 1H, H-7*β*), 2.26 (ddd, *J* = 2.5, 5, 12.7, 1H, H-12*β*), 2.31 (s, 3H, H-21), 3.6 (dddd, *J* = 4.8, 4.8, 11.1, 11.1, 1H, H-3α), 4.65 (dd, *J* = 2.9, 5.4, 1H, H-15α), 6.65 (d, *J* = 2.9, 1H, H-16). *δ* 75-MHz $^{13}$C NMR (MeOH): *δ* 12.65, 21.91, 22.47, 27.57, 29.78, 32.13, 32.22, 36.27, 37.00, 38.00, 38.90, 46.64, 48.09, 56.87, 60.68, 71.90, 73.43, 145.33, 158.47, 200.48. IR (cm$^{-1}$): 3439, 2935, 1671.. Mass spectrum *m/e* (PCI:isobutane): 315 ($M^+$ − 17), 299 ($M^+$ − 34, 100). Anal. Calcd for $C_{21}H_{32}O_3 \cdot 0.7\ H_2O$: C, 73.09; H, 9.54. Found: C, 73.09; H, 9.75. Mp (°C): 181−183. [α]$^{25}_D$ −29 (*c* = 1, MeOH).

**3*β*-[(*tert*-Butyldimethylsilyl)oxy]-15*β*-hydroxy-5α-pregn-16-en-20-one (24).** To a solution of **22** (300 mg, 0.9 mmol) in pyridine (5 mL) and $CH_2Cl_2$ (5 mL) cooled to −78 °C was added a solution of *tert*-butyldimethylsilyl trifluoromethanesulfonate (0.9 mmol, 0.23 mL) in $CH_2Cl_2$ (2 mL) dropwise. Additional TBDMSOTf/$CH_2Cl_2$ solution was then added (0.1 equiv at a time) until the reaction was complete. It was then quenched at −78 °C by addition of a saturated $NH_4Cl$ solution. The aqueous layer was extracted with EtOAc, and the combined organic layers were dried over $MgSO_4$ and condensed under

vacuum. Purification of the residue by flash chromatography on silica gel (3/1 hexane EtOAc) gave **24** as a white solid (363 mg, 90%). 500-MHz $^1$H NMR: $\delta$ 0.05 (s, 6H, $(CH_3)_2SiO$), 0.76 (ddd, $J$ = 4.5, 10.2, 12.1, 1H, H-9α), 0.88 (s, 9H, $(CH_3)_3CSiO$), 0.89 (s, 3H, H-19), 0.95 (ddd, $J$ = 4.5, 13.2, 13.2, 1H, H-1α), 1.09 (dddd, $J$ = 5.7, 11.8, 11.8, 11.8, 1H, H-7α), 1.12 (m, 1H, H-5α), 1.22 (s, 3H, H-18), 1.22 (m, 1H, H-12α), 1.27 (dd, $J$ = 5.4, 12.1, 1H, H-14α), 1.3−1.4 (m, 1H, H-6α), 1.34 (m, 1H, H-6*β*), 1.36 (m, 1H, H-4*β*), 1.44 (m, 1H, H-11*β*), 1.45 (m, 2H, H-2*β*, H-4α), 1.60 (m, 1H, H-11α), 1.67 (m, 1H, H-1*β*), 1.69 (m, 1H, H-2α), 1.82 (dddd, $J$ = 3.8, 12.1, 12.1, 12.1, 1H, H-8*β*), 1.93 (dddd, $J$ = 12.1, 3.8, 3.8, 3.8, 1H, H-7*β*), 2.25 (ddd, $J$ = 2.4, 4.6, 12.8, 1H, H-12*β*), 2.31 (s, 3H, H-21), 3.55 (dddd, $J$ = 5, 5, 10.9, 10.9, 1H, H-3α), 4.65 (bs, 1H, H-15α), 6.65 (d, $J$ = 2.5, 1H, H-16). 75-MHz $^{13}$C NMR: $\delta$ −4.85 (2C), 12.07, 18.04, 20.55, 22.61, 25.74 (3C), 27.43, 28.34, 30.70, 31.08, 31.69, 34.80, 35.71, 36.73, 38.44, 45.26, 46.82, 55.40, 59.13, 72.01, 73.29, 141.92, 158.04, 197.87. IR (cm$^{-1}$): 2931, 1671. Mass spectrum *m*/*e* (PCI:isobutane): 448 ($M^+$ + 1), 432 ($M^+$ − 15, 100), 299 ($M^+$ − 148). Anal. Calcd for $C_{27}H_{46}O_3Si$: C, 72.59; H, 10.38. Found: C, 72.68; H, 10.30. Mp (°C): 178−179. $[\alpha]^{25}_D$ −12 ($c$ = 1, $CHCl_3$).

**3*β*-[(*tert*-Butyldimethylsilyl)oxy]-15*β*-hydroxy-5α-pregnan-20-one (25).** A solution of **24** (0.9 g, 2.02 mmol) in EtOH (50 mL) was added to a flask containing 0.3 g 5% Rh/Alumina. The reaction vessel was then fitted with a balloon filled with hydrogen, and the mixture was stirred for 3 h at rt. The resulting mixture was then filtered through a pad of Celite and concentrated in vacuo, and the residue was subjected to column chromatography (silica gel) using a 3/1 mixture of hexane/EtOAc as the eluent to give **25** as white needles (0.88 g, 97%). 500-MHz $^1$H NMR: $\delta$ 0.05 (s, 6H, $(CH_3)_2SiO$), 0.73 (ddd, $J$ = 3.8, 11.5, 11.5, 1H, H-9α), 0.84 (s, 3H, H-19), 0.88 (s, 12H, $(CH_3)_3CSiO$), H-18), 0.96 (ddd, $J$ = 4.2, 12.7, 12.7, 1H, H-1α), 1.01 (dddd, $J$ = 5.4, 11.5, 11.5, 11.5, 1H, H-7α), 1.02 (dd, $J$ = 5.7, 11.5, 1H, H-14α), 1.10 (m, 1H, H-5α), 1.3−1.4 (m, 1H, H-6α), 1.33 (m, 1H, H-6*β*), 1.34 (m, 2H, H-4*β*, H-11*β*), 1.37 (m, 1H, H-12α), 1.45 (m, 1H, H-4α), 1.45 (m, 1H, H-2*β*), 1.62 (m, 1H, H-11α), 1.68 (m, 1H, H-1*β*), 1.69 (m, 1H, H-2α), 1.74 (dddd, $J$ = 3.8, 11.5, 11.5, 11.5, 1H, H-8*β*), 1.94 (dddd, $J$ = 11.5, 3.7, 3.7, 3.7, 1H, H-7*β*), 1.99 (ddd, $J$ = 2.4, 4.6, 12.8, 1H, H-12*β*), 2.13 (s, 3H, H-21), 2,0.19 (ddd, $J$ = 9.4, 9.6, 15, 1H, H-16), 2.23 (ddd, $J$ = 2.5, 9.4, 15, 1H, H-16′), 2.46 (dd, $J$ = 9.4, 9.4, 1H, H-17α), 3.56 (dddd, $J$ = 4.6, 4.6, 10.8, 10.8, 1H, H-3α), 4.29 (ddd, $J$ = 2.5, 5.7, 9.6, 1H, H-15α). 75-MHz $^{13}$C NMR: $\delta$ −4.82 (2C), 12.11, 15.79, 18.04, 20.94, 25.76 (3C), 28.35, 31.20, 31.46, 35.55, 35.66, 37.04, 38.43, 40.46, 43.72, 45.02, 54.64, 60.95, 63.88, 70.51, 72.00, 208.78. IR (cm$^{-1}$): 2931, 2856, 1701. Mass spectrum *m*/*e* (PCI: isobutane): 431 ($M^+$ − 17), 299 ($M^+$ − 150, 100). Anal. Calcd for $C_{27}H_{48}O_3Si\cdot 0.2H_2O$: C, 71.69; H, 10.78. Found: C, 71.68; H, 10.79. Mp = 200−201 °C. $[\alpha]^{25}_D$ +36 ($c$ = 1, $CHCl_3$).

**3*β*-[(*tert*-Butyldimethylsilyl)oxy]-15*β*-hydroxy-24-nor-5α-chol-20-ene-23-nitrile (26).** To a suspension of NaH (washed 3× with petroleum ether) (83 mg, 3.46 mmol) in THF (4 mL) at rt was added dropwise diethyl cyanomethylphosphonate (0.56 mL, 3.46 mmol). The mixture was stirred at rt for 1 h. A solution of **25** (575 mg, 1.22 mmol) in THF (4 mL) was then added dropwise, and the mixture was stirred at rt for 12 h. Another 3 equiv of ylide was then added, and the reaction mixture was stirred for an additional 12 h. It was then quenched with a saturated $NH_4Cl$ solution. The aqueous layer was extracted with EtOAc, and the combined organic layers were dried over $MgSO_4$ and condensed under vacuum. Purification of the residue by flash chromatography on silica gel (12/1 hexane EtOAc) gave **26** as a white solid (506 mg, 88%). 500-MHz $^1$H NMR: $\delta$ 0.05 (s, 6H, $(CH_3)_2SiO$), 0.71 (ddd, $J$ = 3.8, 12.1, 12.1, 1H, H-9α), 0.83 (s, 3H, H-18), 0.84 (s, 3H, H-19), 0.88 (s, 9H, $(CH_3)_3CSiO$)), 0.95 (ddd, $J$ = 3.8, 12.8, 12.8, 1H, H-1α), 0.98 (dd, $J$ = 5.7, 12.1, 1H, H-14α), 1.01 (dddd, $J$ = 5.4, 13.4, 13.4, 13.4, 1H, H-7α), 1.10 (m, 1H, H-5α), 1.16 (ddd, $J$ = 3.8, 12.8, 12.8, 1H, H-12α), 1.29 (m, 1H, H-11*β*), 1.3−1.4 (m, 1H, H-6α), 1.31 (m, 1H, H-6*β*), 1.34 (m, 1H, H-4*β*), 1.45 (m, 2H, H-4α, H-2*β*), 1.58 (dddd, $J$ = 13.4, 3.8, 3.8, 3.8, 1H, H-11α), 1.68 (m, 1H, H-1*β*), 1.69 (m, 1H, H-2α), 1.73 (m, 1H, H-8*β*), 1.78 (m, 2H, H-16*β*, H-12*β*), 1.89 (dddd, $J$ = 13.4, 3.2, 3.2, 3.2, 1H, H-7*β*), 2.09 (s, 3H, H-21), 2.13 (dd, $J$ = 9.6, 9.6, 1H, H-17α), 2.30 (ddd, $J$ = 16, 9.6, 9.6, 1H, H-16α), 3.55 (dddd, $J$ = 5.1, 5.1, 10.8, 10.8, 1H, H-3α), 4.32 (ddd, $J$ = 2.5, 5.7, 9.6, 1H, H-15α), 5.18 (s, 1H, H-22). 75-MHz $^{13}$C NMR: $\delta$ −4.80 (2C), 12.14, 15.34, 18.08, 20.87, 22.49, 25.78 (3C), 28.33, 31.47, 31.73, 35.57, 37.00, 37.84, 38.41, 39.86, 44.37, 45.00, 54.73, 58.37, 60.78, 70.26, 71.98, 96.01, 117.54, 164.74. IR (cm$^{-1}$): 3494, 2932, 2856, 1618. Mass spectrum *m*/*e* (PCI:isobutane): 472 ($M^+$), 133 ($M^+$ − 339, 100). Anal. Calcd for $C_{29}H_{49}O_2NSi$: C, 73.83; H, 10.47. Found: C, 73.96; H, 10.55. Mp (°C): 193−194. $[\alpha]^{25}_D$ −7 ($c$ = 1, $CHCl_3$).

**3*β*-[(*tert*-Butyldimethylsilyl)oxy]-15*β*-hydroxy-5α-cholest-20-en-23-one (27).** To a solution of **26** (375 mg, 0.8 mmol) in benzene (7 mL) at rt was added a 2 M solution of isobutylmagnesium bromide in ether (2 mL). The reaction mixture was then brought to reflux and stirred for 4 h. After cooling, it was quenched with a saturated $NH_4Cl$ solution. The aqueous layer was extracted with EtOAc, and the combined organic layers were dried over $MgSO_4$ and condensed under vacuum. Purification of the residue by flash chromatography on silica gel (3/1 hexane EtOAc) gave **27** as a white solid (373 mg, 88%). 500-MHz $^1$H NMR: $\delta$ 0.05 (s, 6H, $(CH_3)_2SiO$), 0.72 (ddd, $J$ = 4.3, 12.4, 12.4, 1H, H-9α), 0.82 (s, 3H, H-18), 0.84 (s, 3H, H-19), 0.88 (s, 9H, $(CH_3)_3CSiO$), 0.92 (d, $J$ = 7, 6H, H-26, H-27), 0.95 (m, 1H, H-1α), 1.00 (dd, $J$ = 5.7, 11, 1H, H-14α), 1.03 (dddd, $J$ = 5.4, 11, 11, 11, 1H, H-7α), 1.10 (m, 1H, H-5α), 1.17 (ddd, $J$ = 3.4, 11.9, 11.9, 1H, H-12α), 1.28 (m, 1H, H-11*β*), 1.3−1.4 (m, 1H, H-6α), 1.31 (m, 1H, H-6*β*), 1.34 (m, 1H, H-4*β*), 1.45 (m, 2H, H-4α, H-2*β*), 1.56 (m, 1H, H-11α), 1.68 (m, 1H, H-1*β*), 1.69 (m, 1H, H-2α), 1.73 (m, 1H, H-8*β*), 1.76 (ddd, $J$ = 11.9, 3.1, 3.1, 1H, H-12*β*), 1.89 (ddd, $J$ = 15.8, 8.7, 2.5, 1H, H-16*β*), 1.91 (dddd, $J$ = 11, 3.2, 3.2, 3.2, 1H, H-7*β*), 2.09 (dd, $J$ = 8.7, 8.7, 1H, H-17α), 2.13 (m, 1H, H-25), 2.15 (s, 3H, H-21), 2.26 (ddd, $J$ = 15.8, 8.7, 8.7, 1H, H-16α), 2.30 (d, $J$ = 7.1, 2H, H-24), 3.55 (dddd, $J$ = 4.8, 4.8, 10.9, 10.9, 1H, H-3α), 4.33 (ddd, $J$ = 2.5, 5.7, 8.7, 1H, H-15α), 6.09 (s, 1H, H-22). 75-MHz $^{13}$C NMR: $\delta$ −4.82 (2C), 12.13, 15.42, 18.04, 20.89, 21.04, 22.47, 25.15, 25.76 (3C), 28.37, 31.34, 31.49, 31.73, 35.55, 37.00, 37.74, 38.43, 40.00, 44.24, 45.00, 53.72, 54.84, 60.42, 60.83, 70.53, 71.98, 124.18, 157.15, 201.63. IR (cm$^{-1}$): 3475, 2932, 1677, 1602. Mass spectrum *m*/*e* (PCI:isobutane): 513 ($M^+$ − 18), 133 ($M^+$ − 398, 100),. Anal. Calcd for $C_{33}H_{58}O_3Si$: C, 74.66; H, 11.01. Found: C, 74.73; H, 11.09. Mp (°C): 164−165. $[\alpha]^{25}_D$ −4 ($c$ = 1, $CHCl_3$).

**(20*R*)-3*β*-[(*tert*-Butyldimethylsilyl)oxy]-15*β*-hydroxy-5α-cholestan-23-one and (20*S*)-3*β*-[(*tert*-Butyldimethylsilyl)oxy]-15*β*-hydroxy-5α-cholestan-23-one (28).** A solution of 3*β*-[(*tert*-butyldimethylsilyl)oxy]-15*β*-hydroxy-5α-cholest-20-en-23-one (212 mg, 0.4 mmol) in 50/1 dioxane/AcOH (10 mL) was added to a flask containing $PtO_2$ (21 mg). The reaction vessel was then fitted with a balloon filled with hydrogen, and the mixture was stirred for 4.5 h at rt. It was then filtered through a pad of Celite. After concentration in vacuo, the residue was subjected to column chromatography (silica gel) using a 3/1 mixture of hexane/EtOAc as the eluent to give a 1/1 mixture of (20*R*) and (20*S*) **28** as a white solid (191 mg, 90%). IR (cm$^{-1}$): 2933, 2857, 1707. Mass spectrum *m*/*e* (PCI: isobutane): 515 ($M^+$ − 18), 383 ($M^+$ − 150), 133 ($M^+$ − 400, 100). Anal. Calcd for $C_{33}H_{60}O_3Si$: C, 74.37; H, 11.34. Found: C, 74.16; H, 11.34.

**(20*R*)-3*β*-[(*tert*-Butyldimethylsilyl)oxy]-5α-cholestane-15,23-dione (29a) and (20*S*)-3*β*-[(*tert*-Butyldimethylsilyl)-oxy]-5α-cholestane-15,23-dione (29b).** To a solution of (20*R*)-3*β*-[(*tert*-butyldimethylsilyl)oxy]-15*β*-hydroxy-5α-cholestan-23-one and (20*S*)-3*β*-[(*tert*-butyldimethylsilyl)oxy]-15*β*-5α-hydroxycholestan-23-one (163 mg, 0.3 mmol) in $CH_2Cl_2$ (3 mL) containing some Celite was added PCC (135 mg, 0.6 mmol) in one portion. The reaction mixture was stirred at rt for 1 h. It was then filtered through a pad of Celite. After concentration in vacuo, the residue was subjected to column chromatography (silica gel) using a 4/1 mixture of hexane/EtOAc as the eluent to give a 1/1 mixture of **29a** and **29b** as a white solid (136 mg, 86%). IR (cm$^{-1}$): 2933, 2857, 1735, 1707. Mass spectrum *m*/*e* (PCI:isobutane): 531 ($M^+$, 100), 399 ($M^+$ − 132), 133 ($M^+$ −

398, 100). Anal. Calcd for $C_{33}H_{58}O_3Si$: C, 74.66; H, 11.01. Found: C, 74.73; H, 11.09.

**3*β*-[(*tert*-Butyldimethylsilyl)oxy]-23*β*-hydroxy-16*β*,23-cyclo-5α,14*β*-cholestan-15-one (30).** To a solution of **29a** and **29b** (120 mg, 0.23 mmol) in ethanol (7 mL) and THF (2 mL) was added an aqueous solution of NaOH (0.2 mL, 2 N). The reaction mixture was stirred at rt for 17 h before being neutralized by 10% HCl. It was then evaporated to dryness, and the residue was dissolved in $CHCl_3$ and dried. Purification by flash chromatography (6/1 EtOAc/hexane) afforded **30** (60 mg, >95%) and the recovered unnatural epimer **29b** (60 mg). **30**: 500-MHz $^1$H NMR: $\delta$ 0.05 (s, 6H, $(CH_3)_2SiO$), 0.74 (s, 3H, H-19), 0.88 (s, 9H, $(CH_3)_3CSiO$), 0.89 (m, 1H, H-9α), 0.91 (m, 1H, H-1α), 0.95 (d, $J$ = 7, 3H, H-26), 0.96 (d, $J$ = 7, 3H, H-27), 1.02 (m, 1H, H-12α), 1.09 (d, $J$ = 6.5, 3H, H-21), 1.12 (s, 3H, H-18), 1.17 (m, 1H, H-5α), 1.19 (m, 1H, H-11*β*), 1.2−1.4 (m, 1H, H-6α), 1.21 (m, 1H, H-6*β*), 1.27 (m, 1H, 22α), 1.32 (m, 1H, H-4*β*), 1.39 (m, 2H, H-2*β*, H-7*β*), 1.42 (m, 1H, H-12*β*), 1.47 (m, 1H, H-4α), 1.49 (dd, $J$ = 6.5, 15, 1H, H-24), 1.57−1.64 (m, 1H, H-11-α), 1.59 (m, 1H, H-8*β*), 1.64 (m, 2H, H-1*β*, H-2α), 1.68 (dd, $J$ = 6.5, 15, 1H, H-24′), 1.72 (dd, $J$ = 9.6, 9.6, 1H, H-17α), 1.86 (ddqq, $J$ = 6.5, 6.5, 7, 7, 1H, H-25), 1.94 (dd, $J$ = 5.7, 12.8, 1H, H-22*β*), 2.09 (dd, $J$ = 2.6, 3.8, 1H, H-14*β*), 2.27 (dddq, $J$ = 5.7, 9.6, 12.2, 6.5, 1H, H-20*β*), 2.47 (dddd, $J$ = 4.5, 12.8, 12.8, 12.8, 1H, H-7α), 2.60 (d, $J$ = 9.6, 1H, H-16α), 3.54 (dddd, $J$ = 4.5, 4.5, 11.5, 11.5, 1H, H-3α). 75-MHz $^{13}$C NMR: $\delta$ −4.84 (2C), 12.01, 18.09, 19.70, 20.29, 21.06, 24.35, 24.46, 24.55, 25.80 (3C), 28.72, 28.85, 31.58, 32.68, 34.22, 35.32, 36.85, 38.06, 38.56, 38.75, 44.03, 47.51, 50.73, 51.92, 56.85, 57.42, 62.92, 72.07, 81.97, 220.66. IR (cm$^{-1}$): 2931, 2858, 1720. Mass spectrum *m*/*e* (PCI:isobutane): 513 ($M^+$ − 18, 100), 381 ($M^+$ − 150). Anal. Calcd for $C_{33}H_{58}O_3Si$: C, 74.66; H, 11.01. Found: C, 74.39; H, 10.94. Mp (°C): 55−56. $[\alpha]^{25}_D$ −42 ($c$ = 1, $CHCl_3$).

**3*β*-[(*tert*-Butyldimethylsilyl)oxy]-23-nor-5α-chol-20-en-15*β*-ol (31).** To a solution of methyltriphenylphosphonium bromide (1.53 g, 4.28 mmol) in THF (5 mL) cooled to 0 °C was added a solution of BuLi in hexanes (2.7 mL, 4.28 mmol). The mixture was stirred at 0 °C for 15 min, warmed to rt, and stirred for an additional 20 min. A solution of **25** (875 mg, 1.95 mmol) in THF (5 mL) was added dropwise at rt, and the resulting solution was then refluxed for 3 h. After being cooled to rt, it was quenched with a saturated $NH_4Cl$ solution. The aqueous layer was extracted with EtOAc, and the combined organic layers were dried over $MgSO_4$ and condensed under vacuum. Purification of the residue by flash chromatography on silica gel (4/1 hexane EtOAc) gave **31** as a white solid (630 mg, 73%). 500-MHz $^1$H NMR: $\delta$ 0.05 (s, 6H, $(CH_3)_2SiO$), 0.70 (ddd, $J$ = 4.1, 10.6, 12.5, 1H, H-9α), 0.81 (s, 3H, H-18), 0.83 (s, 3H, H-19), 0.88 (s, 9H, $(CH_3)_3CSiO$), 0.94 (dd, $J$ = 5.7, 11.5, 1H, H-14α), 0.95 (m, 1H, H-1α), 1.02 (dddd, $J$ = 5.4, 12.7, 12.7, 12.7, 1H, H-7α), 1.10 (m, 1H, H-5α), 1.13 (ddd, $J$ = 4, 12.7, 12.7, 1H, H-12α), 1.24−1.38 (m, 1H, H-6α), 1.29 (m, 1H, H-11*β*), 1.31 (m, 1H, H-6*β*), 1.34 (m, 1H, H-4*β*), 1.44 (m, 1H, H-4α), 1.45 (m, 1H, H-2*β*), 1.54 (m, 1H, H-11α), 1.68 (m, 1H, H-1*β*), 1.69 (m, 1H, H-2α), 1.71 (m, 1H, H-8*β*), 1.76 (s, 3H, H-21), 1.81 (m, 1H, H-12*β*), 1.82 (m, 1H, H-16*β*), 1.92 (dddd, $J$ = 12.7, 3.5, 3.5, 3.5, 1H, H-7*β*), 1.94 (dd, $J$ = 7.3, 7.3, 1H, H-17α), 2.25 (ddd, $J$ = 14.6, 7.9, 7.9, 1H, H-16α), 3.55 (dddd, $J$ = 4.6, 4.6, 10.9, 10.9, 1H, H-3α), 4.28 (ddd, $J$ = 2.4, 5.7, 7.9, 1H, H-15α), 4.74 (s, 1H, H-22), 4.87 (s, 1H, H-22′). 75-MHz $^{13}$C NMR: $\delta$ −4.78 (2C), 12.18, 15.25, 18.09, 21.02, 24.36, 25.80 (3C), 28.48, 31.44, 31.62, 31.81, 35.60, 37.09, 38.47, 38.51, 40.22, 42.77, 45.11, 54.97, 57.26, 60.70, 70.71, 72.09, 111.23, 144.89. IR (cm$^{-1}$): 2932, 2857, 1640. Mass spectrum *m*/*e* (PCI: isobutane): 429 ($M^+$ − 18), 297 ($M^+$ − 150, 100). Anal. Calcd for $C_{28}H_{50}O_2Si$: C, 75.27; H, 11.28. Found: C, 75.15; H, 11.30. Mp (°C): 139−140. $[\alpha]^{25}_D$ −16 ($c$ = 1, $CHCl_3$).

**3*β*-[(*tert*-Butyldimethylsilyl)oxy]-23-nor-5α-cholane-15*β*,22-diol (32).** To a nitrogen-purged flask containing borane−methyl sulfide complex (0.38 mL, 4.07 mmol) cooled to 0 °C was added cyclohexene (0.82 mL, 8.14 mmol) dropwise. The mixture was stirred at 0 °C for 30 min and then diluted with THF (6 mL). A solution of **31** (605 mg, 1.35 mmol) in THF (6 mL) was then added dropwise, and the reaction mixture was stirred at 0 °C for 24 h. EtOH (3 mL), 6 N NaOH (1 mL), and 30% $H_2O_2$ (2 mL) were then added successively at 0 °C. The reaction mixture was then warmed to rt and stirred for 24 h. The organic layer was then separated and dried over $MgSO_4$ and condensed under vacuum. Purification of the residue by flash chromatography on silica gel (2/1 hexane EtOAc) gave **32** as a white solid (495 mg, 79%). 500-MHz $^1$H NMR: $\delta$ 0.05 (s, 6H, $(CH_3)_2SiO$), 0.68 (ddd, $J$ = 4.1, 10.5, 12.3, 1H, H-9α), 0.83 (s, 3H, H-19), 0.86 (dd, $J$ = 5.7, 11.4, 1H, H-14α), 0.88 (s, 9H, $(CH_3)_3CSiO$), 0.95 (s, 3H, H-18), 0.95 (m, 1H, H-1α), 1.00 (dddd, $J$ = 5.4, 12.7, 12.7, 12.7, 1H, H-7α), 1.04 (d, $J$ = 7, 3H, H-21), 1.10 (m, 1H, H-5α), 1.13 (m, 1H, H-12α), 1.16 (dd, $J$ = 8.7, 10.1, 1H, H-17α), 1.24−1.40 (m, 1H, H-6α), 1.30 (m, 2H, H-6*β*, H-11*β*), 1.34 (m, 1H, H-4*β*), 1.37 (m, 1H, H-16*β*), 1.44 (m, 1H, H-4α), 1.45 (m, 1H, H-2*β*), 1.50 (m, 1H, H-11α), 1.68 (m, 2H, H-1*β*, H-20), 1.69 (m, 1H, H-2α), 1.71 (m, 1H, H-8*β*), 1.88 (dddd, $J$ = 12.7, 3.5, 3.5, 3.5, 1H, H-7*β*), 1.91 (ddd, $J$ = 12.8, 3.3, 3.3, 1H, H-12*β*), 2.37 (ddd, $J$ = 16.5,0.7.9, 7.9, 1H, H-16α), 3.40 (dd, $J$ = 6.5, 10.5, 1H, H-22), 3.55 (dddd, $J$ = 4.8, 4.8, 10.8, 10.8, 1H, H-3α), 3.64 (dd, $J$ = 3.2, 10.5, 1H, H-22′), 4.28 (ddd, $J$ = 2.4, 5.7, 7.9, 1H, H-15α). 75-MHz $^{13}$C NMR: $\delta$ −4.78 (2C), 12.14, 14.62, 16.64, 18.10, 20.93, 25.80 (3C), 28.46, 31.29, 31.44, 31.81, 35.53, 37.06, 38.17, 38.49, 40.31, 41.17, 42.21, 45.04, 52.66, 54.78, 60.74, 67.83, 70.48, 72.13. IR (cm$^{-1}$): 2932, 2857. Mass spectrum *m*/*e* (PCI:isobutane): 447 ($M^+$ − 18), 315 ($M^+$ − 150, 100). Anal. Calcd for $C_{28}H_{52}O_3Si{\cdot}0.8H_2O$: C, 70.18; H, 11.27. Found: C, 70.17; H, 11.02. Mp (°C): 187−188. $[\alpha]^{25}_D$ −12 ($c$ = 1, $CHCl_3$).

**3*β*-[(*tert*-Butyldimethylsilyl)oxy]-15*β*-hydroxy-24-nor-5α-cholane-23-nitrile (34).** To a solution of TsCl (292 mg, 1.55 mmol) in pyridine (3 mL) at 0 °C was added a solution of **32** (480 mg, 1.03 mmol) in pyridine (4 mL). The reaction mixture was stirred for 24 h at 0 °C. It was then poured into water and extracted with EtOAc. The combined organic layers were dried over $MgSO_4$ and condensed under vacuum. The crude tosylate was obtained (572 mg, 90%) and used without further purification. It was dissolved in DMSO (3 mL) and THF (1 mL). KCN (120 mg, 1.85 mmol) was added, and the reaction mixture was warmed to 60 °C and stirred for 5 h. After cooling the reaction mixture to rt, it was diluted with a 3/1 mixture of hexane and EtOAc and plugged through a pad of silica gel. Further purification by flash chromatography (eluent 3/1 hexane/EtOAc) gave **34** as a white solid (368 mg, 84%). 500-MHz $^1$H NMR: $\delta$ 0.05 (s, 6H, $(CH_3)_2SiO$), 0.69 (ddd, $J$ = 3.9, 10.5, 12.4, 1H, H-9α), 0.84 (s, 3H, H-19), 0.88 (s, 9H, $(CH_3)_3CSiO$), 0.92 (dd, $J$ = 5.7, 11.4, 1H, H-14α), 0.95 (m, 1H, H-1α), 0.96 (s, 3H, H-18), 1.02 (dddd, $J$ = 5.4, 12.7, 12.7, 12.7, 1H, H-7α), 1.10 (m, 1H, H-5α), 1.14 (m, 1H, H-12α), 1.16 (d, $J$ = 7, 3H, H-21), 1.20−1.38 (m, 1H, H-6α), 1.24 (m, 1H, H-17α), 1.31 (m, 2H, H-6*β*, H-11*β*), 1.32 (m, 1H, H-16*β*), 1.34 (m, 1H, H-4*β*), 1.44 (m, 1H, H-4α), 1.45 (m, 1H, H-2*β*), 1.53 (m, 1H, H-11α), 1.68 (m, 1H, H-1*β*), 1.69 (m, 1H, H-2α), 1.71 (dddd, $J$ = 3.6, 11.4, 11.4, 11.4, 1H, H-8*β*), 1.87 (dddd, $J$ = 12.7, 3.5, 3.5, 3.5, 1H, H-7*β*), 1.91 (m, 1H, H-20), 1.92 (m, 1H, H-12*β*), 2.27 (dd, $J$ = 6.6, 16.7, 1H, H-22), 2.35 (dd, $J$ = 3.9, 16.7, 1H, H-22′), 2.39 (ddd, $J$ = 16.5, 7.9, 7.9, 1H, H-16α), 3.55 (dddd, $J$ = 4.8, 4.8, 10.8, 10.8, 1H, H-3α), 4.24 (ddd, $J$ = 2, 5.7, 7.9, 1H, H-15α). 75-MHz $^{13}$C NMR: $\delta$ −4.82 (2C), 12.11, 14.56, 18.07, 19.20, 20.83, 24.64, 25.78 (3C), 28.38, 31.21, 31.34, 31.75, 32.93, 35.49, 37.00, 38.45, 40.40, 40.89, 42.22, 44.96, 54.58, 54.76, 60.77, 70.04, 72.03, 118.80. IR (cm$^{-1}$): 2932, 2857, 2254. Mass spectrum *m*/*e* (PCI:isobutane): 324 ($M^+$ − 150, 100). Anal. Calcd for $C_{29}H_{51}O_2NSi$: C, 73.51; H, 10.85. Found: C, 73.52; H, 10.91. Mp (°C): 172−173. $[\alpha]^{25}_D$ −9 ($c$ = 1, $CHCl_3$).

**3*β*-[(*tert*-Butyldimethylsilyl)oxy]-15*β*-hydroxy-5α-cholestan-23-one (35).** To a solution of **34** (350 mg, 0.74 mmol) in benzene (7 mL) was added at rt a 2 M solution of isobutylmagnesium bromide in ether (1.84 mL). The reaction mixture was then brought to reflux and stirred for 4 h. After cooling to rt, it was quenched with a saturated $NH_4Cl$ solution. The aqueous layer was extracted with EtOAc, and the combined organic layers were dried over $MgSO_4$ and condensed under vacuum. Purification of the residue by flash chromatography on silica gel (6/1 hexane EtOAc) gave **35** as a white solid (321 mg, 82%). 500-MHz $^1$H NMR: $\delta$ 0.05 (s, 6H, $(CH_3)_2SiO$), 0.67

(ddd, $J$ = 3.8, 10.6, 12.4, 1H, H-9α), 0.83 (s, 3H, H-19), 0.87 (m, 1H, H-14α), 0.88 (s, 9H, $(CH_3)_3CSiO$), 0.90 (d, $J$ = 6.5, 3H, H-26), 0.91 (d, $J$ = 6.5, 3H, H-27), 0.92 (d, $J$ = 6, 3H, H-21), 0.95 (m, 1H, H-1α), 0.97 (s, 3H, H-18), 0.99 (m, 1H, H-7α), 1.09 (m, 2H, H-12α, H-17α), 1.10 (m, 1H, H-5α), 1.24−1.38 (m, 1H, H-6α), 1.31 (m, 2H, H-6*β*, H-11*β*), 1.33 (m, 1H, H-16*β*), 1.34 (m, 1H, H-4*β*), 1.44 (m, 1H, H-4α), 1.45 (m, 1H, H-2*β*), 1.50 (m, 1H, H-11α), 1.67 (m, 1H, H-1*β*), 1.69 (m, 1H, H-2α), 1.72 (dddd, $J$ = 3.6, 12.4, 12.4, 12.4, 1H, H-8*β*), 1.89 (dddd, $J$ = 12.4, 3.6, 3.6, 3.6, 1H, H-7*β*), 1.92 (ddd, $J$ = 12.4, 3.3, 3.3, 1H, H-12*β*), 2.11 (m, 1H, H-22), 2.12 (m, 1H, H-20), 2.13 (m, 1H, H-25), 2.24 (d, $J$ = 7, 2H, H-24), 2.33 (ddd, $J$ = 15, 7.9, 7.9, 1H, H-16α), 2.42 (d, $J$ = 12.4, 1H, H-22′), 3.55 (dddd, $J$ = 4.9, 4.9, 10.8, 10.8, 1H, H-3α), 4.19 (dd, $J$ = 5.7, 5.7, 1H, H-15α). 75-MHz $^{13}$C NMR: $\delta$ −4.78 (2C), 12.14, 14.60, 18.09, 19.62, 20.91, 22.40, 22.51, 24.36, 25.80 (3C), 28.46, 31.25, 31.40, 31.81, 32.05, 35.53, 37.05, 38.49, 40.89, 41.20, 42.28, 45.03, 50.26, 52.31, 54.75, 56.27, 61.01, 70.25, 72.10, 211.32. IR (cm$^{-1}$): 2933, 2857. Mass spectrum *m/e* (PCI:isobutane): 515 ($M^+$ − 18, 100), 383 ($M^+$ − 150). Anal. Calcd for $C_{33}H_{60}O_3Si$: C, 74.37; H, 11.35. Found: C, 74.29; H, 11.43. Mp (°C): 182−183. $[\alpha]^{25}_D$ −15 ($c$ = 1, $CHCl_3$).

**(20*R*)-3*β*-[(*tert*-Butyldimethylsilyl)oxy]-5α-cholestane-15,23-dione (29a).** To a solution of **35** (140 mg, 0.26 mmol) in $CH_2Cl_2$ (3 mL) containing some Celite was added PCC (135 mg, 0.6 mmol) in one portion. The reaction mixture was stirred at rt for 1 h and then filtered through a pad of Celite. After concentration in vacuo, the residue was subjected to column chromatography (silica gel) using a 4/1 mixture of hexane/EtOAc as the eluent to give pure **29a** as a white solid (124 mg, 90%). 500-MHz $^1$H NMR: $\delta$ 0.05 (s, 6H, $(CH_3)_2SiO$), 0.62 (ddd, $J$ = 3.6, 10.3, 12.2, 1H, H-9α), 0.77 (s, 3H, H-18), 0.80 (s, 3H, H-19), 0.83 (m, 1H, H-7α), 0.88 (s, 9H, $(CH_3)_3CSiO$), 0.90 (d, $J$ = 5, 3H, H-26), 0.92 (d, $J$ = 5, 3H, H-27), 0.93 (m, 1H, H-1α), 0.99 (d, $J$ = 6.5, 3H, H-21), 1.07 (m, 1H, H-5α), 1.22−1.40 (m, 2H, H-6α, H-12α), 1.27 (m, 1H, H-6*β*), 1.28 (m, 1H, H-11*β*), 1.31 (m, 1H, H-4*β*), 1.43 (m, 1H, H-4α), 1.44 (m, 1H, H-2*β*), 1.55 (m, 1H, H-11α), 1.61 (m, 1H, H-17α), 1.62−1.68 (m, 1H, H-12*β*), 1.65 (m, 1H, H-1*β*), 1.69 (m, 1H, H-2α), 1.71 (dddd, $J$ = 3.6, 12.4, 12.4, 12.4, 1H, H-8*β*), 1.75 (dd, $J$ = 9.8, 18, 1H, H-16*β*), 2.06−2.10 (m, 1H, H-14α), 2.10 (m, 1H, H-20), 2.13 (m, 1H, H-25), 2.19 (dd, $J$ = 9.6, 16.2, 1H, H-22), 2.24 (d, $J$ = 7, 2H, H-24), 2.33 (dd, $J$ = 3, 16.2, 1H, H-22′), 2.36 (dd, $J$ = 8.5, 18, 1H, H-16α), 2.64 (dddd, $J$ = 12.2, 3.6, 3.6, 3.6, 1H, H-7*β*), 3.55 (dddd, $J$ = 4.6, 4.6, 10.9, 10.9, 1H, H-3α). 75-MHz $^{13}$C NMR: $\delta$ −4.78 (2C), 12.07, 12.85, 18.09, 20.01, 20.59, 22.36, 22.47, 24.40, 25.80 (3C), 28.14, 30.56, 31.60, 31.75, 31.79, 35.49, 37.05, 38.37, 39.69, 41.63, 42.34, 44.88, 49.78, 51.08, 52.53, 53.94, 65.94, 71.99, 210.47, 215.43. IR (cm$^{-1}$): 2933, 1735, 1707. Mass spectrum *m/e* (PCI: isobutane): 531 ($M^+$, 100), 513 ($M^+$ − 18), 399 ($M^+$ − 132). Anal. Calcd for $C_{33}H_{58}O_3Si$: C, 74.66; H, 11.01. Found: C, 74.53; H, 11.01. Mp (°C): 206−207. $[\alpha]^{25}_D$ +29 ($c$ = 1, $CHCl_3$).

**3*β*-[(*tert*-Butyldimethylsilyl)oxy]-23*β*-hydroxy-16*β*,23-cyclo-5α,14*β*-cholestan-15-one (30).** To a solution of **29a** (120 mg, 0.23 mmol) in ethanol (7 mL) and THF (2 mL) was added an aqueous solution of NaOH (0.2 mL, 2 N). The reaction mixture was stirred at rt for 17 h before being neutralized by 10% HCl. It was then evaporated to dryness, and the residue was dissolved in $CHCl_3$ and dried. Purification by flash chromatography (6/1 EtOAc/hexane) afforded the fully functionalized C/D/E ring system of the pentacyclic steroid **30** (120 mg, 100%).

**3,3-(Ethylenedioxy)-5-androsten-17*β*-ol (36).**[35] Using a procedure described by Paquette,[35] a mixture of 1.0 g (3.50 mmol) of testosterone, **4**, 0.75 g (12.1 mmol) of ethylene glycol, and 13 mg (0.070 mmol) of *p*-toluenesulfonic acid monohydrate in 18 mL of benzene was refluxed for 24 h with continuous azeotropic removal of water and excess ethylene glycol by means of a Dean−Stark trap. The cooled mixture was diluted with 20 mL of EtOAc and washed with saturated brine and saturated aqueous $NaHCO_3$, and dried over anhydrous $Na_2SO_4$. The solvent was removed in vacuo, and the residue was purified by column chromatography on silica gel (2:1 hexanes−EtOAc) to give 0.98 g (85%) of ketal **36**. $[\alpha]^{589}_{Na}$ = −45.2 ($c$ 7.0, $CHCl_3$). Mp: 179−180 °C. 500 MHz $^1$H NMR $\delta$ 5.35 (ddd, $J$ = 4.8, 2.6, 1.9, 1H, C=C*H*CH$_2$), 3.89−3.99 (m, 4H, (C*H*$_2$O)$_2$C), 3.65 (ddd, $J$ = 8.6, 8.6, 6.0, 1H, C*H*OH), 2.57 (ABddd $J_{AB}$ = 14.0, $J$ = 2.9, 2.9, 2.9, 1H, 4-C*H*H), 2.12 (ABd, $J_{AB}$ = 14.0, 2.9, 1H, 4-CH*H*), 2.03−2.10 (m, 1H, 16-C*H*H), 1.98 (ABddd, $J_{AB}$ = 17.5, $J$ = 5.4, 5.4, 2.9, 7-C*H*H), 1.74−1.85 (m, 3H), 1.40−1.70 (m, 7H), 1.03−1.13 (m, 2H), 1.04 (s, 3H, 19-C*H*$_3$), 0.91−0.99 (m, 1H), 0.76 (s, 3H, 18-C*H*$_3$). 75 MHz $^{13}$C NMR $\delta$ 140.4, 122.0, 109.5, 81.8, 64.4, 64.1, 51.2, 49.7, 42.6, 41.7, 36.6, 36.4, 36.2, 31.8, 31.2, 30.9, 30.3, 23.3, 20.4, 18.7, 10.8. IR (cm$^{-1}$) 3474, 2950, 1460. Mass spectrum (CI) *m/e* 333 (M + 1), 315 (M − OH). Anal. Calcd for $C_{21}H_{32}O_3 \cdot 0.3xH_2O$: C, 74.65; H, 9.72. Found: C, 74.44; H, 9.64.

**3,3-(Ethylenedioxy)-17*β*-methoxy-5-androstene (37).** Using a procedure reported by Heathcock,[40] a solution of 950 mg (2.85 mmol) of **36** in 10 mL of dry THF was added dropwise to a stirred suspension of 490 mg (4.30 mmol) of 35% KH (rendered oil free) in 14 mL of THF. The mixture was stirred for 30 min, and 610 mg (4.30 mmol) of $CH_3I$ was added dropwise. After stirring overnight at rt, the reaction was quenched with water, followed by removal of most of the solvent in vacuo. The aqueous solution was extracted three times with 20 mL portions of EtOAc. The combined extracts were washed with brine and dried over anhydrous $Na_2SO_4$. Evaporation of the solvent yielded a solid which was purified by chromatography (30% EtOAc/hexane) to give 940 mg (95%) of ether **37**. $[\alpha]^{589}_{Na}$ = −47.9 ($c$ 7.0, $CHCl_3$). Mp: 163−165 °C. 500 MHz $^1$H NMR $\delta$ 5.34 (ddd, $J$ = 4.5, 2.6, 1.9, 1H, C=C*H*), 3.89−3.99 (m, 4H, (C*H*$_2$O)$_2$C), 3.35 (s, 3H, CHOC*H*$_3$), 3.24 (dd, $J$ = 8.6, 8.0, 1H, C*H*OCH$_3$), 2.57 (ABddd $J_{AB}$ = 14.3, $J$ = 2.9, 2.9, 2.9, 1H, 4-C*H*H), 2.12 (ABd, $J_{AB}$ = 14.3, $J$ = 2.9, 1H, 4-C*H*H), 1.91−2.06 (m, 3H), 1.73−1.83 (m, 2H), 1.43−1.70 (m, 7H), 1.16−1.37 (m, 3H), 1.06 (ddd, $J$ = 12.1, 11.2, 5.1, 1H), 1.03 (s, 3H, 19-C*H*$_3$), 0.97 (ddd, $J$ = 12.4, 10.8, 7.0, 1H), 0.77 (s, 3H, 18-C*H*$_3$). 75 MHz $^{13}$C NMR $\delta$ 140.5, 122.0, 109.6, 90.8, 64.4, 64.1, 57.8, 51.5, 49.7, 42.6, 41.6, 37.8, 36.5, 36.2, 31.6, 31.2, 30.9, 27.5, 23.2, 20.5, 18.6, 11.2. IR (cm$^{-1}$) 2939, 2874, 1670. Mass spectrum (CI) *m/e* 347 (M + 1), 315 (M − OCH$_3$). Anal. Calcd for $C_{22}H_{34}O_3$: C, 76.26; H, 9.89. Found: C, 76.32; H, 9.88.

**3,3-(Ethylenedioxy)-17*β*-methoxy-5-androsten-7-one (38).** Using a procedure described by Kato,[41] a mixture of 920 mg (2.65 mmol) of **37** and 10.4 g (40.0 mmol) of Collins reagent in 30 mL of dry $CH_2Cl_2$ was stirred at rt for 12 h and then poured into aqueous NaCl. The product was extracted with $CH_2Cl_2$, and the extracts were washed with water, aqueous copper sulfate, and brine and dried. After removal of the solvent, the residue was purified on a silica gel column using 20% EtOAc/hexane as the eluent to give 766 mg (80%) of enone **38**. $[\alpha]^{589}_{Na}$ = −73.4 ($c$ 7.0, $CHCl_3$). Mp: 203−204 °C. 500 MHz $^1$H NMR $\delta$ 5.66 (d, $J$ = 1.9, 1H, C=C*H*), 3.90−4.00 (m, 4H, (C*H*$_2$O)$_2$C), 3.34 (s, 3H, CHOC*H*$_3$), 3.23 (dd, $J$ = 8.9, 7.3, 1H, C*H*OCH$_3$), 2.68 (ABd, $J_{AB}$ = 14.7, $J$ = 2.2, 1H, 4-C*H*H), 2.37−2.44 (m, 1H), 2.33 (ABd, $J_{AB}$ = 14.7, 3.2, 1H, 4-CH*H*), 2.26 (dd, $J$ = 11.8, 11.2, 1H, 8-C*H*), 2.00−2.11 (m, 1H, 15-C*H*H), 1.83−1.95 (m, 3H), 1.71−1.77 (m, 1H), 1.43−1.67 (m, 6H), 1.33 (ddd, $J$ = 11.2, 11.2, 7.0, 1H), 1.21 (s, 3H, 19-C*H*$_3$), 1.15 (ddd, $J$ = 12.2, 12.2, 3.2, 1H), 0.77 (s, 3H, 18-C*H*$_3$). 75 MHz $^{13}$C $\delta$ 201.9, 165.1, 126.7, 109.0, 89.9, 64.5, 64.4, 57.7, 49.7, 45.1, 45.0, 43.2, 41.6, 38.2, 36.6, 35.5, 30.9, 27.5, 25.55, 20.7, 16.7, 11.4. IR (cm$^{-1}$) 2942, 1664. Mass spectrum (CI) *m/z* 361 (M+1), 329 (M − OCH$_3$). Anal. Calcd for $C_{22}H_{32}O_4$: C, 73.30; H, 8.95. Found: C, 73.23; H, 8.92.

**3,3-(Ethylenedioxy)-17*β*-methoxy-androstan-7-one (39).** Using a procedure described by Kato,[41] small pieces of lithium metal (190 mg, 27.0 mmol) were added to liquid ammonia (50 mL, freshly distilled from sodium metal) and the mixture was stirred for a few minutes under nitrogen. A solution of **38** (490 mg, 1.36 mmol) in dry THF (7 mL) was added dropwise, and stirring was continued at −60 °C for 30 min. An excess of

(40) Lodge, E. P.; Heathcock, C. H. *J. Am. Chem. Soc.* **1987**, *109*, 3353.

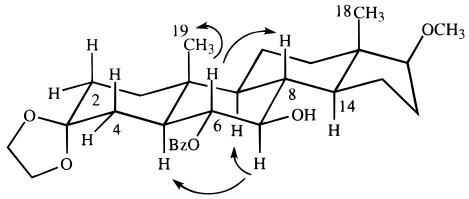
(41) Kato, M.; Kurihara, H.; Yoshikoshi, A. *J. Chem. Soc., Perkin Trans. 1* **1979**, 2740.

$NH_4Cl$ (1.50 g, 35 mmol) was added cautiously, and the stirring was continued while the ammonia was allowed to evaporate. The residue was diluted with water and extracted with EtOAc. The extract was then washed with brine and dried. Evaporation left a white powdery solid which was passed through a silica gel column using hexanes−EtOAc (4:1) to give 470 mg (95%) of ketone **39**. $[\alpha]^{589}_{Na} = -48.1$ (*c* 7.0, $CHCl_3$). Mp: 152−154 °C. 500 MHz $^1$H NMR $\delta$ 3.88−3.95 (m, 4H, $(CH_2O)_2C$), 3.33 (s, 3H, $CHOCH_3$), 3.24 (dd, $J$ = 8.3, 8.3, 1H, $CHOCH_3$), 2.37 (dd, $J$ = 11.5, 11.2, 1H, 8-C*H*), 2.30 (ABd, $J_{AB}$ = 13.7, $J$ = 13.1, 0.6, 1H, 6-C*H*H), 2.17−2.24 (m, 1H, 15-C*H*H), 2.02−2.10 (m, 1H, 16-CH*H*), 2.01 (dd, $J$ = 12.4, 3.5, 1H, 6-CH*H*), 1.81−1.91 (m, 2H), 1.60−1.76 (m, 5H), 1.38−1.55 (m, 4H), 1.10−1.29 (m, 4H), 1.08 (s, 3H, 198-$CH_3$), 0.74 (s, 3H, 18-$CH_3$). 75 MHz$^{13}$C NMR $\delta$ 211.8, 108.7, 89.8, 64.2, 64.1, 57.7, 54.9, 49.5, 45.6, 45.4, 44.0, 42.6, 37.6, 36.6, 35.8, 35.0, 30.9, 27.4, 24.2, 21.4, 11.5, 10.7. IR ($cm^{-1}$) 3052, 2952, 1706. Mass spectrum (CI) *m*/*z* 363(M + 1), 331(M − $OCH_3$). Anal. Calcd for $C_{22}H_{34}O_4$: C, 72.89; H, 9.45. Found: C, 72.78; H, 9.42.

**3,3-(Ethylenedioxy)-7-(trimethylsiloxy)-17β-methoxy-6-androstene (40).** Using a procedure described by Garst,[42] a solution of 0.29 mL (2.04 mmol) of $^i Pr_2NH$ in 3 mL of THF was cooled to −78 °C, and 1.26 mL (2.02 mmol) of 1.6 M *n*-butyllithium in THF was added dropwise. After the addition, the resulting solution was allowed to stir for 30 min at −78 °C. A solution of 370 mg (1.02 mmol) of **39** in 5 mL of THF was added dropwise over 5 min. The resulting solution was stirred at −78 °C for 30 min followed by quenching with 0.26 mL (2.04 mmol) of TMSCl in 0.42 mL (3.06 mmol) of $NEt_3$, warmed to rt, and concentrated on a rotary evaporator. The residue was diluted with water and extracted with EtOAc (30 mL, 3×). The combined extracts were washed with a saturated bicarbonate solution and brine, dried over anhydrous $Na_2SO_4$, and evaporated in vacuo. The residue was passed though a pad of silica gel using 20% EtOAc/hexane, and the solvent was evaporated to give 430 mg (97%) of enol ether **40**. Mp: 196−198 °C. 500 MHz $^1$H NMR $\delta$ 4.39 (dd, $J$ = 1.9, 1.8, 1H, C*H*=C(OTMS)), 3.89−3.97 (m, 4H, $(CH_2O)_2C$), 3.34 (s, 3H, $CHOCH_3$), 3.20 (dd, $J$ = 8.3, 8.3, 1H, $CHOCH_3$), 2.28 (dddd, $J$ = 13.7, 3.5, 3.5, 1.9, 1H), 1.73−2.03 (m, 5H), 1.51−1.68 (m, 3H), 1.36−1.47 (m, 3H), 1.07−1.32 (m, 5H), 0.79 (s, 3H, 19-$CH_3$), 0.73−0.79 (m 1H), 0.77 (s, 3H, 18-$CH_3$), 0.16 (s, 9H, $(CH_3)_3Si$).

**3,3-(Ethylenedioxy)-6α-hydroxy-7β-hydroxy-17β-methoxyandrostane (41).** Using a procedure described by Brown,[43] to a stirred solution of **40** (420 mg, 0.97 mmol) in 8 mL of THF was added 0.97 mL (0.97 mmol) of 1 M $BH_3$·THF in THF dropwise at 0 °C. After stirring at rt for 2 h, the reaction was quenched with ice chips followed by addition of 0.2 mL (3.33 mmol) of 30% aqueous $H_2O_2$ and 1.2 mL of 3 M aqueous KOH. The resulting solution was stirred at rt for 3 h. After the reaction was complete, the solution was diluted with 10 mL of water and extracted with EtOAc (4 × 30 mL). The combined extracts were washed successively with saturated $NaHCO_3$ and brine and dried over anhydrous $Na_2SO_4$. After removing the solvent, the crude product was purified by silica gel chromatography with 50% EtOAc/hexane to give 247 mg (67%) of diol **41**. $[\alpha]^{589}_{Na} = +37.3$ (*c* 7.0, $CHCl_3$). Mp: 171−173 °C. 500 MHz $^1$H NMR $\delta$ 3.88−3.97 (m, 4H, $(CH_2O)_2O$), 3.34 (s, 3H, $CHOCH_3$), 3.23 (obscured ddd, $J$ = 8.6, 8.6, 4.1, 1H, 6-C*H*OH), 3.21 (dd, $J$ = 8.6, 8.6, 1H, 17-C*H*$OCH_3$), 3.12 (ddd, $J$ = 9.6, 9.6, 3.8, 1H, 7-C*H*OH), 1.99−2.07 (m, 3H), 1.96 (ddd, $J$ = 12.4, 2.5, 2.5, 1H), 1.91 (ddd, $J$ = 12.4, 3.5, 3.2, 1H), 1.10−1.71 (m, 13H), 0.87 (s, 3H, 18-$CH_3$), 0.86 (ddd, $J$ = 11.4, 11.4, 4.3, 1H, 14-C*H*). 75 MHz $^{13}$C NMR $\delta$ 109.1, 90.3, 74.8, 64.2, 64.1, 57.7, 51.8, 50.7, 46.6, 43.6, 40.8, 37.7, 36.2, 35.6, 32.0, 30.8, 27.7, 26.0, 20.8, 12.6, 11.5. IR ($cm^{-1}$) 3576, 2952. Mass spectrum (CI) *m*/*z* 381 (M + 1), 363 (M − OH). Anal. Calcd for $C_{22}H_{36}O_5$: C, 69.44; H, 9.54. Found: C, 69.20; H, 9.55.

**3,3-(Ethylenedioxy)-7β-hydroxy-17β-methoxyandrostan-6α-yl Benzoate (42).** A mixture of diol **41** (44 mg, 0.12 mmol), $NEt_3$ (0.086 mL, 0.60 mmol), and DMAP (1.0 mg, 0.008 mmol) in 1.2 mL of $CH_2Cl_2$ was cooled to 0 °C. To this cooled solution was added 0.04 mL (0.36 mmol) of benzoyl chloride dropwise. The resulting solution was then allowed to stir overnight. After the reaction was complete, the reaction was diluted with 50 mL of $CH_2Cl_2$ and was successively washed with saturated $NaHCO_3$ and brine, dried over anhydrous $Na_2SO_4$, and concentrated. Chromatography of the resulting oil on a silica gel column with 20% EtOAc/hexane (1:1) afforded 52 mg (93%) of benzoate **42** as a white solid. $[\alpha]^{589}_{Na} = +35.5$ (*c* 7.0, $CHCl_3$). Mp 82−83 °C. 500 MHz $^1$H NMR $\delta$ 8.06 (ddd, $J$ = 8.3, 2.0, 1.4, 2H, 2,6-Ph*H*), 7.56 (dddd, $J$ = 7.3, 7.0, 1.3, 1.3, 1H, 4-Ph*H*), 7.45 (dddd, $J$ = 8.0, 7.5, 1.6, 1.3, 2H, 3,5-Ph*H*), 5.00 (dd, $J$ = 11.6, 9.0, 1H, 6-C*H*OBz), 3.82−3.94 (m, 4H, $(CH_2O)_2O$), 3.44 (ddd, $J$ = 9.3, 9.3, 6.3, 1H, 7-C*H*OH), 3.34 (s, 3H, $CHOCH_3$), 3.21 (dd, $J$ = 8.3, 8.3, 1H, 17-C*H*$OCH_3$), 1.96−2.04 (m, 1H), 1.93 (ddd, $J$ = 12.6, 3.7, 3.3, 1H), 1.91 (d, $J$ = 5.6, 1H, 7-C*H*OH), 1.10−1.87 (m, 25H), 1.00 (s, 3H, 19-$CH_3$), 0.93 (ddd, $J$ = 11.3, 11.3, 4.0, 1H, 14-C*H*), 0.79 (s, 3H, 18-$CH_3$). 75 MHz $^{13}$C NMR $\delta$ 167.4, 133.2, 130.2, 129.9, 128.5, 108.7, 90.2, 78.5, 77.9, 64.1, 64.0, 57.7, 51.7, 50.7, 45.3, 43.6, 41.7, 37.6, 36.0, 32.3, 30.5, 27.7, 25.9, 20.8, 12.5, 11.6. IR ($cm^{-1}$) 3589, 2953, 1716, 1623. Mass spectrum (CI) *m*/*z* 485 (M + 1), 453, 363 (M − $PhCO_2$), 331. Anal. Calcd for $C_{29}H_{40}O_6 \cdot 2.0xH_2O$: C, 66.09; H, 8.51. Found: C, 66.72; H, 7.60.




| proton (δ) | NOE observations (%) |
|---|---|
| 18-$CH_3$ (0.79) | $OCH_3$ (0.5), 15-H (0.6), 8−H (0.4) |
| 9-H (0.93) | 7-H (4.87), 5-H (9.67), and others |
| 19-$CH_3$ (1.00) | 6-H (3.06), 8-H (4.7) |
| $OCH_3$ (3.34) | 17-H (2.5) |
| 17-H (3.21) | $OCH_3$ (6.2) |
| 6-H (5.00) | 7-H (1.55), OH (4.94), 8-H (5.22), 19-H |
| 7-H (3.44) | 5-H (7.39), OH (6.2), 6-H (1.52), 14-H (2.3), 9-H (4.1) |

**6α-Hydroxy-7β-hydroxy-17β-methoxyandrostan-3-one (43).** A mixture of ketal **41** (150 mg, 0.39 mmol) and *p*-TsOH (1.5 mg, 0.008 mmol) in 2 mL of acetone was stirred at rt for 12 h. The solution was then diluted with 20 mL of water and extracted with EtOAc (4 × 30 mL). The combined organic layers were washed with saturated $NaHCO_3$ and brine, dried, and evaporated in vacuo. The crude product was purified by chromatography with EtOAc/hexane (2/1) to yield 119 mg (90%) of ketone **43**. $[\alpha]^{589}_{Na} = +59.8$ (*c* 7.0, $CHCl_3$). Mp 171−173 °C. 500 MHz $^1$H NMR $\delta$ 3.34 (s, 3H, $CHOCH_3$), 3.31 (ddd, $J$ = 8.6, 8.6, 3.8, 1H, 6-C*H*OH), 3.22 (dd, $J$ = 8.6, 8.3, 1H, 17-C*H*$OCH_3$), 3.14 (ddd, $J$ = 8.6, 8.6, 3.8, 1H, 7-C*H*OH), 2.67 (ABdd, $J_{AB}$ = 15.3, $J$ = 4.2, 2.2, 1H, 4-C*H*H), 2.29−2.43 (m, 4H), 2.22 (dd, $J$ = 14.2, 13.4, 1H, 4-CH*H*), 2.19 (d, $J$ = 4.1, 1H, 6-CHO*H*), 2.00−2.09 (m, 3H), 1.82−1.88 (m, 1H), 1.94 (ddd, $J$ = 12.4, 3.8, 2.9, 1H), 1.33−1,74 (m, 7H), 1.14−1.27 (m, 2H), 1.07 (s, 3H, 19-$CH_3$), 0.88 (ddd, $J$ = 10.8, 10.8, 3.8, 1H, 14-CH), 0.80 (s, 3H, 18-$CH_3$). 75 MHz $^{13}$C NMR $\delta$ 211.8, 90.0, 80.3, 74.8, 57.7, 51.3, 50.5, 49.0, 43.5, 40.5, 39.2, 38.2, 37.5, 35.8, 27.6, 26.0, 21.1, 12.7, 11.6. IR ($cm^{-1}$) 3577, 2949, 1711. Mass spectrum (CI) *m*/*z* 337 (M + 1), 287. Anal. Calcd for $C_{20}H_{32}O_4 \cdot 0.7xH_2O$: C, 68.82; H, 9.64. Found: C, 69.01; H, 9.35.

**3α-Hydroxy-6α-hydroxy-7β-hydroxy-17β-methoxyandrostane (44).** To a solution of ketone **43** (47 mg, 0.14 mmol) in THF at −78 °C was added dropwise 0.49 mL (0.49 mmol) of 1 M L-Selectride as a THF solution. This solution was stirred for 2 h at −78 °C and then allowed to warm to rt (1 h). The reaction mixture was then hydrolyzed with 1 mL of water followed by addition of 1 mL of 3 M KOH and 1 mL of 30%

(42) Garst, M. E.; Bontiglio, J. N.; Grudoski, D. A.; Marks, J. *J. Org. Chem.* **1980**, *45*, 2307.

(43) Brown, H. C.; Sharp, R. L. *J. Am. Chem. Soc.* **1966**, *88*, 5851.

$H_2O_2$. After stirring for another 2 h, the aqueous phase was saturated with NaCl, the organic phase was separated, and the aqueous phase was extracted with three 30 mL portions of EtOAc. The combined extracts were washed with brine (2 × 10 mL) and dried ($NaSO_4$). After removing the solvent in vacuo, the residue was purified by chromatography with EtOAc to give 43 mg (91%) of triol **44**. $[\alpha]^{589}_{Na} = +39.0$ (*c* 7.0, $CH_3OH$). Mp: 215−217 °C. 500 MHz $^1$H NMR ($CD_3OD$) $\delta$ 3.99 (dddd, $J$ = 2.9, 2.9, 2.9, 2.9, 1H, 3-C*H*OH), 3.29 (s, 3H, 17-CHOC$H_3$), 3.21 (dd, $J$ = 8.6, 8.3, 1H, 17-CHOC$H_3$), 3.04 (dd, $J$ = 11.2, 8.6, 1H, 6-C*H*OH), 2.97 (dd, $J$ = 9.9, 8.6, 1H, 7-C*H*OH), 1.93−2.01 (m, 2H), 1.83−1.91 (m, 2H), 1.63 (obscured ABddd, $J_{AB}$ = 11.8, $J$ = 11.8, 11.8, 6.1, 1H, 15-C*H*H), 1.55−1.64 (m, 3H), 1.50 (ddd, $J$ = 10.3, 10.3, 10.3, 1H, 8-C*H*), 1.48 (ddd, $J$ = 11.2, 11.2, 5.2, 1H, 5-CH), 1.39 (obscured ABdd, $J_{AB}$ = 12.8, $J$ = 12.8, 3.2, 1H, 16-C*H*H), 1.38 (obscured ABdd, $J_{AB}$ = 12.4, $J$ = 12.4, 4.1, 4-C*H*H), 1.10−1.36 (m, 5H), 0.83 (ddd, $J$ = 11.2, 11.2, 3.8, 1H, 14-C*H*), 0.81 (s, 3H, 19-C$H_3$), 0.73 (s, 3H, 18-C$H_3$). 75 MHz $^{13}$C NMR $\delta$ 92.0, 81.6, 76.2, 66.5, 58.1, 53.8, 52.5, 44.8, 43.6, 42.1, 39.0, 37.1, 33.7, 31.1, 29.1, 28.7, 27.1, 21.6, 12.8, 12.1. IR ($cm^{-1}$) 3688, 3602, 3054, 2939. Mass spectrum (CI) *m*/*z* 321 (M − 17), 303, 271. Anal. Calcd for $C_{20}H_{34}O_4 \cdot 0.4xH_2O$: C, 68.77; H, 10.16. Found: C, 68.53; H, 9.94.

| proton ($\delta$) | NOE observations (%) |
|---|---|
| 3-H (3.99) | 4-$H_\alpha$ (1.56), 4-$H_\beta$ (2.70), 2-$H_\alpha$/$H_\beta$ (5.26) |
| 17-H (3.29) | 16-H (4.93), 12-H/16-H (10.66) |
| 6-H (3.21) | 8-H (5.45), 4-$H_\beta$ (2.19), 19 $CH_3$ (5.27), 7-H |
| 7-H (2.97) | 5-H (7.25), 14-H (4.52), 9-H (2.87), 6-H |

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