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First total synthesis of xestobergsterol A and active structural analogues of the xestobergsterols

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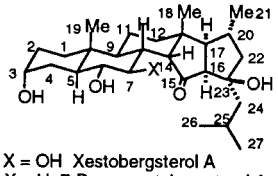
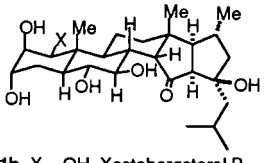
Abstract—The novel pentacyclic polyhydroxylated sterol, xestobergsterol A **1a**, a strong inhibitor of histamine release from rat mast cells induced by anti-IgE, has been synthesized in 24 steps and good overall yield from stigmasterol **7**. The Breslow remote functionalization process has been extended to several more highly functionalized steroid derivatives, especially those with oxygen functionality in the B-ring. The key steps of the synthesis of xestobergsterol A **1a** and its analogues, 7-deoxyxestobergsterol A **1d** and 16,23-*seco*-23-deoxyxestobergsterol A **73**, are the Breslow remote functionalization of oxygenated steroids and for compounds **1a** and **1d**, a novel base-catalyzed epimerization-aldol condensation of a dione to give the desired CD-*cis* ring structure of the xestobergsterols. Thus the known alcohol **75**, prepared from stigmasterol **7**, was taken to the tetraacetate **107** which was then converted via a Breslow remote functionalization into the alkene aldehyde **114** which was transformed in 5 steps to xestobergsterol A **1a**. Testing of the synthetic materials showed that the two analogues, 7-deoxyxestobergsterol A **1b** and 16,23-*seco*-23-deoxyxestobergsterol A **73**, are also potent inhibitors of histamine release with IC_{50} values (IC_{50} 500 nM and 750 nM, respectively) being only 1015 times less than that of xestobergsterol A itself (50 nM).

1. Introduction

The xestobergsterols are intriguing natural products possessing a unique pentacyclic steroid skeleton and exhibiting outstanding biological activity. Umeyama and coworkers first isolated xestobergsterols A **1a** and B **1b** from the Okinawan marine sponge, *Xestospongia bergquistia* Fromont[1] in 1992. Three years later, isolation of xestobergsterols A **1a**, B **1b** and C **1c** from the marine sponge *Ircinia* sp. led to a revision of the C23 stereochemistry and subsequent conformation of the CD *cis* ring juncture in xestobergsterols A and B.[2] Xestobergsterols A and B have demonstrated strong inhibition of histamine release in rat mast cells induced by anti-immunoglobulin B with IC_{50} values of 50 nM and 100 nM, respectively.[2] These compounds 3000–5000 times more potent inhibitors of histamine release than the well-known anti-allergy drug disodium chromoglycate (IC_{50} 262 μM). In the case of xestobergsterol A, it was recently shown that the mechanism of action proceeds via the strong inhibition of phosphatidyl inositol phospholipase C (PI-PLC).[3] PI-PLC functions as a signal amplifier in the inositol phospholipid-dependent trans-membrane signal induction of eukaryotic cells by generating the intracellular secondary messengers, inositol 1,4,5-triphosphate ($InsP_3$), which releases Ca^{2+} from the calcium-sequestering compartment, and diacylglycerol, which activates protein kinase C (PKC). Consequently, xestobergsterol A also inhibits the initial rise of Ca^{2+} and the generation of inositol 1,4,5-trisphosphate ($InsP_3$). Moreover, xestobergsterol A and xestobergsterol C are also mildly cytotoxic against L1210 murine leukemia cells with IC_{50} values of 4.1 and 4.0 μg mL^{-1}, respectively.



1a X = OH Xestobergsterol A
1d X = H 7-Deoxyxestobergsterol A



1b X = OH Xestobergsterol B
1c X = H Xestobergsterol C

Other naturally occurring steroids possessing a 15-keto, *cis* CD ring junction include contignasterol **2**,[4] haliclostanone sulfate **3**,[5] and 15-dehydro-14β-anosmagenin **4**.[6] Although 15-dehydro-14β-anosmagenin, a steroidal aglycon isolated from the saponins of the plant *Solanum vespitilio*, also has the 14β proton configuration, there was considerable doubt whether the 14β configuration exists in the natural product or was formed by epimerization during workup. Although biological activities have not been reported for haliclostanone sulfate or 15-dehydro-14β-anosmagenin, contignasterol strongly inhibited histamine release from rat mast cells induced by anti-IgE in a dose-dependent manner, similar to xestobergsterol A, with an IC_{50} value of 800 nM.[4]

Keywords: xestobergsterols; antihistamines; remote functionalization; steroids; regioselective Mitsunobu reaction; analogues; biological activity.
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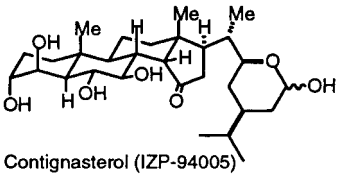
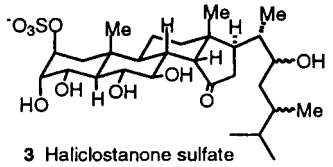
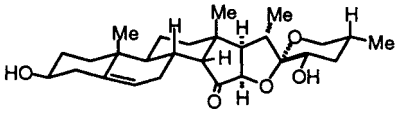


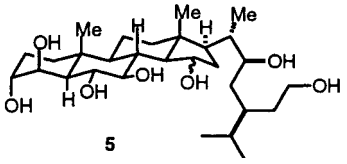
2 Contignasterol (IZP-94005)



3 Haliclostanone sulfate



4 15-Dehydro-14β-anosmagenin



5

It has also been shown to be potent in both in vivo and in vitro models of allergen-induced bronchoconstriction and airway smooth muscle contraction. Consequently, it is very effective as an anti-asthma agent.[7] Interestingly, the contignasterol reduction product **5** did not inhibit histamine release from rat mast cells (IC_{50} approx. 300 μM),[7b] suggesting that either the 15-keto group and/or the hemiacetal is necessary for the inhibition of histamine release. The authors represent the reduction product as having the *trans* C/D ring junction, yet it is doubtful that the reduction conditions would cause epimerization of the 14β hydrogen. Furthermore, although one isomer was purified and tested, the stereochemistry at C15 was not reported.

In addition to our work on the xestobergsterols,[8] only three other reports related to their synthesis, all by Krafft and coworkers,[9] have appeared in the literature. The first two papers[9a,b] utilized an intramolecular Pauson–Khand reaction to generate the D and E rings of the xestobergsterol skeleton. In the third paper,[9c] Krafft abandoned the Pauson–Khand route in favor of ours, namely an intramolecular aldol condensation to form the additional E ring. To date, no synthetic work has been reported on compounds **2**, **3**, or **4**.

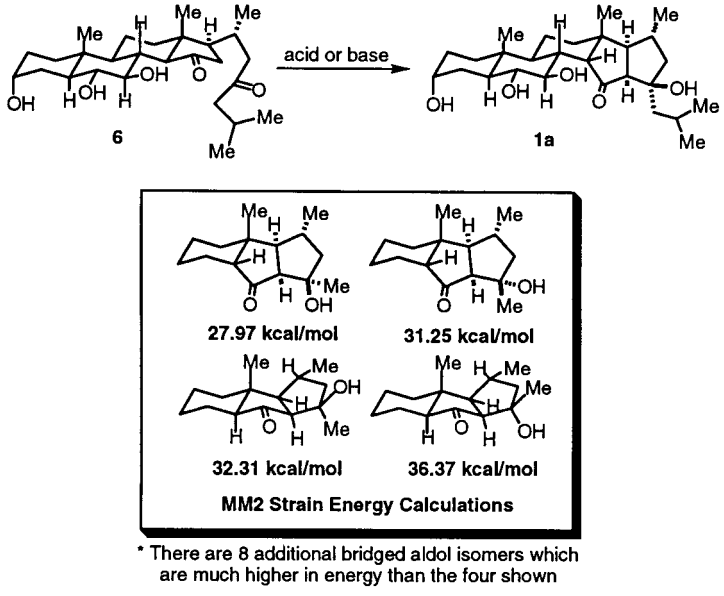
Since the xestobergsterols are β-hydroxy ketones, it is likely that the biogenic precursor is a diketone which has undergone an intramolecular aldol condensation to form the additional five-membered E ring. Therefore we designed our synthesis to use this proposed biosynthesis and to determine if the aldol product **1a** would be produced upon acid or base treatment of diketone **6**. Since twelve aldol isomers are possible from the diketone **6**, molecular mechanics (MM2) strain energy calculations were performed using Macromodel 5.0 to ensure that the desired aldol isomer (that found in the natural products) corresponded to the lowest energy isomer. Of the twelve isomers, eight are bridged and have much higher strain energies than the four fused isomers shown. These calculations clearly demonstrated that the desired aldol isomer was the most stable by at least 3 kcal mol^{-1}, which suggested that the desired isomer should be formed to the exclusion of the remaining eleven under thermodynamic aldol condensation conditions (Scheme 1).

Herein we describe in detail our successful synthesis of xestobergsterol A, **1a**.[8b]

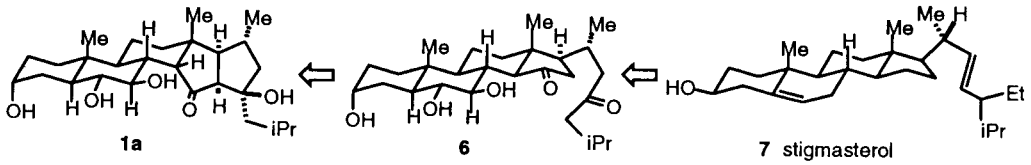
2. Background

2.1. Retrosynthesis

We believed that the xestobergsterols could be produced by an intramolecular aldol condensation of the diketone **6** to



Scheme 1.



Scheme 2.

form the additional E ring with the desired stereochemistry (Scheme 2). Although stigmasterol **7** lacked the 15-keto group needed for the key aldol reaction, it nevertheless seemed to be the most appropriate choice for a starting material since the functionality present in the A and B rings of stigmasterol could be used to functionalize both the B and D rings. More importantly, the side-chain alkene of stigmasterol would allow preparation of the desired 23-ketocholesterol side chain via ozonolysis and extension of the resulting aldehyde. We hoped to install the 15-keto group in ring D by a remote functionalization process, using either the well-known Barton reaction[10] or the Breslow photooxidation process.[11]

Barton and coworkers developed a very useful technique for functionalizing unfunctionalized carbon atoms usually, but not exclusively, in steroids.[10a–c] In addition to the well-known oxidation of the C19 methyl group by photolysis of the C6β nitrite ester, the analogous conversion of an 11α-nitrite ester (derived from the alcohol) via photolysis and hydrolysis provided the Cl ketone in 50% yield.[10b] In order to produce the desired 15-keto functionality in the natural products, photolysis of the 7β-nitrite ester might functionalize C15 of the steroid via an identical mechanism to give the 15-oxime. Acidic hydrolysis of the oxime would provide the 15-ketone, which could possibly be epimerized to the desired *cis* CD 15-ketosteroid.

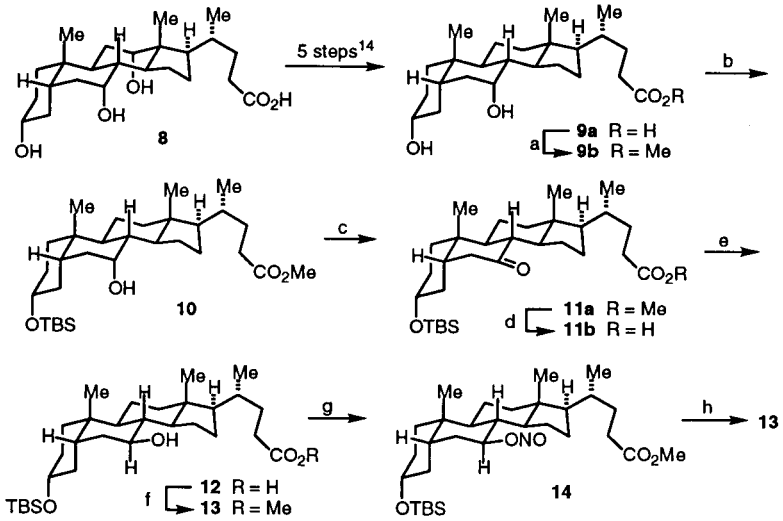
The Breslow remote functionalization technique[11] also allows selective oxidation of C15 in a steroidal skeleton whereby a tertiary hydrogen atom is abstracted by a radical species which is attached usually at C3α of the steroid backbone. Regioselective hydrogen atom abstraction is achieved by choosing a tether of the appropriate length so that the radical species is located nearer to the desired hydrogen atom. Mechanistic studies[11b] showed that photolysis of the benzophenone ester generates a diradical, the oxygen radical of which then abstracts the tertiary hydrogen atom at C14 to provide the tertiary radical at C14. Elimination to provide the C14 alkene occurs exclusively by stereospecific intramolecular abstraction of the 15α-deuterium.

Although there are other remote functionalization techniques available,[12,13] the one using 3α-linked 4-benzophenone acetate best suited our synthetic interests in terms of good yield, excellent selectivity, ease of preparation and tolerance of other functional groups. Conversion of the alkene to the desired ketone at C15 would presumably be straightforward. Hydrolysis of the ester and protection of the alcohol would give the protected 14,15-olefin which on hydroboration–oxidation followed by oxidation should yield the *trans* CD 15-ketosteroid. Epimerization under basic conditions would then provide the desired *cis* CD 15-ketosteroid in very few steps from the photolysis precursor. Accordingly, we decided to investigate both the Barton and Breslow functionalization of steroids as a way of introducing the 15-keto functionality necessary for the xestobergsterols.

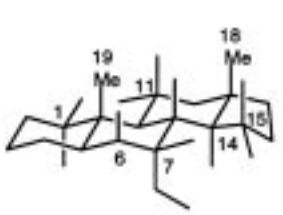
3. Results and discussion

3.1. The Barton reaction

Since the xestobergsterols have a 15-keto group, we believed that the Barton oxidation would be ideal for the oxidation of C15 using the 7β-hydroxyl group, which is also present in the natural products. We decided to test the validity



Scheme 3. a) HCI (cat), MeOH, reflux, 86%; **b)** TBSCI, imidazole, DMF, 82%; **c)** PCC, CH_2CI_2, 98%; **d)** KOH, MeOH:water, reflux, 93%; **e)** Li, NH_3, 85% (3:1, 7β:7α); **f)** CH_2N_2, ether, 98%; **g)** NOCI, pyridine, 97%; **h)** h$\sqrt{}$.



atom-atom	calculated distance (Å)
6βO - 19H (closest approach)	2.23
7βO - 15βH	2.74
7βO - 15αH	2.68
11αO - 1βH	2.40
11βO - 18H (closest approach)	2.23
11βO - 19H (closest approach)	2.08
7αCH$_2$OH - 14αH (closest approach)	1.88

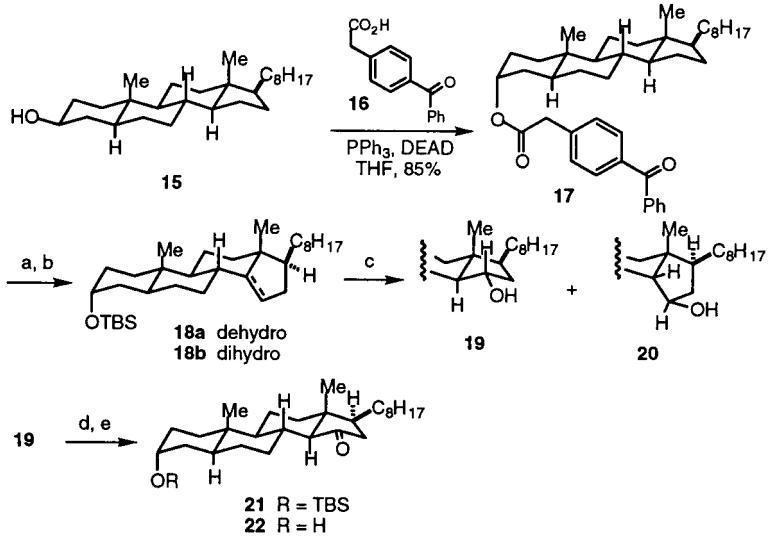
Figure 1.

of this approach by photolysis of the nitrite ester of the alcohol **13**. Commercially available cholic acid **8** (Scheme 3) was converted into the known diol carboxylic acid **9a** in five steps and 35% overall yield.[14] The methyl ester **9b**, prepared in 86% yield, was selectively protected to give the mono silyl ether **10** in 82% yield. Oxidation of the remaining 7α-alcohol of **10** with pyridinium chlorochromate (PCC) afforded the 7-ketone **11a** in 98% yield. Several methods for the reduction of the C7-ketone to the required 7β-alcohol were attempted. Treatment of the ketone **11a** with sodium borohydride or under Meerwein–Pondorf–Verley conditions[15] gave the 7α-alcohol **10** exclusively, in excellent yields, while attempted Mitsunobu inversion of the alcohol **10** provided only starting material. Zhou and coworkers, however, reported that dissolving metal reduction of the 7-keto functionality of cholic acid derivatives gave mainly the 7β-alcohol.[16] Hydrolysis of the ester **11a** produced in 93% yield the carboxylic acid **11b**, which was treated with lithium in ammonia to give an 85% yield of a 3:1 mixture in which the 7β-alcohol **12** predominated over the 7α-alcohol. Re-esterification with diazomethane gave the methyl ester **13**, which was treated with nitrosyl chloride in pyridine to give the nitrite ester **14** in 93% overall yield. The nitrite ester was surprisingly stable, even to silica gel chromatography. Unfortunately, attempts to photolyze the nitrite ester **14** provided only the unfunctionalized 7β-alcohol **13**. Although photochemical cleavage of the O—NO bond occurred, no intramolecular hydrogen atom abstraction from C15 was observed. This approach to xestobergsterol A using the Barton reaction was therefore abandoned.

Further analysis of the steroid skeleton and bond distances using MM2 calculations provided a possible explanation for this ineffectual methodology. Comparison of the successful Barton reactions[10] and our unsuccessful reaction showed significant differences in the calculated atomic distances between the oxygen radical and the hydrogen atom to be abstracted (Fig. 1). For example, the furthest successful distance is 2.40 Å, which is the distance between the equatorial 11β-oxygen atom and the equatorial 1β-hydrogen atom. Since the distance between the 7β-oxygen atom and the 15α-hydrogen atom is 2.68 Å, presumably the additional 0.28 Å required for abstraction of the 15α-hydrogen atom by the oxygen radical is too great for the reaction to occur.

3.2. The Breslow remote functionalization: model studies and analogue preparation

Although the Barton approach for C15 functionalization was unsuccessful, the Breslow remote functionalization technique seemed promising for making the desired D-ring functionalized steroid. We first wanted to show that the C14 olefin produced by the remote functionalization could be transformed into the desired 14β-H 15-ketosteroid. Treatment of cholestanol **15** under Mitsunobu conditions with the known acid **16**[17] provided the inverted ester **17** with the required 3α stereochemistry in 85% yield (Scheme 4). Photolysis of **17** using a 450 W mercury arc lamp with a pyrex filter and subsequent cleavage of the ester with base followed by *tert*-butyldimethylsilyl protection provided an approximately 2:1 mixture of the desired



Scheme 4. a) hν, PhH; 10% KOH, THF:ethanol; **b)** TBSOTf, 2,6-lutidine, CH_2Cl_2, 75% (three steps); **c)** BH_3-THF, THF, 0°C; NaOH, H_2O_2, 17% **(19)**, 3% **(20)**; **d)** PCC, CH_2Cl_2, 100%; **e)** 10% HCl, EtOH, 100%.

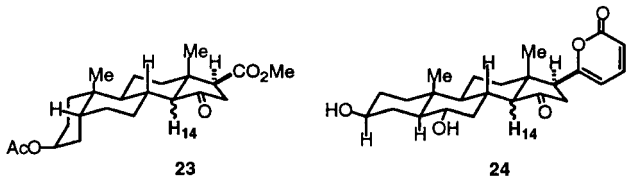


Figure 2.

cholestan-14-en-3α-ol **18a** and the saturated cholestan-3α-ol **18b** in 75% combined yield. Hydroboration–oxidation of the mixture led to an approximately 10:1 mixture of the 14α-H 15α-alcohol **19** and the 14β-H 15β-alcohol **20**, which was separated by flash column chromatography in poor yield. The unreactive TBS-protected cholestan-3α-ol **18b** could also be separated at this stage. Based on the steric hindrance of the approach from the β face of the steroid, the hydroboration–oxidation provided not surprisingly the undesired 14α-H 15α-alcohol **19** as the major isomer. It is unclear why the yield of this hydroboration–oxidation is so low, since thin layer chromatography showed a very clean reaction, and other hydroborations on C14 alkenes have proceeded in good yield in our laboratories (see later schemes). Oxidation of the 14α-H 15α-alcohol **19** provided the 14α-H 15-ketone (*trans* CD ring junction) **21** in excellent yield. Interestingly, treatment of the ketone with base did not provide the desired 14β-H 15-ketosteroid, but instead gave only starting material. Acidic hydrolysis of the *tert*-butyldimethylsilyl ether **21** afforded the pure 14α-H 15-keto-3α-alcohol (*trans* CD ring junction) **22** in quantitative yield.

Two other 15-ketosteroids have also been prepared by other groups and their CD *cis*:*trans* ratios determined. Unlike our simple 15-ketosteroid **22** (Scheme 4), compounds **23**[18] and **24**[19] both favor the *cis* CD ring junction (Fig. 2). These results imply that the side chain at C17 is one important factor in determining the CD *cis*:*trans* ratio. In the *cis* CD compounds, there is a steric interaction between the C18 methyl group and the side chain. Hence, the bigger the side chain, the more unstable the compounds with *cis* CD ring junctions. Both the carbomethoxy group in **23** and the pyrone in **24** are flat and apparently can twist out of the way of the C18 methyl group in the *cis* CD isomers.

Molecular mechanics (MM2) strain energy calculations of model systems show that simple hydrindanone derivatives favor the *cis* CD ring junction by approximately 3 kcal mol^{-1} (Fig. 3). However, substitution of an isopropyl group at C17 to represent a simplified cholesterol side chain, reverses the stabilities of the *trans* and *cis* CD ring junctions resulting in minimal difference between them. These results suggest that for simple cholesterol derivatives, the *trans* CD ring junction should be favored.

Synthesis of the 14β-H 15-ketosteroid (*cis* CD ring junction) consequently proved to be more difficult than anticipated, since simple equilibration could not be used as originally planned. Our next approach involved the Lewis acid mediated rearrangement of a 14α,15α-epoxide to give the 14β-H 15-ketone directly.[20] Morisaki and coworkers have shown that steroidal 14α,15α-epoxides do not give the expected 14β-H 15-ketone directly (Scheme 5). They reported that treatment of the epoxide **25** with boron trifluoride etherate in benzene at room temperature provided the homoallylic alcohol **26** in 75% yield, presumably via the intermediate **I**.[20b] Reichstein and coworkers, however, showed that regioselective and stereoselective reductive opening of steroidal 14α,15α-epoxides could be achieved using hydrogen over platinum catalyst in glacial acetic acid.[21] Reduction of the α-epoxide **27** under these conditions gave a mixture of products (Scheme 6). The desired 14β-H 15α-alcohol **28a** was isolated in 33% yield along with the fully reduced product **28b** in 12% yield, the isomerization product **28c** in 7% yield, and starting material in 4% yield. Although the yields of the desired 14β-H 15α-alcohol **28a** were low, we nevertheless decided to pursue this route since it was precedented to give the product with the desired stereochemistry.

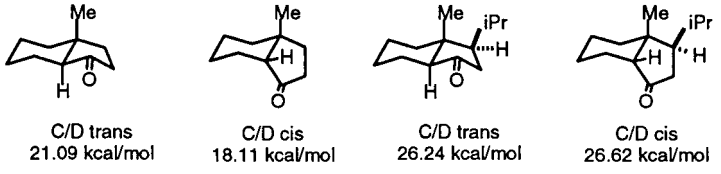
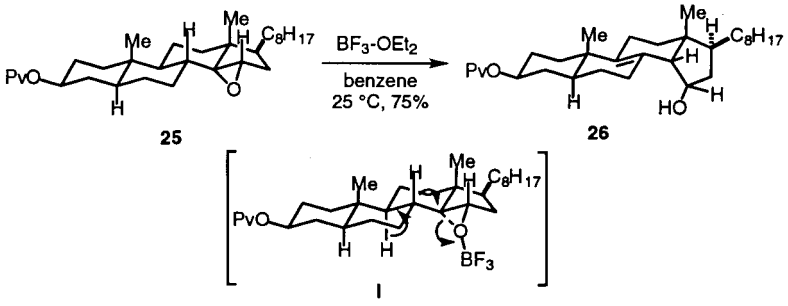
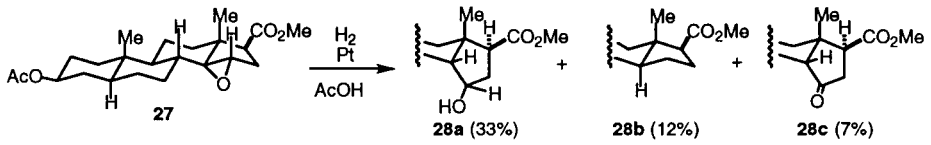


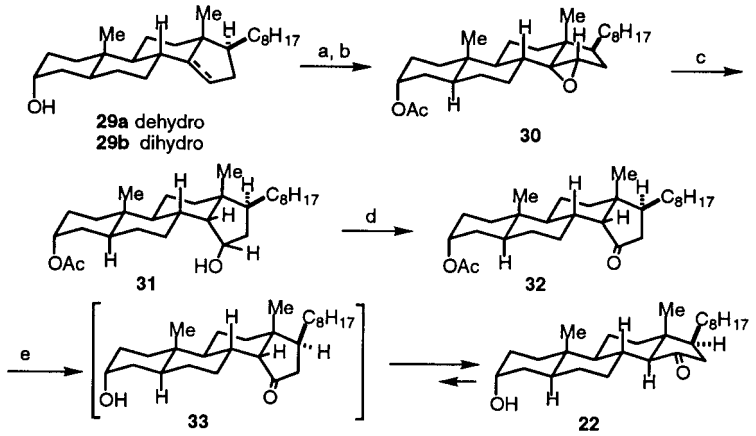
Figure 3.



Scheme 5.



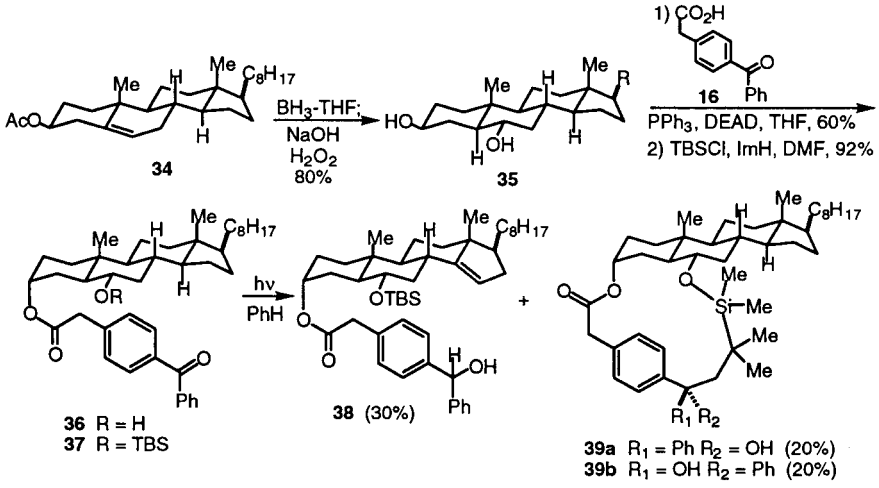
Scheme 6.



Scheme 7. a) Ac_2O, pyr, 97%; **b)** mCPBA, $CHCl_3$, 100% **c)** H_2, PtO_2, AcOH, 42%; **d)** PCC, CH_2Cl_2, 100%; **e)** KOH.

Protection of the mixture of alcohols **29a** and **29b** (Scheme 7) gave the acetate esters in 97% yield. These were subjected to epoxidation using m-CPBA to provide in quantitative yield a 10:1 mixture of α:β epoxidation products, which were separated by flash column chromatography. The unreactive saturated steroid was also separated at this stage. Reduction of the α-epoxide **30** under Reichstein's conditions, namely, hydrogenation over platinum oxide in acetic acid, provided the 14β-H 15α-alcohol **31** in 50% yield. Oxidation of the alcohol **31** with PCC gave the desired 14β-H 15-ketosteroid (*cis* CD ring junction) **32** in quantitative yield. Interestingly, treatment of the ketone **32** with base led to acetate cleavage, but more importantly, epimerization of the 14β hydrogen occurred in the ketone **33** to give an approximately 10:1 ratio of the *trans* CD ketone **22** to the *cis* CD steroid **33**. Thus our results are in agreement with the calculations (Fig. 3).

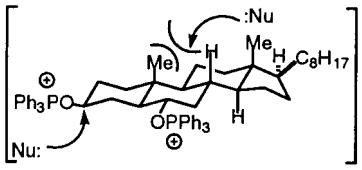
It should be noted that the stereochemistry of the 14-hydrogen (and thus the CD ring junction) is easily established by the chemical shifts and coupling constants of the 7β-protons. In the *trans* CD 15-ketone **22**, the 7β-proton resonates at low field (δ 2.64, dddd, J=13.1, 3.2, 3.2, 3.2 Hz), whereas in the *cis* CD 15-ketone **33**, the 7α-proton resonates at low field (δ 2.51, dddd, J=13.2, 13.2, 13.2, 4.6 Hz). These low-field resonances are due to the deshielding effect of the 15-ketone which has a pseudo 1,3-diaxial interaction with the 7α- or 7β-proton depending on the C14 stereochemistry. The coupling pattern indicates whether the affected proton is equatorial or axial and this, in turn, determines the stereochemistry of the CD ring junction. The CD stereochemistry can also be corroborated by the chemical shift of the C18 methyl group. [Analysis of a variety of 15-ketosteroids from the work of Suginome (see Ref. 13) and also our own work (see Experimental section) showed that the C18 methyl in the cis CD 15-ketosteroids is



Scheme 8.

further downfield in the ^{1}H NMR than in the trans CD 15-ketosteroids.] The compounds with the *trans* CD ring junctions have a resonance for the C18 methyl singlet at 0.70–1.00 ppm, whereas those with the *cis* CD ring junctions have a resonance for the C18 methyl singlet at 1.10–1.30 ppm. For example, in the *trans* CD 15-ketone **22**, C18 resonates at 0.78 ppm, while in the *cis* CD 15-ketone **33**, it resonates at 1.16 ppm. We have used both methods to assign unambiguously the stereochemistry of the CD ring junctions.

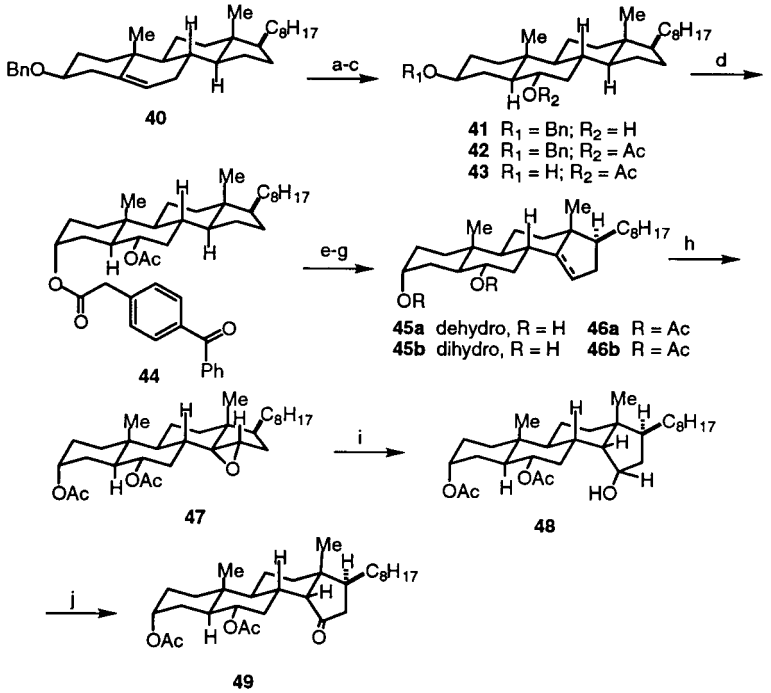
We next determined if substitution at C6 or C7 would have any deleterious effects on the Breslow remote functionalization. The diol **35** was prepared in 80% yield by the hydroboration–oxidation of the commercially available cholesteryl acetate **34** (Scheme 8). A regioselective Mitsunobu reaction[22] with the previously described carboxylic acid **16** provided the ester **36** in 60% yield. Even though both additions are axial, inversion proceeded much faster at C3 than at C6 due to severe steric hindrance encountered in the inversion of the 6α-alcohol, e.g. the 1,3-diaxial interaction of the carboxylate nucleophile with the C18 methyl group, as shown in the intermediate **II**.



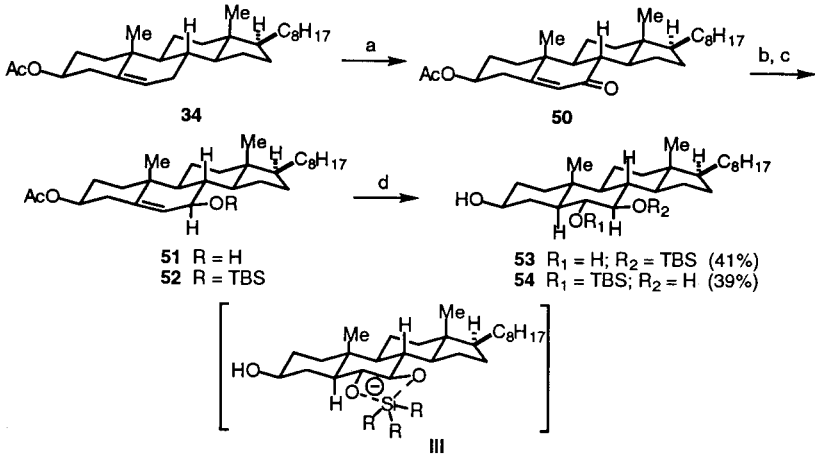
II

Addition of more than one equivalent of the carboxylic acid **16** in this regioselective Mitsunobu reaction results in the inversion of the C6 alcohol as well, so care must be exercised. Finally, protection of the free alcohol at C6 as its *tert*-butyldimethylsilyl ether provided the desired photolysis substrate **37** in 92% yield. Photolysis of **37** afforded the desired olefin **38** in only 30% yield, along with the two diastereomeric lactones **39a** (20%) and **39b** (20%).[23,24]

These undesired photocyclization products could easily be avoided by protection of the C6 alcohol as its acetate ester prior to photolysis. Hydroboration–oxidation of the cholesteryl benzyl ether **40**[25] provided the alcohol **41** in good yield (Scheme 9). Protection of the free alcohol with acetic anhydride gave the ester **42** in 84% yield, which was deprotected at C3 using hydrogen over palladium on carbon catalyst to give **43** in 92% yield. A Mitsunobu reaction was used once again to install the 3a-linked benzophenone tether, which afforded the ester **44** in 86% yield. Photolysis of the steroidal benzophenone **44** followed by complete ester hydrolysis gave an approximately 2:1 mixture of the desired olefinic diol **45a** and the saturated diol **45b**, which were inseparable by conventional flash column chromatography conditions. Protection of the mixture of diols with acetic anhydride proceeded in 68% yield to give a mixture of the unsaturated steroid **46a** and the saturated steroid **46b**. Epoxidation gave the desired α-epoxide **47** in 91% yield (approximately 10:1 ratio of α:β epoxides), which was separable from the saturated diacetate **46b** and the β-epoxide. Reichstein's conditions were again used to reductively open the epoxide **47** regio- and stereoselectively to provide the 14β-H 15α-alcohol **48** in 44% yield. This alcohol was oxidized in 84% yield to the desired 14β-H 15-ketosteroid **49**. Thus the presence of a 6α-alcohol functionality, if properly protected, did not interfere with the remote functionalization process, and the 14β-H 15-ketosteroid **49** could be prepared from the cholesterol derivative **40** in a straightforward manner.

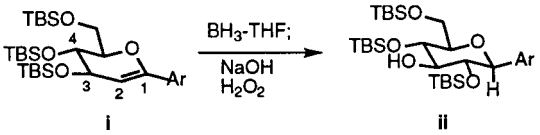


Scheme 9. a) BH_3-THF, THF, 0°C; NaOH, H_2O_2, 89%; **b)** Ac_2O, pyr, 84%; **c)** H_2, Pd/C, THF:EtOH, 92%; **d) 16**, PPh_3, DEAD, THF, 86%; **e)** hν, PhH; **f)** 10% KOH, THF:EtOH:water (1:1:1); **g)** Ac_2O, pyr, 68% (3 steps, combined yield); **h)** mCPBA, $CHCl_3$, 91%; **i)** H_2, PtO_2, AcOH, 44%; **j)** PCC, CH_2Cl_2, 84%.



Scheme 10. a) tBuOOH, $RuCl_3$-H_2O, C_6H_{12}:water, 63%; **b** $NaBH_4$, $CeCl_3$-$7H_2O$, CH_2Cl_2:MeOH (4:1), −78°C to rt, 93%; **c)** TBSCl, imidazole, DMF, 98%; **d)** BH_3-THF, 0°C; 10% NaOH, 30% H_2O_2.

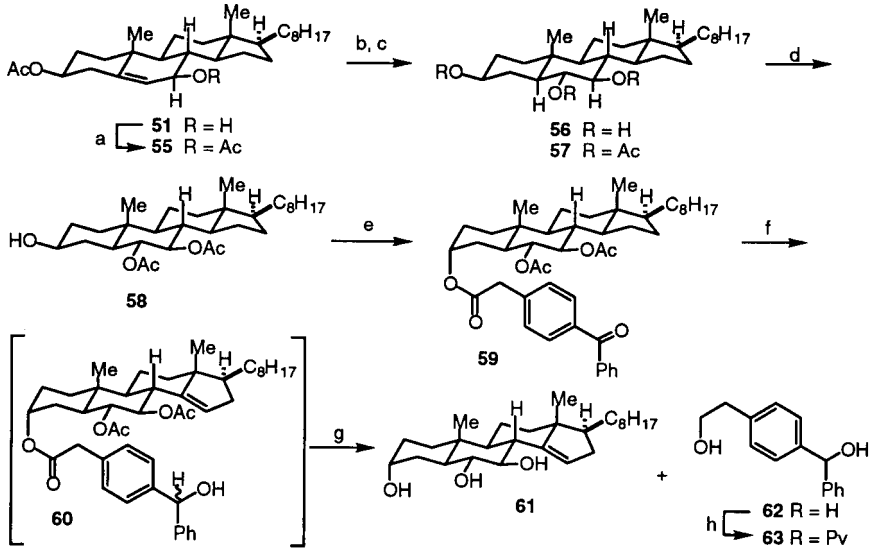
In order to ensure that the photolysis methodology could be used to synthesize xestobergsterol A, we attempted the photolysis with a substrate having oxygen substitution at both C6 and C7, thereby more closely resembling the natural products. After several attempts using catalysts such as copper,[26a] chromium,[26b–d] ruthenium,[26e] and other methods,[26f] we found that the ruthenium-catalyzed allylic oxidation was the most desirable one for the C7 oxidation of protected cholesterol derivatives. Cholesteryl acetate **34** was treated with catalytic ruthenium trichloride and *tert*-butyl hydroperoxide to provide the enone **50** in 63% yield (Scheme 10). Luche reduction of the enone **50** gave reduction exclusively from the α face to afford in 93% yield the 7β-allylic alcohol **51** which was protected with TBSCl to give the silyl ether **52** in 98% yield. Unfortunately, hydroboration–oxidation of the allylic silyl ether **52** gave not only the desired alcohol **53** in 41% yield but also the product **54** in 39% yield in which the silyl group had migrated from the 7β-oxygen to the newly formed 6α-oxygen. Although the 1,2-diol is *trans*, the silyl group is presumably able to migrate via the five-membered transition state **III** to provide the silyl-migrated product **54**.[27] Separation of the two compounds and teatment of the C7 silyl ether **53** under basic conditions gave the more stable C6 silyl ether **54** in quantitative yield. The driving force for the silyl migration is almost certainly alleviation of the severe pseudo 1,3-diaxial interaction between the C7 equatorial silyl ether and the C14–C15 carbon–carbon bond in the D ring of the steroid.[28] [Friesen and coworkers have reported a very similar migration of a silyl group from a more hindered to a less hindered equatorial oxygen. Treatment of the olefin **i** under standard hydroboration–oxidation conditions provided the silyl migrated product **ii** in good yield.



Presumably, migration occurs to give the more stable isomer, which lacks the severe steric interaction between the bulky silyl ether at C4 and the bulky silyl ether at C3. Friesen and co-workers avoided this undesirable migration by oxidative workup with pH 7 phosphate buffer in place of the sodium hydroxide solution.]

We decided instead to protect the C7 alcohol as the acetate which would be cleaved during the hydroboration–oxidation process. Protection of the allylic alcohol **51** went smoothly to provide the allylic acetate **55** in 93% yield (Scheme 11). Hydroboration–oxidation of the olefin gave the triol **56** with a small amount of the triol derived from β addition of the borane, which could easily be separated by flash column chromatography. Attempts at protecting the triol **56** as the triacetate using acetic anhydride/DMAP resulted in slow reaction times and poor yields. However, treatment of the triol **56** with acetic anhydride catalyzed by trimethylsilyl triflate gave the fully protected steroid **57** in 79% yield from **55**. We found that the acetate protecting groups at C6 and C7 were sufficiently hindered relative to the one at C3 so that treatment of the triacetate **57** with mild base gave excellent yields of the mono-deprotected product (e.g. treatment with 10% KOH in 1:1 THF:95% ethanol gave the alcohol **58** in 92% yield). Once again, the Mitsunobu inversion of the C3 alcohol **58** with the carboxylic acid **16** proceeded smoothly to provide the inverted ester **59** in 87% yield. Photolysis of the ester **59** also produced the remote functionalized steroid **60** in fair yield. Flash column chromatography prior to hydrolysis allowed for the facile separation of the unsaturated and the saturated steroids and provided the pure olefin. The olefinic steroid **60** was treated with lithium aluminum hydride to afford the olefinic triol **61** in 58% yield from **58**. In addition, the reduced benzophenone tether **62** was also isolated.

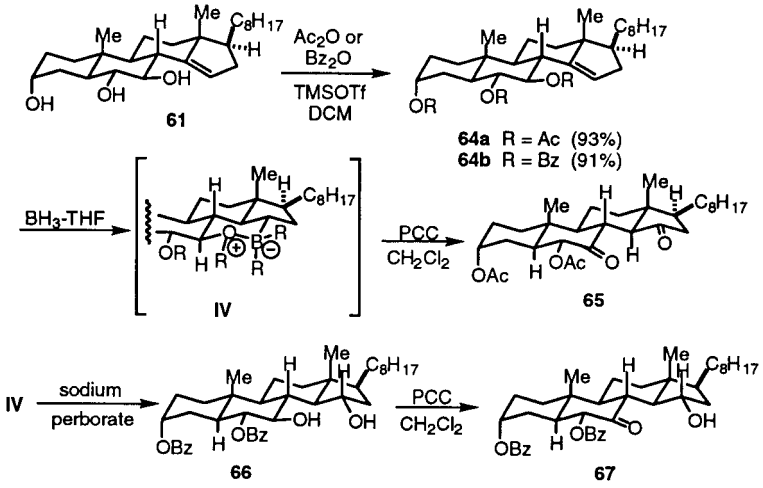
In order to determine the extent of asymmetric induction in forming the benzhydryl alcohol **62** during photolytic reduction of the benzophenone, we selectively protected the diol **62** as the pivaloate ester to give the alcohol **63** in 74% yield. Analysis for enantiomeric purity using the method of Alexakis[29] using ^{31}P NMR revealed an interesting 4:1 mixture of diastereomers (60% de during the photolytic process). We have not yet determined the absolute configuration of the major enantiomer. Breslow also



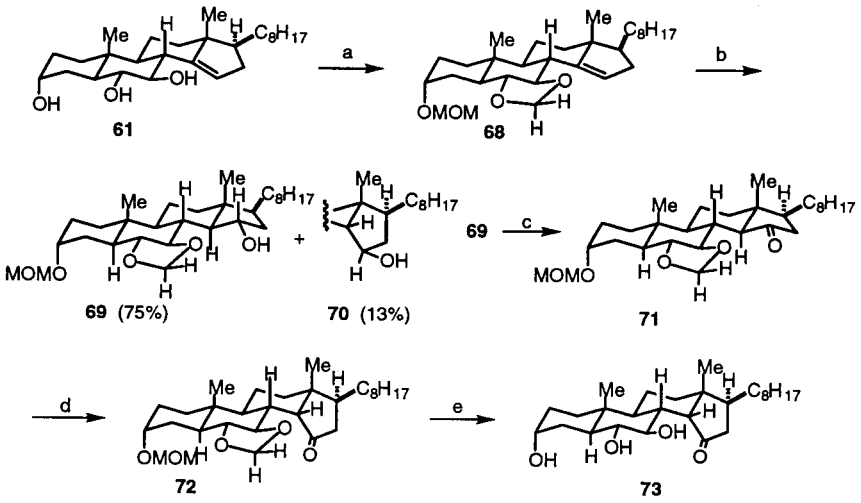
Scheme 11. Ac_2O, DMAP (cat), pyridine, 93%; **b)** BH_3-THF; 10% NaOH, 30% H_2O_2; **c)** Ac_2O, TMSOTf (cat), 79% (two steps); **d)** 10% KOH, THF:95% EtOH (1:1), 92%; **e)** **16**, PPh_3, DEAD, THF, 87%; **f)** hν, PhH; **g)** $LiAlH_4$, THF, 58% (two steps); **h)** PvCl (1.5 eq), pyr, rt, 74%.

looked at asymmetric induction during the reduction of the benzophenone carbonyl with the hydrogens from the steroid backbone and found very little asymmetric induction (approximately 55:45 ratio of diastereomers) with simple steroidal benzophenone esters derived from cholestanol.[11b] In the same paper, Breslow examined asymmetric induction during reduction of the benzophenone carbonyl and found that varying solvents had only slight effects on the amount of asymmetric induction. Thus, the presence of the 6α- and 7β-acetates greatly improves asymmetric induction during reduction.

Our first attempts at protecting the olefinic triol **61** were unsuccessful. Treatment of the triol with either *tert*-butyldimethylsilyl triflate or triethylsilyl triflate led to the formation of the 3,6-bis-protected products in moderate yields but, even at elevated temperatures, none of the desired tris-protected products was detected. Likewise, treatment of the triol with 18-Crown-6/KH/*tert*-butyldimethylsilyl chloride, which is known to protect hindered or tertiary alcohols, failed to give the tris-protected products.[30] Because the C7 equatorial alcohol is pseudo 1,3-diaxial to the C14–C15 carbon–carbon double bond, it is therefore much more hindered than one might assume. Moreover, protection of the C6 oxygen with a bulky group increases the steric hindrance around the C7 alcohol, thus making it much more difficult to protect. Hence a protecting group small enough to protect all three alcohols and one that could be easily removed was required. We tried to fully protect the olefinic triol **61** by treating it with acetic anhydride and catalytic trimethylsilyl triflate, which had been used successfully in our labs to protect hindered alcohols. The desired olefinic triacetate **64a** and tribenzoate **64b** were produced in 93% and 91% yield, respectively (Scheme 12). Since we did not want to cleave the ester protecting groups upon hydroboration–oxidation of the olefin, we used very mild conditions for the oxidation of the intermediate organoborane. The olefinic triacetate



Scheme 12.



Scheme 13. a) $CH_2(OME)_2$, P_2O_5, 63%; **b)** BH_3-THF; NaOH, H_2O_2; **c)** PCC, CH_2Cl_2, 80% **d)** 10% NaOH, THF/EtOH, >95%; **e)** 10% HCl, THF, 50%.

64a was hydroborated and oxidized with pyridinium chlorochromate to give the 7,15-dione **65**, rather than the desired 15-ketosteroid. Similarly, the benzoate **64b** was hydroborated and oxidized with sodium perborate,[31] but again loss of the protecting group at C7 provided the 7β,15α-diol **66**, rather than the desired 15α-alcohol. This loss is presumably facilitated by the intramolecular chelation of the oxygen atom at C7 to the Lewis acidic boron atom forming the zwitterionic six-membered intermediate **IV**. Selective oxidation of the 7β,15α-diol **66** using pyridinium chlorochromate provided the C7 ketone **67** exclusively rather than the desired C15 ketone. It is unclear why the C7 alcohol is oxidized faster than the C15 alcohol although it might be assumed that this is due to a combination of steric and electronic effects.

The pure olefinic triol **61** was successfully protected using methylal and phosphorous pentoxide[32] to give the fully protected ether **68** in 63% yield (Scheme 13). Surprisingly, instead of protecting the three alcohols as methoxymethyl (MOM) ethers, these conditions gave the MOM ether at C3 and the methylene acetal between the C6 and C7 alcohols. Although the C6 and C7 acetonide was found to be highly unstable toward mildly acidic conditions, the methylene acetal in contrast was very robust toward mildly acidic and strongly basic conditions. Hydroboration–oxidation of the protected olefin **68** gave an approximately 6:1 mixture of the 14α-H 15α-alcohol **69** (75% yield) and the 14β-H 15β-alcohol **70** (13% yield), which were separable by flash column chromatography. The 14α-H 15α-alcohol **69** was oxidized[33] to the corresponding ketone **71**, which upon treatment with base, epimerized completely to give the more stable 14β-H 15-ketosteroid **72**. Presumably, epimerization to the more stable 14β-H 15-ketosteroid alleviates the severe steric interaction between 7β oxygen and both the C14–C15 carbon–carbon bond and especially the carbonyl group at C15. Finally, deprotection under acidic conditions provided the *cis* CD keto-triol, 16,23-seco-23-deoxyxestobergsterol A, **73** in 50% yield.

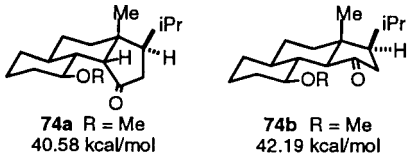
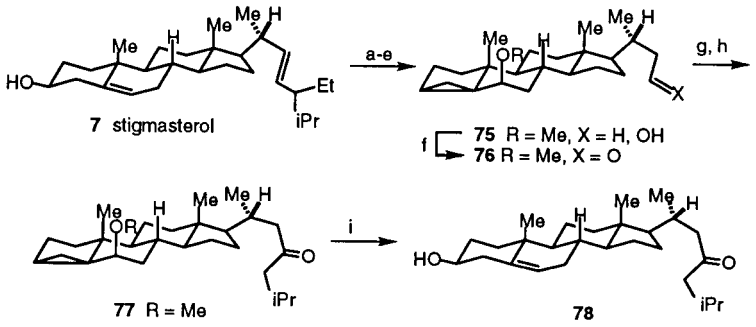


Figure 4.

Molecular mechanics (MM2) strain energy calculations on model structures are in agreement with our experimental results. As shown in Fig. 4, calculations show that the *cis* CD ketone **74a** is more stable than the *trans* CD ketone **74b** by approximately 1.60 kcal mol^{-1}. Presumably, the 7β-methoxy substituent has a strong unfavorable steric interaction with the C14–C15 carbon–carbon bond and the C15-keto group. This severe steric interaction can be alleviated in the *cis* CD isomer, because the C14–C15 carbon–carbon bond is no longer pseudo 1,3-diaxial with the C7–oxygen bond and the C15-keto group interacts with the 7α-hydrogen rather than the bulky methoxy substituent.

3.3. Synthesis of 23-ketocholesterol: a model for side-chain formation

With the cholesterol side-chain analogues of the xestobergsterols fully developed and a well-tested method in place for their synthesis, we set about synthesizing the xestobergsterol skeleton. It only remained for us to find a starting steroid that not only had functionality in the A and B rings of the steroid, but also on the side chain. The inexpensive steroid stigmasterol **7** proved to be the best choice. It was converted into the known alcohol **75** in five steps and 66% overall yield by the following sequence (Scheme 14).[34] Protection of stigmasterol **7** with mesyl chloride gave the mesylate which on refluxing with methanol and pyridine provided the cyclopropyl carbinyl ether via a stabilized homoallylic cation. Ozonolysis of the side-chain olefin and Wittig olefination of the resulting aldehyde, with final hydroboration–oxidation gave the alcohol **75**. Oxidation of the alcohol **75** with pyridinium chlorochromate proceeded smoothly to afford in 88% yield the aldehyde **75**, which was treated with isobutylmagnesium bromide to give an equal

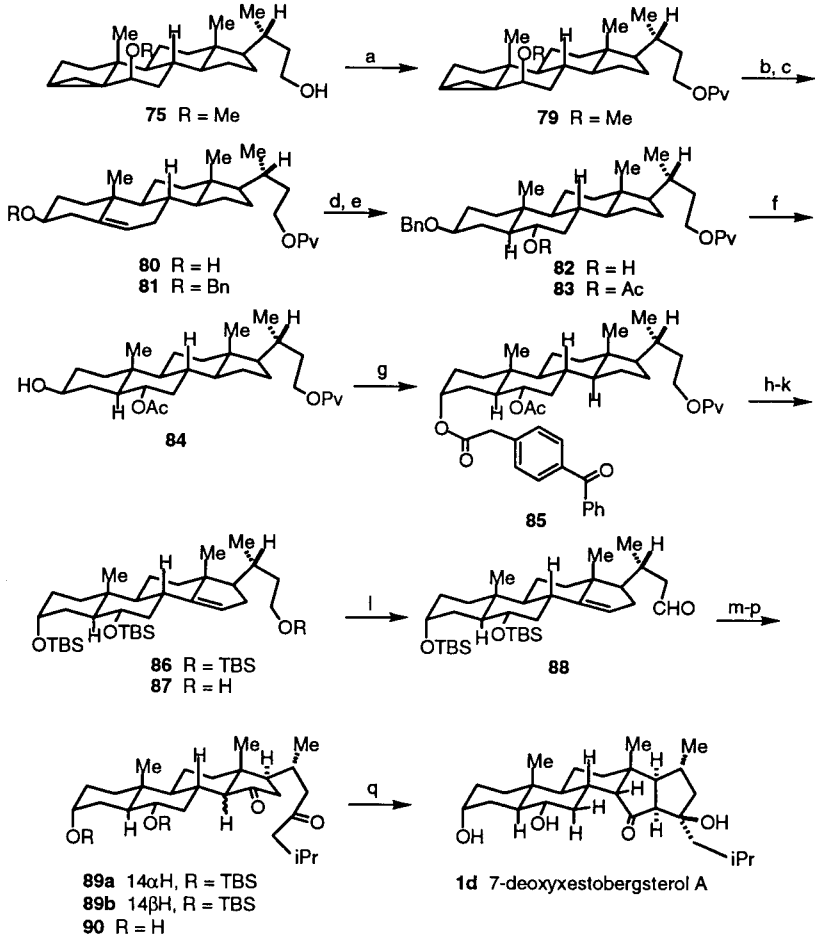


Scheme 14. MsCl, pyr, rt, 99% **b)** MeOH, pyr, reflux, 89%; **c)** O_3; DMS, 100%; **d)** CH_2PPh_3, THF, 93%; **e)** BH_3-THF; NaOH, H_2O_2, 81%; **f)** PCC, KOAc, DCM, 88% **g)** iBuMgBr, ether, 79%; **h)** PCC, pyridine:DCM (2%), 100% **i)** TsOH (cat), dioxane:water (4:1), reflux, 94%.

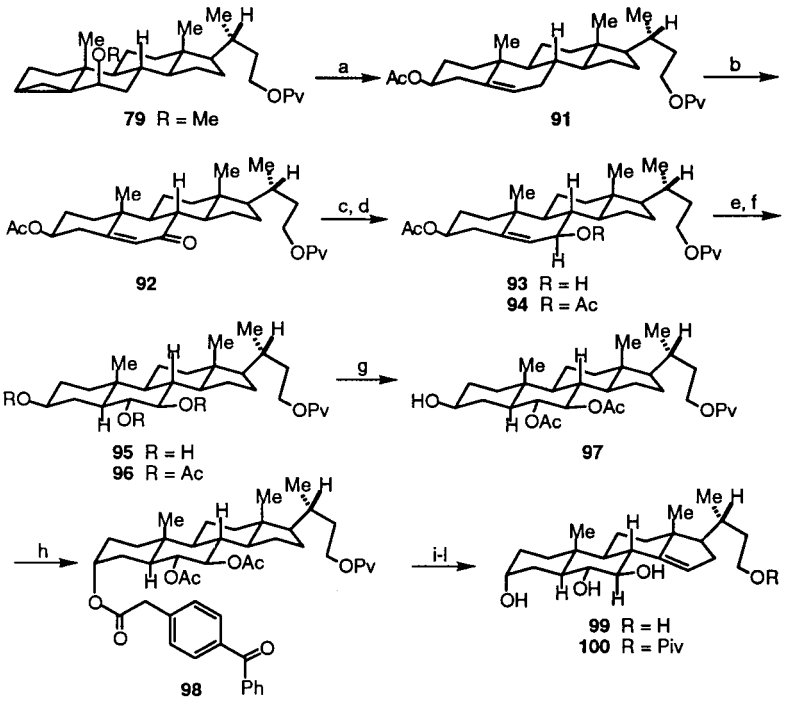
mixture of diastereomeric alcohols in 79% yield. At this point, all of the carbons for the xestobergsterols were in place. Oxidation of the mixture of alcohols provided the 23-ketone **77** in quantitative yield. Acid-catalyzed hydrolysis of the cyclopropylmethyl methyl ether gave the homoallylic alcohol **78** in 94% yield. Unfortunately, all attempts to protect the C23 carbonyl proved unsuccessful.[35] Therefore, instead of fully developing the side chain at the beginning of the synthesis, we decided to postpone the formation of the fully oxidized side chain until near the end of the synthesis in order to avoid protection of the 23-ketone.

3.4. Synthesis of 7-deoxyxestobergsterol A

Having developed a general method for the synthesis of the 14β-H 15-ketone and a good substrate for the side-chain elaboration identified, we decided to continue with the synthesis of xestobergsterol A. The alcohol **75**, derived in five steps and 66% overall yield from stigmasterol, was

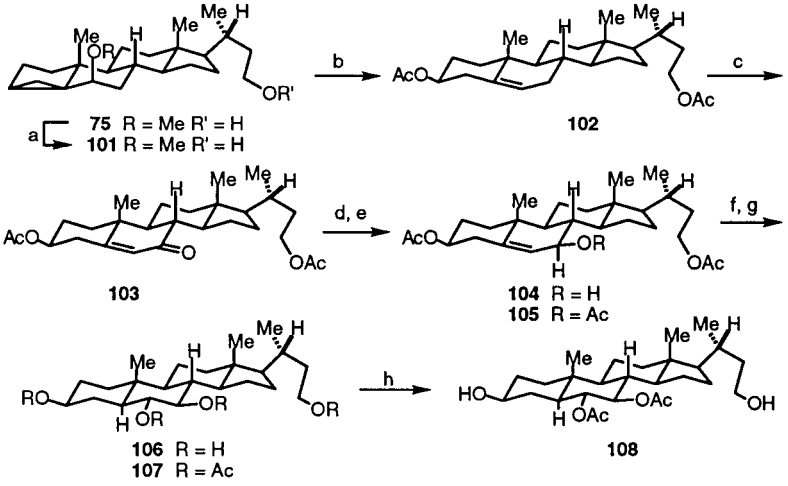


Scheme 15. a) PvCl, pyr, 92%; **b)** TsOH, water:dioxane, reflux, 97%; **c)** NaH, BnBr, TBAl (cat), THF, 83%; **d)** BH_3-THF; 10% NaOH, 30% H_2O_2, 60%; **e)** Ac_2O, pyr, 100%; **f)** H_2, Pt, THF/EtOH, 96%; **g)** **16**, PPh_3, DEAD, 90%; **h)** hν, PhH; **i)** KOH (aq), THF/EtOH; **j)** TBSOTf, 2,6-lutidine, CH_2Cl_2, 48% (3 steps); **k)** AcOH, THF/H_2O, 86%; **l)** PCC, CH_2Cl_2, 83%; **m)** i-BuMgBr, ether, 0°C, 90%; **n)** BH_3-THF; 10% NaOH, 30% H_2O_2; **o)** Pcc, CH_2Cl_2, 79% (two steps); **p)** 10% HCl, THF, 48 hr, >95%; **q)** 10% NaOH, EtOH, >95%.

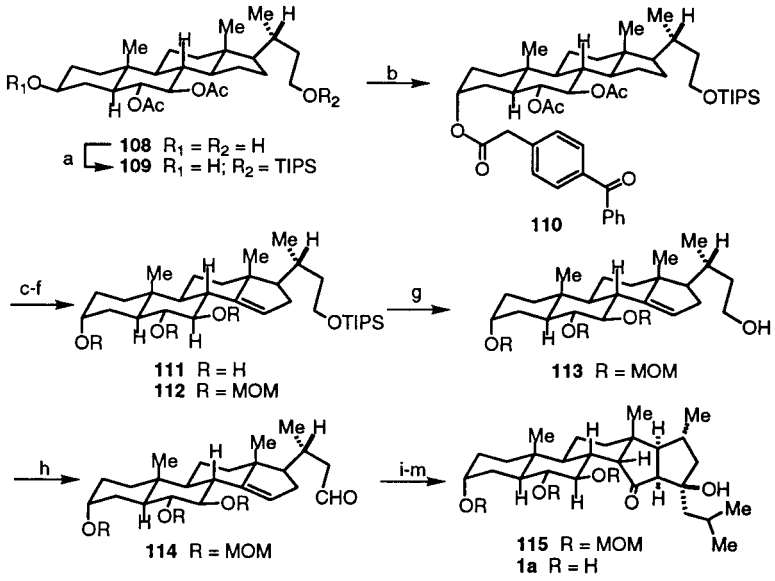


Scheme 16. AcOH, reflux, 94%; **b)** $RuCl_3$, TBHP, C_6H_{12}, 65%; **c)** $NaBH_4$, $CeCl_3$, DCM:MeOH, 97%; **d)** Ac_2O, DMAP, pyr, 98%; **e)** BH_3-THF; NaOH, H_2O_2, 57%; **f)** Ac_2O, TMSOTf, 95%; **g)** 10% NaOH, THF:EtOH, 89%; **h)** **16**, PPh_3, DEAD, THF, 93%; **i)** hν, PhH, 61%; **j)** PCC, DCM, 87%; **k)** $LiAlH_4$, THF, 79% **l)** PvCl, pyr, 83%.

protected with pivaloyl chloride to provide the ester **79** in 92% yield (Scheme 15). The cyclopropylmethyl methyl ether was opened with catalytic acid to give the homoallylic alcohol **80** in 97% yield, which was protected as the benzyl ether **81** in 83% yield. Hydroboration–oxidation of the olefin gave the 6α-alcohol **82** in 60% yield. During the oxidation of the organoborane under basic hydrogen peroxide conditions, it was necessary to maintain low temperature to prevent the removal of the pivaloate ester by hydrogen peroxide anion. Partial loss of the protecting group may account for the somewhat lower yield. Protection of the alcohol provided the acetate **83** in 100% yield. Debenzylation using hydrogen gas with a platinum catalyst gave the alcohol **84** in 96% yield. The alcohol was subjected to the Mitsunobu reaction with the acid **16** to provide the inverted ester **85** in 90% yield. Photolysis of **85** followed by complete basic hydrolysis and exhaustive protection with *tert*-butyldimethylsilyl triflate provided in 48% yield for the three steps the fully protected C14 olefin **86**, which was separated from the saturated steroid by silver nitrate-impregnated silica gel flash column chromatography.[36] Mono-deprotection of the primary silyl ether with aqueous acetic acid gave the primary alcohol **87** in 86% yield. Oxidation of the alcohol **87** provided in 83% yield the aldehyde **88**, to which was added isobutylmagnesium bromide to give a 1:1 mixture of the diastereomeric alcohols



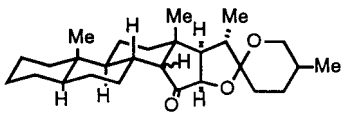
Scheme 17. a) Ac_2O, pyr, 97%; **b)** AcOH, reflux, 97%; **c)** $RuCl_3$, TBHP, DCE, 65%; **d)** $NaBH_4$, $CeCl_3$, DCM:MeOH, 98%; **e)** Ac_2O, pyr, 97%; **f)** BH_3-THF; NaOH, H_2O_2, 50%; **g)** Ac_2O, TMSOTf, 97%; **h)** 10% NaOH, THF:EtOH, 95%.



Scheme 18. a) TlPSCl, imidazole, DMF, 76%; **b) 59**, PPh_3, DEAD, 74%; **c)** hν, benzene, 48%; **d)** PCC, DCM, 63%; **e)** $LiAlH_4$, THF, 91%; **f)** MOMCl, NaI, DCE, reflux, 80%; **g)** TBAF, THF, 92%; **h)** PCC, DCM, 82%; **i)** iBuMgBr, ether, 80%; **j)** BH_3-THF; NaOH, H_2O_2; **k)** Dess-Martin, DCM; **l)** 10% NaOH, EtOH, 73% (3 steps); **m)** 50% HCl, THF:EtOH, 100%.

in 90% yield. Hydroboration–oxidation of the alkene gave an approximately 10:1 ratio of the 14α-H 15α,23-diol and the 14β-H 15β,23-diol, which were oxidized to the corresponding 14α-H 15,23-dione **89a** and the 14β-H 15,23-dione **89b**, respectively, and separated by flash column chromatography. Acidic hydrolysis of the silyl ethers of the major ketone **89a** gave the diol **90**, which undewent base-catalyzed intramolecular aldol condensation giving 7-deoxyxestobergsterol A **1d** as the only aldol isomer in quantitative yield for the two steps. Even though the *trans* CD ring junction is more stable in the tetracyclic system, once the new E ring has been formed, the *cis* CD ring junction is even more stable. Thus the calculations in the model system were borne out in the full steroidal skeleton (Scheme 1).

The structure was assigned by comparison of the chemical shifts and coupling constants to those reported for xestobergsterol A and by a NOESY experiment which showed correlation between the angular 16-H and the hydrogens at C24 and C25, thus establishing the stereochemistry at C23. Accordingly, 7-deoxyxestobergsterol A **1d** is available in 17 steps and 10% overall yield from the known alcohol **75** (22 steps and 7% overall yield from stigmasterol **7**). [Another pentacyclic steroid similar to 7-deoxyxestobergsterol A was prepared and its CD *cis*:*trans* ratio determined. Upon treatment with methanolic potassium hydroxide, the 15-ketosteroid **iii** gave exclusively the *cis* CD ring junction.



iii 14βH:14αH (>98:2)

Evidently the 5,5-*cis* fusion of the D and E rings places additional strain on the D ring of steroids which can be relieved by epimerization to the more stable *cis* CD isomer.]

3.5. Synthesis of xestobergsterol A

The pivaloate ester **79** was again prepared from stigmasterol **7** as described before. Opening of the cyclopropylmethyl methyl ether with glacial acetic acid afforded the homoallylic acetate **91** in 94% yield (Scheme 16). Allylic oxidation under the previously described conditions ($RuCl_3$, *t*-BuOOH) yielded in 65% yield the enone **92**, which was reduced under Luche conditions to provide the 7β-alcohol **93** as the only detectable isomer in 97% yield. Protection of the allylic alcohol with acetic anhydride and catalytic DMAP gave the allylic acetate **94** in 98% yield, which was hydroborated and oxidized to give only a modest yield (57%) of the desired triol **95**. The somewhat low yield of the triol can be attributed to loss of the pivaloate ester under the strongly basic hydrogen peroxide conditions giving the tetrol. Nonetheless, the triol was carried on. Acid-catalyzed acetylation of the triol **95** led to the triacetate **96** in a gratifying yield of 95%. Selective deacetylation at C3 with mild base, as described before, provided the C3 alcohol **97** with superb selectivity in 89% yield. Reaction of the C3 alcohol of **97** with the acid **16** under Mitsunobu conditions provided the inverted ester **98** in 93% yield. Photolysis of this benzophenone ester gave the olefinic steroid in 61% yield, which was oxidized with pyridinium chlorochromate to aid in purification by flash column chromatography. Reductive cleavage of all the esters with lithium aluminum hydride afforded the pure olefinic tetrol **99** in 42% overall yield from the benzophenone **98**. The olefinic tetrol was selectively protected to give the primary pivaloate ester **99** in 83% yield. Unfortunately, attempted protection of the triol **99** with phosphorous pentoxide and methylal, as described before, led to decomposition of the substrate. This effectively ended all routes using the pivaloate protecting group for the C23 alcohol. Although this first route for

the synthesis of xestobergsterol A was unsuccessful, it did provide valuable information which helped in designing the synthesis which eventually led to the first total synthesis of xestobergsterol A.

Treatment of the known alcohol **75** with acetic anhydride provided the acetate ester **101** in 97% yield (Scheme 17). The cyclopropylmethyl methyl ether of **101** was opened with glacial acetic acid to give in 97% yield the homoallylic acetate **102**, which was subjected to the same allylic oxidation conditions as previously described ($RuCl_3$, tBuOOH) to give the enone **103** in 65% yield. Once again the enone **103** was reduced under Luche conditions to give the allylic 7β-alcohol **104** as the only detectable diastereomer in 98% yield. Protection of the alcohol as the acetate provided the allylic acetate **105** in 97% yield, which was hydroborated and treated with basic hydrogen peroxide to yield the pure tetrol **106** (after column chromatography to remove the minor isomer produced from addition of the borane to the β-face of the alkene). Simple acetylation of the tetrol gave mainly the triacetate in which the 7β-alcohol was unprotected. Since the 7β-alcohol is quite sterically hindered, it was necessary to use acetic anhydride and catalytic trimethylsilyl triflate in order to produce the tetraacetate **107** in excellent yield (97%). The C6 and C7 acetates are again sufficiently hindered relative to the acetates at C3 and C23 to allow selective deprotection using mildly basic conditions to afford the diol **108** in 95% yield.

Protection of the C23 primary alcohol, in preference to the C3 secondary alcohol, as its triisopropylsilyl (TIPS) ether produced the alcohol **109** in 76% yield, which was reacted with the known acid **16** using Mitsunobu conditions to give the photolysis precursor **110** in 74% yield (Scheme 18). Photolysis of the fully protected steroid provided the remote functionalized product in 48% yield. The lower yield may be attributed to loss of the triisopropylsilyl ether via hydrolysis or oxidation since photolysis of the substrate with the C23 alcohol protected as the pivaloate gave much better yields of the remote functionalized product. Nonetheless, the photolysis product was oxidized with PCC to facilitate purification by conventional flash column chromatography and reduced to yield the triol **111** in 28% overall yield from the benzophenone **110**. Since we had encountered difficulties protecting a similar triol with methylal and phosphorous pentoxide, we decided to use basic conditions to introduce three methoxymethyl (MOM) ether protecting groups. Treatment of the triol **111** with excess chloromethyl methyl ether and sodium iodide[37] (to generate the iodomethyl methyl ether in situ) gave the differentially fully protected ether **112** in 80% yield. Removal of the primary silyl ether gave in 92% yield the alcohol **113**, which was oxidized with pyridinium chlorochromate to provide the aldehyde **114** in 82% yield. Addition of isobutylmagnesium bromide gave an equal mixture of diastereomeric alcohols in 80% yield. Hydroboration–oxidation followed by oxidation with the Dess–Martin periodinane and finally base-catalyzed intramolecular aldol condensation gave the β-hydroxy ketone **115** in 73% yield for the three steps. Final deprotection of the three MOM ethers was accomplished using acidic conditions to give xestobergsterol A **1a** in 100% yield, which was identical in all respects to the natural product. [For characterization data for xestobergsterol A, please see Refs 1 and 2. Natural xestobergsterol A: $[\alpha]_D^{25}=-37.7°$ (*c* 2.8, $CHCl_3$); natural xestobergsterol B: $[\alpha]_D^{25}=-35.0°$ (*c* 0.89, $CHCl_3$), private communication from Dr. Maseo Takei (Japan National Cancer Research Institute).]

3.6. Biological activity of analogues

Since the *cis* CD 15-keto functionality appears to be an important factor in inhibition of histamine release, it was important to prepare analogues to prove their efficacy. Interestingly, when 16,23-*seco*-23-deoxyxestobergsterol A **73** (see Scheme 13) was tested for its inhibitory activity against histamine release in rat peritoneal mast cells, it was shown to be quite active (IC_{50} 750 nM). These results suggest that the simple cholesterol side chain is tolerated quite well and that the presence of both the E ring and the additional hydroxyl group at C23 are not extremely important for activity. Since analogues containing the cholesterol side chain are easier and cheaper to make, it is likely that compounds based on the keto triol structure **73** will be useful as antihistamine drugs. 7-Deoxyxestobergsterol A **1d** (Scheme 15) was also tested for its inhibitory activity against histamine release in rat peritoneal mast cells. Like the ketotriol **73**, 7-deoxyxestobergsterol A **1d** was also quite active (IC_{50} 500 nM). Although these compounds are 10–15 times less active than xestobergsterol A **la**, they have somewhat better activity than contignasterol **2** (IC_{50} 800 nM), which is being explored as a potential lead compound for inhibiting histamine release. Further testing of these analogues for cytotoxicity is underway.

4. Conclusion

In summary, we have utilized the Breslow remote functionalization process to achieve the first total synthesis of xestobergsterol A as well as the synthesis of several simpler analogues. In addition to completing the synthesis of xestobergsterol A, we have determined that the Breslow remote functionalization process can be carried out on substrates with functionality in the A and B rings of steroids without any deleterious effects or loss in yields compared to the simpler substrates used by Breslow. Furthermore, side-chain structure, substitution or lack of substitution at C7, and formation of the 5,5-fused DE ring system in steroids are all important factors determining the relative stabilities of the *trans* and *cis* CD ring junctions. Finally, biological testing provided valuable information suggesting that the structural moiety necessary for biological activity is the *cis* CD 15-keto functionality. Other changes in the structure, such as replacement of the additional E ring in the xestobergsterols with a simple cholesterol side chain, also produce active analogues, which may be potentially useful in the development of potent antihistamine agents.

5. Experimental section

5.1. General

All reactions were carried out under argon with the

exclusion of moisture. Reagents were purchased from Aldrich Chemical Company and were used without further purification unless otherwise noted. The following solvents and reagents were distilled from the indicated agent under argon: tetrahydrofuran (THF) and diethyl ether from sodium benzophenone ketyl; dichloromethane, benzene, and toluene from calcium hydride; and triethylamine from potassium hydroxide. Flash column chromatography was carried out in the indicated solvent system on 230–400 mesh silica gel. Analytical thin layer chromatography was done on Merck silica gel F_{254} 0.2 mm precoated plates. The proton nuclear magnetic resonance spectra (^{1}H NMR) were recorded on a Bruker ARX-400 spectrometer operating at 400.132 MHz. The ^{13}C NMR spectra were also recorded on a Bruker ARX-400 operating at 100.622 MHz. Spectra were taken in the indicated solvent at ambient temperature unless otherwise specified, and the chemical shifts are reported in parts per million (ppm) relative to the lock of the solvent used. Resonance patterns are reported with the following notations: app (apparent), b (broad), s (singlet), d (doublet), t (triplet), q (quartet), quin (quintet), and m (multiplet). The infrared (IR) spectra were recorded on a Nicolet 510 PCIR spectrometer and are reported in reciprocal centimeters (cm^{-1}). High-resolution mass spectra (MS) were recorded on a VG Autospec at the UCLA Mass Spectrometry Laboratory and are reported in *m/z* units for the most abundant peaks.

5.1.1. Methyl 3α,7α-dihydroxycholan-24-oate (9b). To a stirring solution the carboxylic acid **9a** (348 mg, 0.886 mmol) in refluxing methanol (15 mL) was added 4 drops of concentrated hydrochloric acid. The solution was cooled to 25°C and neutralized with saturated sodium bicarbonate. The volatile components were removed under reduced pressure and water was added. The mixture was extracted three times with ethyl acetate (3×5 mL). The combined organic extracts were dried over magnesium sulfate, filtered, and concentrated under reduced pressure to give the methyl ester **9b** (310 mg, 86%) as a white solid, which was used without further purification. ^{1}H NMR ($CDCl_3$, 200 MHz) δ: 3.91 (1H, m), 3.69 (3H, s), 3.50 (1H, m), 2.50–0.50 (28H, m), 0.92 (3H, d, *J*=7.0 Hz), 0.91 (3H, s), 0.66 (3H, s). FTIR (thin film): 3391, 2832, 2867, 1740, 1437, 1167, 1078 cm^{-1}.

5.1.2. Methyl 3α-[((1,1-dimethyl)ethyl)dimethylsilyloxy]-7α-hydroxycholan-24-oate (10). To a stirring solution of the diol **9b** (87 mg, 0.214 mmol) in DMF (1.5 mL) at 25°C was added imidazole (36 mg, 0.535 mmol) followed by *tert*-butyldimethylsilyl chloride (39 mg, 0.257 mmol) and the reaction was stirred overnight. Water was added and the mixture was extracted with ethyl acetate (3×5 mL). The combined organic extracts were dried over magnesium sulfate, filtered, and concentrated under reduced pressure. Flash column chromatography of the crude residue (silica gel, 4:1 hexanes:ethyl acetate) provided the silyl ether **10** (92 mg, 82%) as a clear glass. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 3.81 (1H, m), 3.64 (3H, s), 3.42 (1H, m), 1.85 (1H, ddd, *J*=15.3, 10.0, 5.0 Hz), 2.20 (1H, m), 2.10–0.50 (25H, m), 0.90 (3H, d, *J*=6.4 Hz), 0.87 (3H, s), 0.86 (9H, s), 0.63 (3H, s), 0.02 (6H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 174.7, 72.9, 68.5, 55.8, 51.5, 50.4, 42.7, 41.6, 40.1, 39.6, 39.5, 35.5, 35.4, 35.1, 34.6, 32.7, 31.1, 31.00, 30.98, 28.2, 26.0, 23.7, 22.8, 20.6, 18.3, 18.2, 11.8, −4.5, −4.6. FTIR (thin film): 3521, 2930, 2857, 1742, 1254, 1090, 835 cm^{-1}.

5.1.3. Methyl 3α-[((1,1-dimethyl)ethyl)dimethylsilyloxy]-7-ketocholan-24-oate (11a). To a stirring solution of the alcohol **10** (328 mg, 0.630 mmol) in dichloromethane (10 mL) at 25°C was added anhydrous potassium acetate followed by pyridinium chlorochromate (406 mg, 1.892 mmol) and the reaction was stirred overnight. Celite (400 mg) was added and the solution was diluted with ether (10 mL). The mixture was filtered through Celite and the volatile components were removed under reduced pressure. The residue was dissolved in ether and passed through a short plug of silica gel, eluting with ether. The ether was removed under reduced pressure to give the ketone **11a** (318 mg, 98%) as a white solid (mp 89–90°C). ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 3.65 (3H, s), 3.54 (1H, m), 2.81 (1H, dd, *J*=12.6, 6.0 Hz), 2.50–0.50 (25H, m), 1.16 (3H, s), 0.90 (3H, d, *J*=6.2 Hz), 0.85 (9H, s), 0.63 (3H, s), 0.02 (6H, s). ^{13}C NMR ($CDCl_3$, 50 MHz) δ: 211.9, 174.6, 71.6, 54.8, 51.5, 49.5, 48.9, 46.2, 45.5, 42.7, 42.5, 38.9, 37.7, 35.2, 35.2, 34.3, 31.1, 30.5, 28.3, 25.9, 24.9, 23.1, 21.7, 18.4, 18.2, 12.1 (3 high-field carbons unresolved). FTIR (thin film): 2934, 2861, 1742, 1713, 1462, 1377, 1252, 1167, 1092 cm^{-1}. High-resolution MS (EI, *m/z*): 519.3867, calcd for $C_{31}H_{55}O_4Si$ $(M+H)^+$ 519.3870.

5.1.4. 3α-[((1,1-Dimethyl)ethyl)dimethylsilyloxy]-7-ketocholan-24-oic acid (11b). To a stirring solution of the methyl ester **11a** (318 mg, 0.613 mmol) in methanol (8 mL) was added 10% KOH (aqueous, 8 mL) and the mixture was refluxed for 1 h. The mixture was cooled to 25°C, acidified to pH 3, and extracted with ether (310 mL). The combined organic extracts were dried over magnesium sulfate, filtered, and concentrated under reduced pressure to give the pure carboxylic acid **11b** (289 mg, 93%). ^{1}H NMR ($CDCl_3$, 200 MHz) δ: 3.56 (1H, m), 2.81 (1H, dd, *J*=12.6, 6.0 Hz), 2.50–0.50 (26H, m), 1.16 (3H, s), 0.91 (3H, d, *J*=5.7 Hz), 0.85 (9H, s), 0.63 (3H, s), 0.01 (6H, s). FTIR (thin film): 3500–2500, 2934, 2857, 1705, 1254, 1092, 909, 835 cm^{-1}.

5.1.5. Methyl 3α-[((1,1-dimethyl)ethyl)dimethylsilyloxy]-7β-hydroxycholan-24-oate (13). To a stirring solution of the ketone **11b** (289 mg, 0.572 mmol) in ammonia (25 mL), tetrahydrofuran (5 mL), and methanol (3 mL) cooled to −78°C was added lithium metal (250 mg) in small chunks. The solution was stirred for 20 min, quenched with ammonium chloride, and then allowed to warm to 25°C. Water was added, the mixture was acidified to a pH of 3, and extracted with ether (3×10 mL). The combined organic extracts were dried over magnesium sulfate, filtered, and concentrated under reduced pressure to give a 3:1 mixture of the 7β-alcohol **12** and the 7α-alcohol **10** (247 mg, 85%). The crude products were dissolved in ether (10 mL) at 0°C and a solution of diazomethane in ether was added dropwise until the starting material had disappeared by TLC. The reaction was quenched with ammonium chloride, water was added, and the mixture was extracted with ether (3×10 mL). The combined organic extracts were dried over magnesium sulfate, filtered, and concentrated under reduced pressure. Flash column chromatography (silica

gel, 4:1 hexanes:ethyl acetate) of the residue gave the pure 7β-alcohol **13** (57% from the ketone **11b**) as a clear glass. ^{1}H NMR ($CDCl_3$, 200 MHz) δ: 3.66 (3H, s), 3.55 (1H, m), 2.50–0.50 (28H, m), 0.92 (3H, s), 0.90 (3H, d, J= 6.2 Hz), 0.88 (9H, s), 0.66 (3H, s), 0.05 (6H, s). FTIR (thin film): 3391, 2932, 2859, 1742, 1453, 1373, 1252, 1082, 835 cm^{-1}.

5.1.6. Methyl 3α-[((1,1-dimethyl)ethyl)dimethylsilyloxy]-7β-nitrosyloxycholanoate (14). Through a stirring solution of the alcohol **13** (27 mg, 0.052 mmol) in pyridine (6 mL) at 25°C was bubbled excess nitrosyl chloride gas. The excess pyridine was removed by high-vacuum rotovaporator and the crude material was dissolved in ether and passed through a short plug of silica gel, eluting with ether. Concentration under reduced pressure gave the pure nitrite ester **14** (28 mg, 97%) as a clear glass. ^{1}H NMR ($CDCl_3$, 200 MHz) δ: 5.37 (1H, m), 3.65 (3H, s), 3.57 (1H, m), 2.50–0.50 (26H, m), 1.02 (3H, s), 0.93 (3H, d, J=6.2 Hz), 0.92 (9H, s), 0.63 (3H, s), 0.06 (6H, s).

5.1.7. 3α-[((1,1-Dimethyl)ethyl)dimethylsilyloxy]-5α,14α-cholestan-15α-ol (19). To a stirring solution of the steroidal olefin **18a** (35 mg, 0.070 mmol) in 5 mL of THF cooled to 0°C was added borane tetrahydrofuran complex (1.0 M, 279 μL, 0.279 mmol). The reaction mixture was stirred at 25°C for 12 h. The reaction mixture was cooled to 0°C and 279 μL of 10% NaOH was added dropwise followed by 279 μL of 30% hydrogen peroxide. The reaction was stirred vigorously for 1 h. Water was added and the products were extracted with ether (3×5 mL). The organic layers were combined and dried over anhydrous magnesium sulfate, filtered, and evaporated under reduced pressure to give a white solid. Flash column chromatography of the crude solid (silica gel, 20:1 hexanes:ether) gave the alcohol **19** (6 mg, 17%) as a clear glass. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 3.95 (2H, m), 2.00–0.50 (30H, m), 0.91 (3H, d, J=6.2 Hz), 0.88 (9H, s), 0.862 (3H, d, J=6.6 Hz), 0.858 (3H, d, J=6.6 Hz), 0.77 (3H, s), 0.68 (3H, s), 0.01 (6H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 74.0, 66.8, 64.0, 54.3, 53.8, 44.1, 40.5, 40.2, 39.5, 38.8, 36.7, 36.1, 36.0, 35.3, 35.1, 32.5, 32.4, 29.7, 28.5, 28.0, 25.0, 23.7, 22.8, 22.6, 20.7, 18.5, 18.1, 13.4, 11.5, −4.8 (1 high-field carbon unresolved). FTIR (thin film): 3335, 2930, 2855, 1472, 1252, 1059 cm^{-1}. High-resolution MS (EI, m/z): 517.4428, calcd for $C_{33}H_{62}O_2Si$ 517.4441.

5.1.8. 3α-[((1,1-Dimethyl)ethyl)dimethylsilyloxy]-5α,14α-cholestan-15-one (21). To a stirring solution of the alcohol **19** (4 mg, 0.008 mmol) in dichloromethane (5 mL) was added pyridinium chlorochromate (5 mg, 0.023 mmol) and the reaction was stirred for 2 h. The solution was diluted with an equal volume of ether and Celite (50 mg) was added. The solution was filtered and concentrated under reduced pressure to provide the ketone **21** (4 mg, 100%) as a clear glass. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 3.95 (1H, m), 2.51 (1H, dddd, J=13.2, 3.1, 3.1, 3.1 Hz), 2.42 (1H, dd, J=18.8, 8.7 Hz), 2.10 (1H, ddd, J=12.5, 3.4, 3.4 Hz), 1.90–0.60 (25H, m), 1.76 (1H, dd, J=18.7, 9.4 Hz), 0.98 (3H, d, J=6.4 Hz), 0.88 (9H, s), 0.864 (3H, d, J=6.6 Hz), 0.860 (3H, d, J=6.6 Hz), 0.75 (3H, s), 0.73 (3H, s), 0.01 (6H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 216.4, 66.8, 66.0, 53.9, 51.6, 42.4, 42.0, 39.9, 39.3, 39.0, 36.6, 36.1, 36.0, 35.4, 32.4, 31.9, 30.8, 29.7, 28.2, 28.0, 25.9, 23.8, 22.8, 22.5, 20.4, 19.0, 18.1, 13.0, 11.3, −4.8, −4.9. FTIR (thin film): 2953, 2928, 2855, 1742, 1462, 1385, 1372, 1252, 1057 cm^{-1}. High-resolution MS (EI, m/z): 517.4453, calcd for $C_{33}H_{61}O_2Si$ $(M+H)^+$ 517.4441.

5.1.9. 3α-Hydroxy-5α,14α-chlolestan-15-one (22). To a stirring solution of the silyl ether **21** (4 mg, 0.008 mmol) in ethanol (4 mL) at 25°C was added concentrated hydrochloric acid (several drops) and the reaction was stirred for 1 h. The ethanol was removed under reduced pressure and water was added. The mixture was extracted with ether (3×5 mL). The combined organic extracts were dried over magnesium sulfate, filtered, and concentrated under reduced pressure to yield the pure keto alcohol **22** (4 mg, 100%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 4.04 (1H, m), 2.65 (1H, dddd, J=13.1, 3.2, 3.2, 3.2 Hz), 2.43 (1H, dd, J=18.8, 8.6 Hz), 2.11 (1H, ddd, J=12.4, 3.3, 3.3 Hz), 1.90–0.50 (27H, m), 0.97 (3H, d, J=6.4 Hz), 0.863 (3H, d, J=6.6 Hz), 0.859 (3H, d, J=6.6 Hz), 0.78 (3H, s), 0.74 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 216.4, 66.5, 66.0, 53.9, 51.5, 42.4, 42.0, 39.9, 39.3, 39.1, 36.2, 36.0, 35.8, 35.4, 32.1, 31.9, 30.6, 29.7, 28.9, 28.1, 28.0, 23.8, 22.8, 22.5, 20.3, 19.0, 13.0, 11.1 (1 additional low-field carbon). FTIR (thin film): 3289, 2923, 2851, 1736, 1449, 1366, 999 cm^{-1}. High-resolution MS (EI, m/z): 402.3497, calcd for $C_{27}H_{46}O_2$ 402.3498.

5.1.10. 3α-Acetyloxy-14α,15α-epoxy-5α-cholestane (30). To a stirring solution of the olefinic alcohol **29a** and the saturated alcohol **29b** (55 mg, 0.142 mmol, combined) in pyridine at 25°C was added acetic anhydride (29 mg, 0.284 mmol). The solution was stirred for 18 h and then was quenched with ice chips. Water was added and the mixture was extracted with ether (3×5 mL). The combined organic extracts were dried over magnesium sulfate, filtered, and concentrated under reduced pressure. Column chromatography (silica gel, 3:1 hexanes:ethyl acetate) of the crude product gave a mixture of the unsaturated and saturated acetates (59 mg, 97%). To a stirring solution of the olefin (30 mg, 0.070 mmol) in chloroform (5 mL) at 0°C was added m-chloroperbenzoic acid (18 mg, 0.105 mmol) and the reaction was stirred for 1 h. Water was added and the mixture was extracted with ether (3×5 mL). The combined organic extracts were dried over magnesium sulfate, filtered, and concentrated under reduced pressure. Flash column chromatography of the crude residue (silica gel, 10:1 hexanes:ether) provided the epoxide **30** (31 mg, 100%) as a clear glass. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 4.99 (1H, m), 3.32 (1H, s), 2.30–0.60 (27H, m), 2.03 (3H, s), 1.85 (1H, m), 0.856 (3H, d, 6.6 Hz), 0.851 (3H, d, J=6.5 Hz), 0.847 (3H, s), 0.839 (3H, d, J=6.4 Hz), 0.81 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 170.8, 74.1, 70.0, 58.1, 50.1, 48.6, 41.1, 39.5, 39.0, 35.8, 35.8, 35.7, 33.7, 32.8, 32.7, 32.1, 32.0, 28.0, 27.4, 26.1, 25.3, 23.7, 22.8, 22.5, 21.5, 20.6, 18.7, 14.6, 11.2. FTIR (thin film): 2936, 2867, 1736, 1468, 1456, 1364, 1250, 1238, 1020 cm^{-1}. High-resolution MS (EI, m/z): 444.3607, calcd for $C_{29}H_{48}O_3$ 444.3603.

5.1.11. 3α-Acetyloxy-5α,14β-cholestan-15α-ol (31). To a stirring solution of the epoxide **30** (107 mg, 241 mmol) in glacial acetic acid (5 mL) at 25°C was added PtO_2 (107 mg) and the flask was evacuated using a high-vacuum pump. The

flask was back-filled with hydrogen gas from a balloon. This process of evacuating and back-filling was repeated two times and the reaction was stirred for 1 h. The solution was filtered through Celite and evaporated under reduced pressure to yield a crude oil. Flash column chromatography (silica gel, 6:1 hexanes:ether) of this oil provided the alcohol **31** (45 mg, 42%) as a clear glass. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 5.01 (1H, m), 4.26 (1H, dd, *J*=3.6, 3.7 Hz), 2.05 (3H, s), 1.50–0.80 (30H, m), 1.00 (3H, s), 0.92 (3H, d, *J*=6.3 Hz), 0.867 (3H, d, *J*=6.6 Hz), 0.864 (3H, d, *J*=6.6 Hz), 0.74 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 170.8, 74.3, 70.2, 56.0, 55.6, 49.5, 43.2, 40.4, 39.7, 39.5, 39.2, 36.1, 35.3, 33.8, 33.5, 32.9, 32.8, 31.6, 28.8, 28.0, 26.0, 24.5, 22.8, 22.6, 21.8, 21.6, 21.2, 20.3, 10.3. FTIR (thin film): 3497, 2932, 2857, 1736, 1373, 1366, 1269, 1256, 1237, 1020 cm^{-1}. High-resolution MS (EI, *m*/*z*): 446.3760, calcd for $C_{29}H_{50}O_3$ 446.3760.

5.1.12. 3α-Acetyloxy-5α,14β-cholestan-15-one (32). To a stirring solution of the alcohol **31** (30 mg, 0.067 mmol) in dichloromethane (5 mL) at 25°C was added pyridinium chlorochromate (29 mg, 0.134 mmol) and the reaction was stirred for 3 h. The solution was diluted with an equal volume of ether and Celite (50 mg) was added and the solution was filtered through Celite and concentrated under reduced pressure. Flash column chromatography of the residue (silica gel, 6:1 hexanes:ether) provided the ketone **32** (30 mg, 100%) as a clear glass. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 5.00 (1H, m), 2.51 (1H, dddd, *J*=13.2, 13.2, 13.2, 4.6 Hz), 2.34 (1H, dd, *J*=19.8, 10.0 Hz), 2.17 (1H, m), 2.12 (1H, m), 2.05 (3H, s), 1.92 (1H, m), 1.80–0.60 (27H, m), 1.16 (3H, s), 0.85 (9H, d, *J*=6.6 Hz), 0.74 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 220.8, 170.8, 70.0, 57.9, 48.4, 47.2, 42.1, 39.3, 39.1, 38.3, 37.6, 35.8, 33.5, 33.3, 32.9, 32.6, 31.8, 29.0, 28.5, 28.0, 25.9, 25.5, 22.7, 22.5, 21.6, 21.2, 19.2, 19.1, 11.2. FTIR (thin film): 2951, 2930, 2869, 1736, 1462, 1453, 1248, 1237 cm^{-1}. High-resolution MS (EI, *m*/*z*): 444.3605, calcd for $C_{29}H_{48}O_3$ 444.3603.

5.1.13. 3α-((4-Benzoyl)phenylacetyloxy)-5α-cholestan-6α-ol (36). To a stirring solution of the diol **35** (300 mg, 0.741 mmol) in THF (10 mL) at 25°C was added triphenylphosphine (389 mg, 1.482 mmol) and the carboxylic acid **16** (196 mg, 1.482 mmol) followed by the dropwise addition of diethyl azodicarboxylate (233 μL, 1.482 mmol). The reaction was stirred for 0.5 h and then quenched with water. The mixture was extracted with ether (3×10 mL). The combined organic layers were dried over magnesium sulfate, filtered, and concentrated under reduced pressure. Flash column chromatography of the residue (silica gel, 3:1 hexanes:ethyl acetate) provided the ester **36** (280 mg, 60%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.90–7.30 (9H, m), 5.11 (1H, m), 3.68 (2H, s), 3.29 (1H, ddd, *J*=10.6, 10.6, 4.3 Hz), 2.20–0.50 (30H, m), 0.88 (3H, d, *J*=6.5 Hz), 0.857 (3H, d, *J*=6.6 Hz), 0.855 (3H, d, *J*=6.6 Hz), 0.74 (3H, s), 0.62 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 196.0, 170.0, 139.3, 137.4, 136.1, 132.3, 130.3, 129.9, 129.3, 128.2, 70.2, 69.3, 56.1, 56.0, 53.6, 46.8, 42.4, 41.8, 41.6, 39.6, 39.4, 36.3, 36.0, 35.6, 34.0, 32.9, 28.0, 27.9, 27.0, 25.6, 24.0, 23.7, 22.7, 22.5, 20.6, 18.6, 12.4, 11.9. FTIR (thin film): 3497, 2944, 2869, 1732, 1659, 1607, 1279, 1468, 1447 cm^{-1}. High-resolution MS (EI, *m*/*z*): 626.4323, calcd for $C_{42}H_{58}O_4$ 626.4335.

5.1.14. 3α-((4-Benzoyl)phenylacetyloxy)-6α-[((1,1-dimethyl)ethyl)dimethylsilyloxy]-5α-cholestane (37). To a stirring solution of the alcohol **36** (143 mg, 0.228 mmol) in dry *N*,*N*-dimethylformamide (5 mL) at 25°C was added imidazole (31 mg, 0.456 mmol) followed by *tert*-butyldimethylsilyl chloride (38 mg, 0.251 mmol) and the reaction was stirred for 4 h. Water was added and the mixture extracted with ether (3×10 mL). The combined organic layers were dried over magnesium sulfate, filtered, and concentrated under reduced pressure. Flash column chromatography of the residue (silica gel, 8:1 hexanes:ether) provided the silyl ether **37** (155 mg, 92%) as a clear glass. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.90–7.70 (4H, m), 7.65–7.30 (5H, m), 5.09 (1H, m), 3.69 (2H, s), 3.29 (1H, ddd, *J*=10.6, 10.6, 4.4 Hz), 1.90–0.60 (29H, m), 0.88 (3H, d, *J*=6.7 Hz), 0.856 (3H, d, *J*=6.6 Hz), 0.852 (3H, d, *J*=6.6 Hz), 0.82 (9H, s), 0.75 (3H, s), 0.63 (3H, s), −0.01 (3H, s), −0.02 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 195.8, 169.9, 139.4, 137.7, 136.0, 132.2, 130.4, 129.9, 129.3, 128.2, 70.5, 70.2, 56.1, 53.7, 46.8, 42.5, 42.0, 41.9, 39.8, 39.6, 36.4, 36.2, 35.8, 34.1, 33.2, 28.2, 28.0, 27.5, 25.9, 25.8, 24.1, 23.9, 22.9, 22.7, 22.6, 20.7, 18.7, 18.0, 12.5, 12.1, −3.8, −4.7. FTIR (thin film): 2936, 2857, 1732, 1661, 1609, 1472, 1447 cm^{-1}. High-resolution MS (CI, *m*/*z*): 741.5276, calcd for $C_{48}H_{73}O_4Si$ $(M+H)^+$ 741.5278.

5.1.15. 6α-[((1,1-Dimethyl)ethyl)dimethylsilyloxy]-3α-((4-hydroxyphenylmethyl)-phenylacetyloxy)-5α-cholest-14-ene (38), Lactone (39a), and Lactone (39b). The ester **37** (604 mg, 0.815 mmol) was photolyzed (450 W mercury arc lamp, pyrex filter) in degassed benzene (815 mL) for 10 h at 25°C. The solvent was removed under reduced pressure and the residue subjected to column chromatography to give the olefin **38** (181 mg, 30%), the lactone **39a** (120 mg, 20%), and lactone **39b** (120 mg, 20%) as clear glasses.

39a: ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.80–7.00 (9H, m), 5.10 (1H, s), 4.99 (1H, m), 3.63 (1H, d, *J*=13.1 Hz), 3.49 (1H, d, *J*=13.1 Hz), 3.28 (1H, ddd, *J*=10.6, 10.6, 4.4 Hz), 2.43 (1H, d, *J*=14.9 Hz), 2.20 (1H, d, *J*=14.9 Hz), 2.10–0.60 (29H, m), 0.91 (3H, d, *J*=5.3 Hz), 0.886 (3H, d, *J*=6.2 Hz), 0.881 (3H, d, *J*=6.5 Hz), 0.878 (3H, s), 0.73 (3H, s), 0.70 (3H, s), 0.67 (3H, s), 0.27 (3H, s), −0.07 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 170.7, 149.2, 145.1, 133.3, 131.3, 128.8, 128.0, 127.0, 126.3, 126.0, 125.3, 78.1, 71.8, 69.0, 57.2, 56.3, 56.0, 53.8, 46.6, 42.9, 42.6, 41.8, 39.8, 39.5, 36.7, 36.2, 35.9, 34.6, 33.3, 31.6, 28.8, 28.2, 28.1, 28.0, 27.7, 25.8, 24.2, 23.9, 22.9, 22.8, 22.7, 22.6, 20.7, 18.7, 14.2, 12.3, 12.1, −2.0, −4.3 (3 additional high-field carbons). FTIR (thin film): 3409, 2946, 2861, 1732, 1468, 1381, 1250 cm^{-1}. High-resolution MS (EI, *m*/*z*): 741.5262, calcd for $C_{48}H_{73}O_4Si$ $(M+H)^+$ 741.5278.

39b: ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.80–7.00 (9H, m), 5.04 (1H, m), 3.64 (1H, d, *J*=12.7 Hz), 3.42 (1H, d, *J*=12.7 Hz), 3.23 (1H, ddd, *J*=10.3, 10.3, 4.5 Hz), 2.95 (1H, d, *J*=14.6 Hz), 2.20–0.70 (30H, m), 2.07 (1H, d, *J*=14.6 Hz), 1.08 (3H, s), 0.92 (3H, d, *J*=6.5 Hz), 0.874 (3H, d, *J*=6.6 Hz), 0.870 (3H, d, *J*=6.6 Hz), 0.75 (3H, s), 0.67 (3H, s), 0.44 (3H, s), 0.03 (3H, s), −0.19 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 170.7, 150.2, 145.5, 132.4, 129.9, 128.8, 128.3, 127.4, 127.0, 125.9, 125.6, 80.6, 70.0, 69.3, 56.3, 56.3, 54.0, 47.5, 46.3, 42.8, 42.6, 42.4, 39.9, 39.5,

36.5, 36.2, 35.9, 34.1, 33.5, 28.2, 28.0, 27.7, 27.4, 26.0, 24.2, 23.9, 22.8, 22.6, 21.2, 20.7, 20.6, 18.7, 12.4, 12.1, −2.9, −6.3. FTIR (thin film): 3505, 2944, 2869, 1732, 1466, 1381, 1248 cm^{-1}. High-resolution MS (EI, *m/z*): 739.5114, calcd for $C_{48}H_{71}O_4Si$ $(M-H)^+$ 739.5122.

5.1.16. 3β-Phenylmethoxy-5α-cholestan-6α-ol (41). To a stirring solution of the olefin **40** (401 mg, 0.841 mmol) in THF (5 mL) at 0°C was added borane tetrahydrofuran complex (1.0 M, 4.2 mL, 4.2 mmol) and the solution was stirred overnight at 25°C. The solution was cooled to 0°C and 10% sodium hydroxide (4.2 mL) was added dropwise followed by 30% hydrogen peroxide (4.2 mL). The mixture was stirred vigorously for several hours. Water was added and the mixture was extracted with ether (3×15 mL). The combined organic extracts were dried over magnesium sulfate, filtered, and concentrated under reduced pressure. Flash column chromatography of the residue (silica gel, 4:1 hexanes:ethyl acetate) gave the alcohol **41** (380 mg, 89%) as a white solid. ^1H NMR ($CDCl_3$, 200MHz) δ: 7.50–7.10 (5H, m), 4.61 (1H, d, *J*=23.7 Hz), 4.53 (1H, d, *J*=23.7 Hz), 3.60–3.10 (2H, m), 2.50–2.25 (1H, m), 2.30–0.50 (38H, m), 0.89 (3H, s), 0.65 (3H, s). ^{13}C NMR ($CDCl_3$, 50 MHz) δ: 139.1, 128.4, 127.6, 127.4, 76.5, 70.0, 69.5, 56.2, 53.9, 51.7, 42.6, 41.7, 39.9, 39.6, 37.4, 36.6, 35.8, 28.8, 28.2, 28.2, 28.1, 24.3, 23.9, 22.9, 22.8, 22.6, 21.2, 18.7, 13.5, 12.1 (2 high-field carbons unresolved). FTIR (thin film): 3546, 2946, 1497, 1464, 1375, 1111, 1042, 909, 734 cm^{-1}.

5.1.17. 6α-Acetyloxy-3β-phenylmethoxy-5α-cholestane (42). To a stirring solution of the alcohol **41** in pyridine (20 mL) at 25°C was added acetic anhydride (310 μL, 3.24 mmol) and the reaction was stirred overnight. Water was added and the mixture was extracted with ether (3×20 mL). The organic layers were dried over magnesium sulfate, filtered, and concentrated under reduced pressure. Excess pyridine was removed by high-vacuum rotovaporation. Flash column chromatography of the residue (silica gel, 100% $CHCl_3$) provided the ester **42** (1.21 g, 84%) as a white solid (mp 146–148°C). ^1H NMR ($CDCl_3$, 200 MHz) δ: 7.50–7.10 (5H, m), 4.67 (1H, ddd, *J*=10.4, 10.4, 4.6 Hz), 4.57 (1H, d, *J*=23.8 Hz), 4.51 (1H, d, *J*=23.8 Hz), 3.31 (1H, m), 2.30–0.50 (41H, m), 2.02 (3H, s), 0.66 (3H, s). ^{13}C NMR ($CDCl_3$, 50 MHz) δ: 170.6, 139.1, 128.4, 127.6, 127.4, 77.9, 72.6, 70.1, 56.3, 53.8, 48.7, 42.7, 39.9, 39.6, 37.8, 37.2, 36.9, 36.2, 35.8, 34.2, 29.2, 28.2, 28.0, 27.9, 24.2, 24.0, 22.9, 22.7, 21.3, 21.2, 18.8, 13.4, 12.1. FTIR (thin film): 3031, 2944, 2869, 1740, 1455, 1375, 1242, 1026 cm^{-1}. High-resolution MS (EI, *m/z*): 536.4232, calcd for $C_{36}H_{55}O_3$ $(M-H)^+$ 536.4229.

5.1.18. 6α-Acetyloxy-5α-cholestan-3β-ol (43). The benzyl ether **42** (492 mg, 0.917 mmol) was dissolved in THF:ethanol (10:1, 12 mL) at 25°C and activated palladium on carbon catalyst (49 mg) was added. The flask was evacuated and back-filled with hydrogen gas from a balloon. This process of evacuation and back-filling was repeated two times and the reaction was stirred for 2 h. The mixture was filtered through a small plug of Celite and concentrated under reduced pressure to give the pure alcohol **43** (375 mg, 92%) as a white solid (mp 84°C). ^1H NMR ($CDCl_3$, 200 MHz) δ: 4.67 (1H, ddd, *J*=10.4, 10.4, 4.6 Hz), 3.55 (1H, m), 2.30–0.50 (42H, m), 2.03 (3H, s), 0.64 (3H, s). ^{13}C NMR ($CDCl_3$, 50 MHz) δ: 170.7, 72.6, 70.7, 60.4, 56.2, 53.7, 48.7, 42.6, 39.8, 39.5, 37.7, 37.2, 36.6, 36.1, 35.7, 34.1, 32.1, 31.1, 28.2, 28.0, 24.1, 23.8, 22.8, 22.6, 21.2, 18.7, 14.2, 13.2, 12.0. FTIR (thin film): 3395, 2946, 2869, 1740, 1242. High-resolution MS (EI, *m/z*): 446.3763, calcd for $C_{29}H_{50}O_3$ 446.3760.

5.1.19. 3α-((-4-Benzoyl)phenylacetyloxy)-6α-acetyloxy-5α-cholestane (44). To a stirring solution of the alcohol **43** (250 mg, 0.560 mmol) in THF (10 mL) at 25°C was added triphenyl-phosphine (294 mg, 1.120 mmol) and the carboxylic acid **16** (161 mg, 0.672 mmol) followed by the dropwise addition of DEAD (176 μL, 1.120 mmol) and the reaction was stirred for 1 h. Water was added and the mixture was extracted with ether (3×5 mL). The combined organic extracts were dried over magnesium sulfate, filtered, and concentrated under reduced pressure. Flash column chromatography of the crude residue (silica gel, 6:1 hexanes:ethyl acetate) provided the benzophenone ester **44** (322 mg, 86%) as a clear glass (mp 56–57°C). $[\alpha]_D^{25}=+18.3°$ (*c* 0.75, CH_2Cl_2). ^1H NMR ($CDCl_3$, 400 MHz) δ: 7.85–7.63 (4H, m), 7.60–7.48 (1H, m), 7.48–7.30 (4H, m), 5.05 (1H, m), 4.57 (1H, ddd, *J*=10.4, 10.4, 4.3 Hz), 3.69 (2H, s), 2.10–0.40 (29H, m), 1.95 (3H, s), 0.873 (3H, d, *J*=5.4 Hz), 0.841 (6H, d, *J*=6.4 Hz), 0.79 (3H, s), 0.60 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 195.8, 170.7, 169.9, 139.4, 137.6, 136.2, 132.4, 130.4, 129.9, 129.3, 128.3, 72.5, 70.0, 56.1, 56.1, 53.6, 44.0, 42.6, 42.0, 39.7, 39.5, 37.6, 36.7, 36.1, 35.7, 33.9, 32.9, 28.1, 28.0, 27.1, 25.6, 24.0, 23.8, 22.8, 22.6, 21.2, 20.6, 18.7, 12.4, 12.0. FTIR (thin film): 2948, 2869, 1732, 1661, 1607, 1447, 1375, 1244, 1148, 756 cm^{-1}. High-resolution MS (CI, *m/z*): 669.4515, calcd for $C_{44}H_{61}O_5$ $(M+H)^+$ 669.4519.

5.1.20. 3α,6α-Diacetyloxy-14α,15α-epoxy-5α-cholestane (47). The benzophenone ester **44** (444 mg, 0.664 mmol) in purified, degassed benzene (664 mL) at 25°C was photolyzed using a 450 W mercury arc lamp for 10 h. The mixture was concentrated under reduced pressure to give a crude oil. The crude oil was dissolved in 10% KOH (4 mL), ethanol (12 mL) and THF (4 mL) and the mixture stirred at 25°C for 18 h. Water was added and the mixture was extracted with ether (3×20 mL). The combined organic extracts were dried over magnesium sulfate, filtered, and concentrated under reduced pressure to give a pale yellow solid. The crude olefinic diol was dissolved in pyridine (5 mL) at 25°C and excess acetic anhydride was added and the mixture was stirred overnight. Water was added and the mixture was extracted with ether (3×5 mL). The combined organic extracts were dried over magnesium sulfate, filtered, and concentrated under reduced pressure. Flash column chromatography (silica gel, 8:1 hexanes:ethyl acetate) of the crude solid gave a mixture of the olefinic diacetate **46a** and the saturated diacetate **46b** (220 mg, 68% combined yield). To a stirring solution of the olefin mixture (116 mg, 0.238 mmol) in chloroform (5 mL) cooled to 0°C was added *m*-chloroperbenzoic acid (62 mg, 0.357) and the reaction was stirred for approximately 1 h. Saturated sodium thiosulfate (0.1 mL) was added followed by water and the mixture was extracted with dichloromethane (2×10 mL). The combined organic layers were dried over magnesium sulfate, filtered, and evaporated under reduced pressure to

yield a crude oil. Flash column chromatography (silica gel, 10:1 hexanes:ethyl acetate) of the crude oil provided the epoxide **47** (109 mg, 91% based on the amount of olefin as judged by ^{1}H NMR in the previous step) as a colorless glass. $[\alpha]_D^{25}=+51.3°$ (*c* 0.75, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 4.99 (1H, m), 4.57 (1H, ddd, *J*=11.3, 11.3, 4.6 Hz), 3.25 (1H, m), 2.24 (1H, ddd, *J*=12.1, 12.1, 4.1 Hz), 2.10–0.60 (40H, m), 2.00 (3H, s), 1.94 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 170.9, 170.4, 73.5, 72.3, 68.8, 58.2, 49.4, 48.5, 43.1, 41.0, 39.4, 36.8, 35.7, 35.4, 33.6, 32.7, 31.9, 31.2, 30.8, 27.9, 27.1, 25.6, 23.6, 22.8, 22.5, 21.5, 21.2, 20.4, 18.7, 14.5, 12.3. FTIR (thin film): 2951, 2872, 1738, 1240, 1022 cm^{-1}.

5.1.21. 3α,6α-Diacetyloxy-5α,14β-cholestan-15α-ol (48). To a stirring solution of the epoxide **47** (95 mg, 197 mmol) in glacial acetic acid (5 mL) was added Pt (95 mg) and the flask was evacuated using a high-vacuum pump. The flask was back-filled with hydrogen gas from a balloon. This process of evacuating and back-filling was repeated two times and the reaction was allowed to stir at 25°C for 12 h. The solution was filtered through Celite and evaporated under reduced pressure to yield a crude oil. Flash column chromatography (silica gel, 6:1 hexanes:ethyl acetate) of the crude oil provided the alcohol **48** (42 mg, 44%) as a clear glass. $[\alpha]_D^{25}=+75.8°$ (*c* 1.2, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 5.05 (1H, m), 4.64 (1H, ddd, *J*=8.6, 8.6, 4.5 Hz), 4.22 (1H, dd, *J*=3.5, 3.5 Hz), 2.10–0.60 (28H, m), 2.05 (3H, s), 2.01 (3H, s), 0.98 (3H, s), 0.90 (3H, d, *J*=6.4 Hz), 0.85 (3H, d, *J*=5.2 Hz), 0.84 (3H, d, *J*=6.6 Hz), 0.79 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 171.0, 170.7, 74.1, 73.3, 69.1, 55.6, 55.2, 48.3, 43.7, 43.6, 42.8, 40.4, 39.5, 39.4, 37.0, 37.0, 35.2, 33.4, 32.8, 32.2, 28.0, 27.3, 25.6, 24.5, 22.8, 22.6, 21.7, 21.3, 21.1, 20.2, 11.7. FTIR (thin film): 3530, 2951, 2870, 1736, 1466, 1248, 1022 cm^{-1}.

5.1.22. 3α,6α-Diacetyloxy-5α,14β-cholestan-15-one (49). To a stirring solution of the alcohol **48** (31 mg, 0.061 mmol) in dichloromethane (5 mL) at 25°C was added pyridinium chlorochromate (26 mg, 0.122 mmol) and the reaction was stirred for 3 h. The solution was diluted with an equal volume of ether and Celite (50 mg) was added. The solution was filtered and concentrated under reduced pressure. Flash column chromatography of the crude residue (silica gel, 8:1 hexanes:ethyl acetate) provided the ketone **49** (31 mg, 84%) as a clear glass. $[\alpha]_D^{25}=+37.2°$ (*c* 1.2, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 5.04 (1H, m), 4.52 (1H, ddd, *J*=8.6, 8.6, 4.5 Hz), 2.54 (1H, bddd, *J*=11.4, 8.6, 8.6 Hz), 2.10–0.60 (29H, m), 2.06 (3H, s), 2.00 (3H, s), 1.14 (3H, s), 0.85 (9H, d, *J*=6.7 Hz), 0.80 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 220.4, 171.2, 170.7, 73.1, 68.9, 57.0, 48.3, 46.4, 43.0, 42.0, 39.3, 38.0, 37.4, 36.8, 34.5, 33.3, 32.6, 31.9, 31.7, 27.9, 27.2, 25.5, 22.7, 22.5, 21.6, 21.3, 21.0, 19.2, 19.0, 12.3 (1 high-field carbon unresolved). FTIR (thin film): 2950, 2870, 1734 (broad), 1466, 1373, 1437, 1364, 1244, 1022 cm^{-1}.

5.1.23. 3β-Acetyloxycholest-5-en-7-one (50). A mixture of the olefin **34** (2.158 g, 5.034 mmol) and ruthenium trichloride monohydrate (7 mg) in cyclohexane:water (5:1, 30 mL) was stirred at 25°C. *tert*-Butyl hydroperoxide (70% aqueous, 6.52 mL) was added dropwise over 6 h and the mixture was allowed to stir for an additional 18 h. Sodium sulfite (2.158 g) was added and the mixture allowed to stir for 1 h. Water was added and the mixture was extracted with ether (3×30 mL). The combined organic extracts were dried over magnesium sulfate, filtered, and concentrated under reduced pressure. Flash column chromatography (silica gel, 7:1 hexanes:ethyl acetate) of the residue provided the enone **50** (1.409 g, 63%) as a white solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 5.67 (1H, d, *J*=1.0 Hz), 4.69 (1H, dddd, *J*=11.4, 11.4, 4.6, 4.6 Hz), 2.60–2.30 (3H, m), 2.20 (1H, dd, *J*=10.7, 10.7 Hz), 2.10–0.50 (22H, m), 2.02 (3H, s), 1.19 (3H, s), 0.90 (3H, d, *J*=6.5 Hz), 0.840 (3H, d, *J*=6.6 Hz), 0.836 (3H, d, *J*=6.6 Hz), 0.66 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 201.9, 170.2, 163.8, 126.7, 72.2, 54.8, 49.9, 49.8, 45.4, 43.1, 39.5, 38.6, 38.3, 37.7, 36.2, 36.0, 35.7, 28.5, 28.0, 27.4, 26.3, 23.8, 22.8, 22.6, 21.2, 21.2, 18.9, 17.2, 12.0. FTIR (thin film): 2951, 1728, 1672, 1636, 1468, 1248, 1038, 911, 731 cm^{-1}.

5.1.24. 3β-Acetyloxycholest-5-en-7β-ol (51). To a stirring solution of the enone **50** (1.150 g, 2.598 mmol) in dichloromethane:methanol (4:1, 30 mL) cooled to −78°C was added cerium trichloride heptahydrate (1.936 g, 5.196 mmol) followed by sodium borohydride (0.197 g, 5.196 mmol). The solution was stirred and allowed to warm to 25°C slowly. The solution was acidified with 10% HCl and extracted with ether (3×100 mL). The combined organic extracts were dried over magnesium sulfate, filtered, and concentrated under reduced pressure to yield the allylic alcohol **51** (1.070 g, 93%) as a white solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 5.28 (1H, s), 4.59 (1H, m), 3.81 (1H, d, *J*=7.4 Hz), 2.50–2.20 (2H, m), 2.20–0.50 (27H, m), 2.00 (3H, s), 1.03 (3H, s), 0.89 (3H, d, *J*=6.3 Hz), 0.84 (6H, d, *J*=6.6 Hz), 0.66 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 170.5, 142.2, 126.4, 73.4, 73.1, 55.9, 55.4, 48.2, 42.9, 40.7, 39.52, 39.50, 37.6, 36.7, 36.5, 36.2, 35.7, 28.5, 28.0, 27.7, 26.4, 23.8, 22.8, 22.6, 21.4, 21.0, 19.1, 18.8, 11.8. FTIR (thin film): 3328, 2944, 2870, 2853, 1732, 1468, 1375, 1248, 1138, 1036 cm^{-1}.

5.1.25. 3β-Acetyloxy-7β-[((1,1-dimethyl)ethyl)dimethylsilyloxy]-cholest-5-ene (52). To a stirring solution of the alcohol **51** (219 mg, 0.491 mmol) in DMF (10 mL) at 25°C was added imidazole (50 mg, 0.737 mmol) followed by *tert*-butyl dimethylsilyl chloride (185 mg, 1.228 mmol) and the reaction was stirred for 18h. Water was added and the mixture was extracted with ether (3×5 mL). The combined organic extracts were dried over magnesium sulfate, filtered and concentrated under reduced pressure. Flash column chromatography of the crude residue (silica gel, 20:1 hexanes: ether) afforded the olefin **52** (269 mg, 98%) as a clear glass. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 5.29 (1H, s), 4.61 (1H, m), 3.93 (1H, d, *J*=7.8 Hz), 2.40–2.20 (2H, m), 2.20–0.50 (24H, m), 2.01 (3H, s), 1.04 (3H, s), 0.90 (3H, d, *J*= 6.5 Hz), 0.86 (9H, s), 0.852 (3H, d, *J*=6.6 Hz), 0.848 (3H, d, *J*=6.6 Hz), 0.66 (3H, s), 0.05 (3H, s), 0.04 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 170.4, 140.9, 127.4, 74.6, 73.5, 56.2, 55.5, 48.4, 43.0, 40.5, 39.6, 39.5, 37.8, 36.8, 36.4, 36.2, 35.8, 28.5, 28.0, 27.8, 26.8, 26.3, 25.7, 23.8, 22.8, 22.6, 21.4, 21.1, 18.9, 18.8, 18.2, 11.9, −2.6, −3.3. FTIR (thin film): 2932, 2855, 1736, 1470, 1443, 1375, 1248, 1057, 1088 cm^{-1}. High-resolution MS (EI, *m*/*z*): 558.4469, calcd for $C_{35}H_{62}O_3Si$ 558.4468.

5.1.26. 7β-[((1,1-Dimethyl)ethyl)dimethylsilyloxy]-5α-cholestan-6α,3β-diol (53) and 6α-[((1,1-dimethyl)-ethyl)dimethylsilyloxy]-5α-cholestan-3β,7β-diol (54). To a stirring solution of the olefin **52** (265 mg, 0.474 mmol) in THF (10 mL) at 25°C was added borane tetrahydrofuran complex (1.0 M, 2.37 mL, 2.371 mmol) and the reaction was stirred for 18 h. 3 mL of 10% sodium hydroxide was added followed by the addition of 30% hydrogen peroxide and the mixture was stirred for 1 h. Water was added and the mixture was extracted with ether (3×5 mL). The combined organic extracts were dried over magnesium sulfate, filtered, and concentrated under reduced pressure. Flash column chromatography (silica gel, 3:1 hexanes:ethyl acetate) of the crude solid provided the diol **53** (104 mg, 41%) and the diol **54** (100 mg, 39%) as clear glasses.

53: ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 3.54 (1H, m), 3.29 (1H, dd, *J*=8.8, 8.4 Hz), 3.23 (1H, dd, *J*=10.3, 8.3 Hz), 2.30–0.50 (32H, m), 0.89 (9H, s), 0.89 (3H, d, *J*=6.5 Hz), 0.851 (3H, d, *J*=6.6 Hz), 0.846 (3H, d, *J*=6.6 Hz), 0.82 (3H, s), 0.65 (3H, s), 0.14 (3H, s), 0.12 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 83.4, 74.8, 71.0, 56.5, 55.4, 52.8, 48.2, 43.6, 42.0, 40.0, 39.5, 37.3, 36.2, 35.8, 35.1, 32.8, 30.8, 28.4, 28.0, 27.5, 26.8, 23.9, 22.8, 22.6, 21.8, 19.0, 18.8, 13.6, 12.4, −1.4, −2.3. FTIR (thin film): 3391, 2853, 1472, 1385, 1252, 1096 cm^{-1}. High-resolution MS (EI, *m/z*): 535.4546, calcd for $C_{33}H_{63}O_3Si$ $(M+H)^+$ 535.4546.

54: ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 3.53 (1H, m), 3.28 (1H, dd, *J*=10.3, 8.2 Hz), 3.08 (1H, dd, *J*=8.3, 8.2 Hz), 2.20–0.50 (32H, m), 0.91 (9H, s), 0.90 (3H, d, *J*=6.5 Hz), 0.857 (3H, d, *J*=6.6 Hz), 0.852 (3H, d, *J*=6.6 Hz), 0.83 (3H, s), 0.67 (3H, s), 0.12 (3H, s), 0.09 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 80.6, 71.3, 56.2, 55.4, 52.3, 48.1, 43.6, 40.9, 40.0, 39.5, 37.5, 36.2, 35.8, 35.7, 33.4, 31.0, 28.6, 28.0, 27.0, 26.2, 23.9, 22.8, 22.6, 21.5, 18.8, 18.4, 13.7, 12.3, −3.4, −3.8. FTIR (thin film): 3613, 3384, 2951, 2857, 1471, 1253, 1125, 1092 cm^{-1}.

5.1.27. 3β,7β-Diacetyloxycholest-5-ene (55). To a stirring solution of the allylic alcohol **51** (1.314 g, 2.955 mmol) in pyridine (10 mL) at 25°C was added acetic anhydride (0.418 mL, 4.432 mmol) followed by DMAP (4 mg). The reaction was stirred overnight and then ice chips were added. Water was added and the mixture was extracted with ether (3×20 mL). The combined organic extracts were dried over magnesium sulfate, filtered and concentrated under reduced pressure. The excess pyridine was removed by a high-vacuum rotovaporator to provide the allylic acetate **55** (1.343 g, 93%) as a clear glass. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 5.19 (1H, bs), 4.98 (1H, d, *J*=8.6 Hz), 4.54 (1H, m), 2.40–2.20 (2H, m), 2.10–0.50 (24H, m), 1.97 (3H, s), 1.96 (3H, s), 1.03 (3H, s), 0.86 (3H, d, *J*=6.5 Hz), 0.814 (3H, d, *J*=6.6 Hz), 0.810 (3H, d, *J*=6.6 Hz), 0.64 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 170.9, 170.2, 144.1, 122.3, 75.4, 73.2, 55.5, 55.4, 48.1, 42.8, 39.4, 39.3, 37.5, 36.5, 36.4, 36.1, 35.6, 28.4, 28.0, 27.6, 25.1, 23.8, 22.8, 22.5, 21.6, 21.3, 21.0, 19.0, 18.7, 11.8 (1 high-field carbon unresolved). FTIR (thin film): 2948, 2870, 2857, 1736, 1732 cm^{-1}.

5.1.28. 5α-Cholestan-3β,6α,7β-triol (56). To a stirring solution of the olefin **55** (1.010 g, 2.075 mmol) at 0°C in THF (10 mL) was added borane–tetrahydrofuran complex (1.0 M, 8.3 mL, 8.300 mmol) and the mixture was allowed to warm to 25°C and stir overnight. The solution was cooled to 0°C and 10% NaOH (8 mL) was added followed by 30% hydrogen peroxide (8 mL) and the mixture was stirred vigorously for 2 h. Water was added and the mixture was extracted with ether (3×30 mL). The combined organic extracts were dried over magnesium sulfate, filtered and concentrated under reduced pressure to yield a white solid. Flash column chromatography of the crude residue (silica gel, 12:1 chloroform:methanol) provided the triol **56** (700 mg, 80%) as a white solid. ^{1}H NMR (acetic acid-d_4, 400 MHz) δ: 3.63 (1H, m), 3.39 (1H, dd, *J*=8.8, 10.8 Hz), 3.21 (1H, dd, *J*=9.5, 9.1 Hz), 2.30–0.50 (30H, m), 0.95 (3H, d, *J*=6.5 Hz), 0.875 (3H, s), 0.875 (3H, d, *J*=6.6 Hz), 0.872 (3H, d, *J*=6.5 Hz), 0.70 (3H, s). ^{13}C NMR ($CDCl_3$ with acetic acid-d_4, 100 MHz) δ: 80.3, 74.6, 70.9, 55.9, 55.3, 52.1, 47.6, 43.4, 40.8, 39.8, 39.5, 37.2, 36.2, 35.7, 35.6, 31.9, 30.2, 28.6, 28.0, 26.8, 23.8, 22.8, 22.5, 21.4, 18.8, 13.4, 12.1. FTIR (thin film): 3339, 2950, 2869, 1470, 1445, 1375, 1368, 1090, 1053, 737 cm^{-1}.

5.1.29. 3β,6α,7β-Triacetyloxy-5α-cholestane (57). To a stirring solution of the triol **56** (21 mg, 0.050 mmol) in dichloromethane (1 mL) at 25°C was added acetic anhydride (21 μL, 0.225 mmol) followed by trimethylsilyl triflate (1 μL) and the reaction mixture was stirred for 30 min. Saturated sodium bicarbonate was added and the mixture allowed to stir for an additional 30 min. The mixture was extracted with dichloromethane (3×10 mL) and the combined organic extracts were dried over magnesium sulfate, filtered, and concentrated under reduced pressure. Flash column chromatography of the residue (silica gel, 5:1 hexanes:ethyl acetate) yielded the triacetate **57** (27 mg, 100%) as a white solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 4.84 (1H, dd, *J*=10.0, 10.0 Hz), 4.66 (1H, dd, *J*=10.0, 10.0 Hz), 4.53 (1H, dddd, *J*=11.3, 11.3, 4.9, 4.9 Hz), 2.20–0.50 (27H, m), 2.01 (3H, s), 1.99 (3H, s), 1.95 (3H, s), 0.95 (3H, s), 0.89 (3H, d, *J*=6.5 Hz), 0.852 (3H, d, *J*=6.6 Hz), 0.847 (3H, d, *J*=6.6 Hz), 0.66 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 170.9, 170.8, 170.5, 77.9, 74.5, 72.7, 55.0, 54.7, 51.7, 46.0, 43.6, 39.4, 39.4, 39.1, 36.7, 36.1, 35.8, 35.5, 28.4, 28.3, 28.0, 27.0, 24.8, 23.7, 22.8, 22.6, 21.5, 21.4, 21.3, 20.9, 18.8, 13.3, 12.0. FTIR (thin film): 2953, 2869, 1746, 1468, 1449, 1375, 1248, 1240, 1034 cm^{-1}.

5.1.30. 6α,7β-Diacetyloxy-5α-cholestan-3β-ol (58). To a stirring solution of the triacetate **57** (10 mg, 0.018 mmol) in THF:ethanol (1:2, 1 mL) was added 10% NaOH solution (4 drops, 0.055 mmol) and the reaction mixture was stirred at 0°C for 1 h. 10% HCl was added and the mixture was extracted with ether (3×2 mL). The combined organic extracts were dried over magnesium sulfate, filtered, and concentrated under reduced pressure. Flash column chromatography of the residue (silica gel, 1:1:0.25 hexanes:ethyl acetate:chloroform) yielded the alcohol **58** (9 mg, 92%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 4.83 (1H, dd, *J*=11.2, 9.3 Hz), 4.72 (1H, dd, *J*=9.9, 9.3 Hz), 3.51 (1H, dddd, *J*=11.1, 11.1, 4.6, 4.6 Hz), 2.30–0.50 (28H, m), 1.98 (3H, s), 1.94 (3H, s), 0.93 (3H, s), 0.88 (3H, d, *J*=6.5 Hz), 0.840 (3H, d, *J*=6.6 Hz), 0.835 (3H, d, *J*=6.6 Hz), 0.65 (3H, s). ^{13}C NMR

($CDCl_3$, 100 MHz) δ: 171.0, 170.8, 78.0, 74.6, 70.7, 55.0, 54.8, 51.8, 46.2, 43.6, 39.44, 39.43, 39.1, 37.0, 36.1, 35.8, 35.5, 32.1, 31.0, 28.4, 28.0, 24.9, 23.7, 22.8, 22.6, 21.5, 21.3, 20.8, 18.8, 13.4, 12.0. FTIR (thin film): 3509, 3195, 2952, 2869, 1757, 1740, 1468, 1447, 1377, 1235 cm^{-1}.

5.1.31. 6α,7β-Diacetyloxy-3α-((4-benzoyl)phenylacetyloxy)-5α-cholestane (59). To a stirring solution of the bis-protected triol **58** (37 mg, 0.073 mmol) in 4 mL of THF at 25°C was added triphenylphosphine (39 mg, 0.147 mmol) and the carboxylic acid **16** (21 mg, 0.088 mmol) followed by the dropwise addition of DEAD (23 μL, 0.147 mmol) and the solution was stirred for 5 min. The reaction mixture was quenched with water and extracted with ether (3×5 mL). The organic layers were combined and dried over anhydrous magnesium sulfate, filtered, and evaporated under reduced pressure to give a pale orange oil. Flash column chromatography of the crude oil (silica gel, 3:1 hexanes:ethyl acetate) gave the ester **59** (46 mg, 87%) as a white solid. ^1H NMR ($CDCl_3$, 400 MHz) δ: 7.79 (4H, m), 7.57 (1H, m), 7.47 (2H, m), 7.40 (2H, m), 5.06 (1H, m), 4.80 (1H, dd, *J*=10.9, 9.3 Hz), 4.73 (1H, dd, *J*=9.8, 9.3 Hz), 3.70 (2H, s), 1.97 (3H, s), 1.95 (3H, s), 1.90–0.60 (27H, m), 0.89 (3H, s), 0.88 (3H, d, *J*=5.4 Hz), 0.854 (3H, d, *J*=6.6 Hz), 0.850 (3H, d, *J*=6.6 Hz), 0.64 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 196.0, 170.85, 170.76, 170.0, 139.0, 137.6, 136.4, 132.4, 130.4, 130.0, 129.3, 128.3, 77.8, 74.6, 69.5, 55.0, 54.8, 52.0, 43.5, 41.8, 43.6, 39.5, 39.4, 39.0, 36.1, 36.0, 35.5, 32.8, 28.5, 28.0, 27.2, 25.5, 24.9, 23.7, 22.8, 22.6, 21.5, 20.8, 20.7, 18.8, 12.5, 12.0. FTIR (thin film): 2951, 2869, 1742, 1659, 1607, 1377, 1277, 1246, 1026 cm^{-1}.

5.1.32. 4-(2-Hydroxyethyl)-α-phenylbenzenemethanol (62). A solution of the benzophenone ester **59** (800 mg, 1.100 mmol) at 25°C in degassed benzene (1100 mL) was photolyzed using a 450 W mercury arc lamp for 10 h. The solution was concentrated under reduced pressure and subjected to flash column chromatography (silica gel, 3:1 hexanes:ethyl acetate) to give the epimeric alcohols **60** (545 mg, 68%), which were carried on to the next step as a mixture. To a stirring mixture of alcohols **60** (500 mg, 0.688 mmol) in THF (10 mL) at 25°C was added lithium aluminum hydride (261 mg, 6.88 mmol) in portions. The mixture was stirred for 1 h. Water (261 μL) was added slowly at 0°C followed by 10% NaOH (261 μL), which was followed by addition of water (1 mL) again. The mixture was warmed to 25°C and then stirred for 15 min. Magnesium sulfate was added and the mixture was filtered and concentrated under reduced pressure. Flash column chromatography (silica gel, 5:4 hexanes:ethyl acetate followed by 20:1 chloroform:methanol) gave the pure diol **62** (no yield recorded) followed by the desired olefinic triol **61** (263 mg, 91%), which was not characterized at this step. ^1H NMR ($CDCl_3$, 400 MHz) δ: 7.50–7.00 (9H, m), 5.76 (1H, s), 3.75 (2H, t, *J*=6.9 Hz), 2.79 (2H, t, *J*=6.9 Hz), 2.27 (1H, bs). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 143.9, 142.1, 137.8, 129.2, 128.5, 127.5, 126.8, 126.5, 76.0, 63.5, 38.8. FTIR (thin film): 3335, 3090, 3031, 2930, 2874, 1453, 1493, 1043, 1017 cm^{-1}.

5.1.33. 4-(2-(1,1-Dimethylpropanoyloxy)ethyl)-α-phenylbenzenemethanol (63). To a stirring solution of the diol **62** (93 mg, 0.407 mmol) in 4 mL of pyridine cooled to 0°C was added pivaloyl chloride (50 μL, 0.407 mmol) dropwise. The reaction mixture was warmed to 25°C and stirred for an additional 4 h. Sodium bicarbonate solution was added and the mixture was extracted with ether (3×10 mL). The organic layers were combined, dried over anhydrous magnesium sulfate, filtered, and evaporated under reduced pressure. Excess pyridine was removed by a high-vacuum rotovaporator. Flash column chromatography of the crude solid (silica gel, 6:1 hexanes:ethyl acetate) gave the alcohol **63** (94 mg, 74%) as a white solid. ^1H NMR ($CDCl_3$, 400 MHz) δ: 7.50–7.00 (9H, m), 5.79 (1H, s), 4.24 (2H, t, *J*=6.9 Hz), 2.92 (2H, t, *J*=6.9 Hz), 2.61 (1H, bs), 1.16 (9H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 178.6, 144.0, 142.2, 137.3, 129.1, 128.5, 127.5, 126.7, 126.6, 76.0, 64.8, 38.7, 34.8, 27.2. FTIR (thin film): 3451, 3029, 2973, 2936, 2909, 2872, 1727, 1482, 1287, 1159 cm^{-1}.

5.1.34. 3α,6α-Bis[((1,1-dimethyl)ethyl)dimethylsilyloxy]-5α-cholest-14-en-7β-ol. To a stirring solution of the triol **61** (24 mg, 0.057 mmol) in dichloromethane (1 mL) cooled to 0°C was added 2,6-lutidine (53 μL, 0.459 mmol) followed by *tert*-butyldimethylsilyl triflate (79 μL, 0.342 mmol). The mixture was warmed to 25°C and stirred overnight. Water was added and the mixture was extracted with dichloromethane (3×2 mL). The combined extracts were dried over magnesium sulfate, filtered, and concentrated under reduced pressure to yield an oil. Flash column chromatography (silica gel, 4:1 hexanes:benzene) of the crude oil provided the bis-silyl ether (24 mg, 65%) as a clear glass. ^1H NMR ($CDCl_3$, 400 MHz) δ: 5.57 (1H, s), 4.02 (1H, m), 3.49 (1H, dd, *J*=9.7, 8.3 Hz), 3.30 (1H, dd, *J*=11.1, 8.2 Hz), 2.50–0.50 (37H, m), 0.91 (9H, s), 0.86 (9H, s), 0.80 (3H, s), 0.12 (3H, s), 0.06 (3H, s), 0.01 (3H, s), 0.00 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 151.8, 119.1, 76.3, 66.1, 58.4, 52.0, 47.6, 42.7, 41.7, 41.5, 39.6, 36.2, 36.1, 35.8, 33.9, 32.6, 31.5, 29.2, 28.0, 26.1, 25.8, 23.7, 22.8, 22.6, 22.1, 19.0, 18.4, 18.1, 17.0, 12.6, −3.6, −3.9, −4.9, −5.0 (1 high-field carbon unresolved). FTIR (thin film): 3615, 1930, 2892, 2857, 1472, 1464, 1252, 1059, 835, 775 cm^{-1}.

5.1.35. 3α,6α-Bis(triethylsilyloxy)-5α-cholest-14-en-7β-ol. To a stirring solution of the triol **61** (242 mg, 0.578 mmol) in dichloromethane (5 mL) cooled to 0°C was added 2,6-lutidine (404 μL, 3.468 mmol) followed by triethylsilyl triflate (523 μL, 2.312 mmol). The mixture was stirred at 25°C overnight. Water was added and the mixture extracted with dichloromethane (3×10 mL). The combined organic layers were dried over magnesium sulfate, filtered, and concentrated under reduced pressure to yield an oil. Flash column chromatography (silica gel, 3:1 hexanes: benzene) of the crude oil provided the bis-silyl ether (352 mg, 80%) as a clear glass. ^1H NMR ($CDCl_3$, 400 MHz) δ: 5.53 (1H, s), 4.05 (1H, m), 3.48 (1H, dd, *J*=9.7, 8.3 Hz), 3.35 (1H, dd, *J*=11.1, 8.2 Hz), 2.29 (1H, ddd, *J*=15.2, 7.8, 2.1 Hz), 2.22 (1H, m), 2.15–0.50 (47H, m), 0.867 (3H, d, *J*=6.6 Hz), 0.865 (3H, d, *J*=6.6 Hz), 0.79 (3H, s), 0.65 (6H, q, *J*= 7.8 Hz), 0.55 (6H, q, *J*=8.0 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 151.7, 119.0, 77.2, 76.5, 65.9, 58.4, 52.0, 47.6, 42.8, 41.8, 41.5, 39.6, 36.3, 36.1, 35.8, 33.9, 32.6, 31.2, 29.3, 28.0, 23.8, 22.8, 22.6, 22.1, 19.0,

17.0, 12.6, 7.1, 7.0, 5.5, 4.9. FTIR (thin film): 3615, 2955, 2932, 2911, 2876, 1466, 1372, 1238, 1100, 1007 cm^{-1}.

5.1.36. 3α,6α,7β-Triacetyloxy-5α-cholest-14-ene (64a). To a stirring solution of the triol olefin **61** (90 mg, 0.215 mmol) and acetic anhydride (91 μL, 967 mmol) in dichloromethane (5 mL) at 25°C was added trimethylsilyl triflate (1 μL) and the reaction was allowed to stir for 10 min. Saturated sodium bicarbonate was added and the mixture was extracted with dichloromethane (3×5 mL). The organic layers were dried over magnesium sulfate, filtered, and concentrated under reduced pressure. Flash column chromatography (silica gel, 6:1 hexanes:ethyl acetate) of the residue provided the triacetate **64a** (94 mg, 93%) as a white solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 5.08 (1H, s), 5.05 (2H, m), 4.87 (1H, dd, *J*=11.6, 9.2 Hz), 2.37 (1H, dd, *J*=11.9, 11.9 Hz), 2.24 (1H, ddd, *J*=15.8, 7.2, 2.2 Hz), 2.15–0.50 (22H, m), 2.00 (3H, s), 1.98 (3H, s), 1.93 (3H, s), 0.91 (3H, s), 0.88 (3H, s), 0.87 (3H, d, *J*=7.2 Hz), 0.829 (3H, d, *J*=6.6 Hz), 0.826 (3H, d, *J*=6.6 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 170.91, 170.86, 170.4, 149.4, 118.1, 75.5, 74.6, 68.5, 58.3, 51.9, 47.6, 42.5, 40.7, 40.0, 39.4, 36.1, 35.9, 33.8, 32.7, 28.0, 27.1, 25.4, 23.8, 22.8, 22.5, 22.2, 21.4, 21.2, 20.8, 19.0, 16.8, 12.3 (1 high-field carbon unresolved). FTIR (thin film): 2953, 2934, 2870, 1744, 1364, 1246, 1024, 733 cm^{-1}.

5.1.37. 3α, 6α,7β-Tribenzoyloxy-5α-cholest-14-ene (64b). To a stirring solution of the triol olefin **61** (31 mg, 0.074 mmol) and benzoic anhydride (75 μL, 333 mmol) in dichloromethane (2 mL) at 25°C was added trimethylsilyl triflate (1 μL) and the reaction was allowed to stir for 1 h. Saturated sodium bicarbonate was added and the mixture was extracted with dichloromethane (3×5 mL). The organic layers were dried over magnesium sulfate, filtered, and concentrated under reduced pressure. Flash column chromatography (silica gel, 6:1 hexanes:ethyl acetate) of the residue provided the tribenzoate **64b** (49 mg, 91%) as a white solid. ^{1}H NMR (C_6D_6, 400 MHz) δ: 8.40–8.00 (6H, m), 7.30–6.80 (9H, m), 6.07 (1H, dd, *J*=10.2, 9.5 Hz), 5.81 (1H, dd, *J*=11.3, 10.1 Hz), 5.77 (1H, s), 5.32 (1H, m), 2.86 (1H, m), 2.15–0.50 (23H, m), 1.01 (3H, d, *J*=5.9 Hz), 0.99 (3H, s), 0.98 (6H, d, *J*=6.6 Hz), 0.86 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 166.65, 166.55, 165.6, 149.3, 132.9, 132.8, 132.6, 130.8, 130.4, 129.8, 129.6, 129.5, 128.4, 128.2, 128.1, 118.7, 75.9, 75.3, 69.1, 58.4, 52.4, 47.8, 42.6, 41.9, 40.5, 39.4, 36.6, 36.0, 35.9, 33.8, 33.2, 28.0, 27.7, 25.6, 23.8, 22.8, 22.6, 22.4, 19.1, 16.9, 12.7 (1 aromatic carbon unresolved). FTIR (thin film): 2953, 2932, 2869, 1721, 1451, 1275, 1113, 710 cm^{-1}.

5.1.38. 3α,6α-Diacetyloxy-5α-cholestane-7,15-dione (65). To a stirring solution of the triacetate olefin **64a** (94 mg, 0.173 mmol) in THF (5 mL) at 0°C was added borane–tetrahydrofuran complex (1.0 M, 692 μL, 0.692 mmol) and the reaction was warmed to 25°C and stirred for 3 h. The solution was cooled again to 0°C and water was added dropwise. The mixture was extracted with ether (3×5 mL) and the combined organic extracts were concentrated under reduced pressure. The crude oil obtained was re-dissolved in dichloromethane (5 mL) at 25°C and pyridinium chlorochromate (149 mg, 0.692 mmol) was added and the mixture stirred for 15 h. Celite (150 mg) was added followed by ether (5 mL). The mixture was filtered through Celite and the filtrate was concentrated under reduced pressure. Flash column chromatography (silica gel, 2:1 hexanes:ethyl acetate) of the crude residue afforded the diketone **65** (29 mg, 33%) as a clear glass. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 5.089 (1H, d, *J*=12.5 Hz), 5.087 (1H, m), 2.70 (1H, dd, *J*=11.9, 11.0 Hz), 2.57 (1H, dd, *J*=17.1, 7.6 Hz), 2.43 (1H, d, *J*=10.6 Hz), 2.20–0.60 (22H, m), 2.14 (3H, s), 2.02 (3H, s), 1.15 (3H, s), 0.97 (3H, d, *J*=6.5 Hz), 0.853 (3H, d, *J*=6.6 Hz), 0.848 (3H, d, *J*=6.6 Hz), 0.70 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 211.4, 203.41, 170.4, 170.0, 76.7, 68.4, 58.7, 54.7, 52.0, 46.8, 42.9, 41.2, 41.1, 39.2, 38.5, 36.9, 35.9, 35.5, 32.7, 28.3, 27.9, 25.6, 23.8, 22.8, 22.5, 21.4, 21.0, 20.7, 19.0, 12.8, 12.1. FTIR (thin film): 2951, 2869, 1754, 1732, 1366, 1375, 1242, 1211, 1022 cm^{-1}.

5.1.39. 3α,6α-Benzoyloxy-5α-cholestane-7β,15α-diol (66). To a stirring solution of the tribenzoate olefin **64b** (48 mg, 0.066 mmol) in THF (2 mL) at 0°C was added borane–tetrahydrofuran complex (1.0 M, 263 μL, 0.263 mmol) and the reaction was warmed to 25°C and stirred for 3 h. The solution was cooled again to 0°C and water was added dropwise. The mixture was extracted with ether (3×5 mL) and the combined organic extracts were concentrated under reduced pressure. The crude oil obtained was re-dissolved in THF (3 mL) and water (1 mL) at 25°C and sodium perborate (20 mg, 0.132 mmol) was added and the mixture stirred overnight. Water was added and the mixture was extracted with ether (3×5 mL). The combined organic extracts were dried over magnesium sulfate, filtered, and concentrated under reduced pressure. Flash column chromatography (silica gel, 3:1 hexanes:ethyl acetate) of the crude residue afforded the diol **66** (no yield recorded) as a clear glass. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.20–7.90 (4H, m), 7.30–7.70 (6H, m), 5.31 (1H, m), 5.04 (1H, dd, *J*=11.3, 9.1 Hz), 4.12 (1H, m), 3.62 (1H, bt), 2.10–0.75 (41H, m), 1.02 (3H, s), 0.91 (3H, d, *J*=5.9 Hz), 0.864 (3H, d, *J*=6.6 Hz), 0.861 (3H, d, *J*=6.6 Hz), 0.76 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 168.1, 165.7, 133.3, 132.9, 130.9, 129.8, 129.7, 129.5, 128.5, 77.8, 72.8, 69.4, 62.6, 53.4, 51.3, 44.4, 42.5, 41.9, 39.0, 39.4, 38.5, 36.4, 36.0, 35.5, 33.3, 29.7, 28.0, 27.8, 25.8, 23.7, 22.8, 22.6, 20.6, 18.7, 13.6, 12.7. FTIR (thin film): 3366, 2951, 2870, 1717, 1314, 1279, 1113, 710 cm^{-1}.

5.1.40. 3α,6α-Benzoyloxy-15α-hydroxy-5α-cholestan-7-one (67). To a stirring solution of the diol **66** (10 mg, 0.013 mmol) in dichloromethane (3 mL) at 0°C was added pyridinium chlorochromate (0.003, 0.013 mmol) in smaller portions over 1 h. Ether (3 mL) was added followed by Celite (10 mg) and the reaction was filtered through Celite. The filtrate was concentrated under reduced pressure and the crude oil was subjected to flash column chromatography (silica gel, 5:1 hexanes:ethyl acetate) to provide the pure ketone **67** (no yield recorded, although the reaction was very clean by TLC) as a clear glass. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.20–7.90 (4H, m), 7.30–7.70 (6H, m), 5.40 (1H, m), 5.29 (1H, d, *J*=13.0 Hz), 3.93 (1H, ddd, *J*=8.6, 8.6, 2.9 Hz), 2.83 (1H, dd, *J*=11.1, 11.0 Hz), 2.10–0.75 (39H, m), 1.25 (3H, s), 0.91 (3H, d, *J*=6.5 Hz), 0.859 (3H, d, *J*=6.6 Hz), 0.856 (3H, d, *J*=6.6 Hz), 0.75 (3H, s).

5.1.41. 3α-Methoxymethoxy-6α,7β-methylenedioxy-5α, 14α-cholestan-15α-ol (69) and 3α-methoxymethoxy-6α,7β-methylenedioxy-5α,14β-cholestan-15β-ol (70). To a stirring solution of the olefinic triol **61** (86 mg, 0.205 mmol) in dimethoxymethane (5 mL) at 25°C was added excess phosphorus pentoxide. The solution was stirred overnight, or until the reaction was judged to be complete by TLC. Saturated sodium carbonate solution was added and the mixture was extracted with ether (3×10 mL). The combined organic extracts were dried over magnesium sulfate, filtered, and concentrated under reduced pressure. Flash column chromatography (silica gel, 8:1 hexanes:ethyl acetate) of the crude product provided the protected olefin **68** (62 mg, 63%). To a stirring solution of the steroidal olefin **68** (62 mg, 0.131 mmol) in 3 mL of THF cooled to −78°C was added borane–tetrahydrofuran complex (1.0 M, 393 μL, 0.393 mmol). The reaction mixture was allowed to warm to 25°C and stirred for 12 h. The reaction mixture was cooled to 0°C and 393 μL of 10% NaOH was added dropwise followed by 393 μL of 30% hydrogen peroxide. The reaction was stirred vigorously for 1 h. Water was added and the solution was extracted with ether (3×5 mL). The organic layers were combined, dried over anhydrous magnesium sulfate, filtered, and evaporated under reduced pressure to give a white solid. Flash column chromatography of the crude solid (silica gel, 3.5:1 hexanes:ethyl acetate) gave the alcohol **69** (30 mg, 75%) as a white solid and the alcohol **70** (6 mg, 13%) as a white solid.

69: ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 5.118 (1H, d, *J*=0.6 Hz), 5.036 (1H, d, *J*=0.6 Hz), 4.64 (2H, s), 4.24 (1H, bs), 3.92 (2H, m), 3.35 (3H, s), 3.13 (1H, dd, *J*=11.0, 8.7 Hz), 3.06 (1H, dd, *J*=8.7, 8.7 Hz), 2.20–0.50 (25H, m), 0.88 (3H, d, *J*=6.2 Hz), 0.87 (3H, s), 0.849 (3H, d, *J*=6.6 Hz), 0.846 (3H, d, *J*=6.6 Hz), 0.72 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 95.3, 94.5, 84.7, 79.2, 72.3, 69.9, 61.9, 55.2, 53.7, 52.2, 43.4, 40.9, 40.0, 39.4, 38.0, 37.8, 37.3, 36.0, 35.5, 33.2, 28.0, 28.0, 26.2, 23.6, 22.8, 22.6, 20.3, 18.6, 13.7, 13.3. FTIR (thin film): 3503, 2946, 2940, 2878, 1101, 1080, 1042 cm^{-1}.

70: ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 5.12 (1H, s), 5.05 (1H, s), 4.66 (1H, d, *J*=6.9 Hz), 4.64 (1H, d, *J*=6.9 Hz), 4.23 (1H, m), 3.91 (1H, m), 3.37 (3H, s), 3.13 (1H, dd, *J*=11.2, 8.6 Hz), 3.04 (1H, dd, *J*=10.3, 8.6 Hz), 2.99 (1H, bs), 2.20–0.50 (25H, m), 0.94 (3H, s), 0.91 (3H, d, *J*=7.7 Hz), 0.90 (3H, s), 0.864 (3H, d, *J*=6.6 Hz), 0.860 (3H, d, *J*=6.6 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 95.7, 94.5, 84.9, 79.4, 70.8, 69.9, 60.0, 56.2, 55.2, 53.0, 42.0, 40.9, 40.7, 39.4, 38.6, 37.5, 36.0, 35.1, 35.0, 33.2, 28.0, 26.2, 23.7, 22.8, 22.6, 20.7, 18.7, 14.0, 13.7 (1 high-field carbon unresolved). FTIR (thin film): 3542, 2934, 2890, 1468, 1443, 1385, 1042 cm^{-1}.

5.1.42. 3α-Methoxymethoxy-6α,7β-methylenedioxy-5α, 14α-cholestan-15-one (71). To a stirring solution of the alcohol **69** (50 mg, 0.101 mmol) in 4 mL of dichloromethane at 25°C was added Dess–Martin periodinane (86 mg, 0.202 mmol) in portions. The reaction mixture was stirred for 5 h. Sodium bisulfate solution (10% aqueous) was added and the mixture was extracted with ether (3×10 mL). The organic layers were combined, dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. Flash column chromatography of the crude solid (silica gel, 3:1 hexanes:ethyl acetate) gave the ketone **71** (40 mg, 80%) as a white solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 5.19 (1H, s), 5.04 (1H, s), 4.63 (1H, d, *J*= 6.9 Hz), 4.61 (1H, d, *J*=6.9 Hz), 3.88 (1H, m), 3.33 (3H, s), 3.19 (1H, dd, *J*=11.5, 8.5 Hz), 2.94 (1H, dd, *J*=9.3, 8.7 Hz), 2.50 (1H, dd, *J*=18.4, 9.3 Hz), 2.20–0.50 (24H, m), 0.96 (3H, d, *J*=6.5 Hz), 0.837 (3H, d, *J*=6.5 Hz), 0.840 (3H, s), 0.832 (3H, d, *J*=6.4 Hz), 0.73 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 212.3, 95.6, 94.4, 85.8, 78.6, 69.8, 64.5, 55.2, 52.3, 51.6, 42.1, 41.4, 41.1, 39.7, 39.2, 37.1, 35.8, 35.5, 34.5, 33.3, 28.1, 27.9, 26.3, 23.9, 22.8, 22.5, 20.0, 19.2, 13.4, 13.1. FTIR (thin film): 2944, 2938, 1752, 1468, 1366, 1040 cm^{-1}.

5.1.43. 3α-Methoxymethoxy-6α,7β-methylenedioxy-5α, 14β-cholestan-15-one (72). To a stirring solution of the 14α,15-ketosteroid **71** (40 mg, 0.082 mmol) in 1:1 THF:ethanol (4 mL) at 25°C was added 10% NaOH (0.5 mL) and the reaction mixture was stirred for 4 h. Water was added and the mixture was extracted with ether (3×5 mL). The combined organic extracts were washed with brine, dried over anhydrous magnesium sulfate, filtered, and evaporated under reduced pressure to yield the 14β,15-ketosteroid **72** (40 mg, 100%) as a clear glass, which was used without further purification. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 5.16 (1H, s), 5.11 (1H, s), 4.65 (1H, d, *J*=6.9 Hz), 4.63 (1H, d, *J*=6.9 Hz), 4.26 (1H, dd, *J*=11.2, 8.8 Hz), 3.88 (1H, m), 3.36 (3H, s), 2.97 (1H, dd, *J*=11.4, 8.8 Hz), 2.57 (1H, m), 2.37 (1H, dd, *J*=20.0, 10.1 Hz), 2.21 (1H, d, *J*=20.0 Hz), 2.10–0.70 (22H, m), 1.18 (3H, s), 0.87 (3H, d, *J*=6.5 Hz), 0.856 (3H, d, *J*=6.4 Hz), 0.852 (3H, d, *J*=6.8 Hz), 0.82 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 219.4, 96.2, 94.6, 80.2, 79.9, 70.0, 55.4, 53.1, 48.8, 46.6, 41.5, 40.4, 39.3, 38.4, 37.9, 37.4, 36.4, 33.2, 32.9, 31.9, 28.3, 28.1, 26.4, 25.7, 22.9, 22.7, 21.1, 19.4, 19.1, 13.8. FTIR (thin film): 2934, 2872, 1736, 1468, 1368, 1385, 1089 cm^{-1}.

5.1.44. 3α,6α,7β-Trihydroxy-5α,14β-cholestan-15-one (73). To a stirring solution of the 14β,15-ketosteroid **72** (40 mg, 0.082 mmol) in THF (4 mL) was added 50% concentrated HCl (0.5 mL) and the reaction mixture was stirred at 25°C for 1 h. Water was added and the products were thoroughly extracted with ethyl acetate (3×10 mL). The combined organic extracts were dried over anhydrous magnesium sulfate, filtered, and evaporated under reduced pressure. Flash column chromatography (silica gel, 14:1 chloroform:methanol) of the residue yielded the ketone triol **73** (15 mg, 50%) as a white solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 4.27 (1H, dd, *J*=9.9, 9.6 Hz), 4.13 (1H, m), 3.16 (1H, dd, *J*=10.1, 9.4 Hz), 2.67 (1H, m), 2.41 (1H, dd, *J*=19.8, 10.2 Hz), 2.20 (1H, bd, *J*=19.6 Hz), 2.10–0.70 (25H, m), 1.15 (3H, s), 0.87 (3H, d, *J*=7.4 Hz), 0.857 (3H, d, *J*=6.7 Hz), 0.853 (3H, d, *J*=6.6 Hz), 0.79 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 222.1, 75.1, 74.8, 65.8, 52.5, 49.0, 46.4, 41.8, 41.7, 40.0, 38.7, 38.2, 38.1, 36.8, 33.3, 32.2, 31.9, 30.2, 28.3, 28.1, 25.7, 23.0, 22.7, 20.9, 19.5, 19.4, 12.6. FTIR (thin film): 3453, 3359, 2951, 2936, 2872, 2859, 1736, 1453, 1385, 1020 cm^{-1}. High-resolution MS (EI, *m/z*): 435.3476, calcd for $C_{27}H_{47}O_4$ $(M+H)^+$ 435.3474.

5.1.45. 3α,5-Cyclo-6β-methoxy-24-norcholan-23-al (76). To a stirring solution of the alcohol **75** (830 mg, 2.300 mmol) in 2% pyridine:dichloromethane (25 mL) at 25°C was added pyridinium chlorochromate (1.751 g, 8.150 mmol) and the reaction mixture was stirred for 1 h. Ether (25 mL) was added followed by Celite (25 g) and the mixture was filtered. The filtrate was concentrated under reduced pressure and flash column chromatography (silica gel, 14:1 hexanes:ethyl acetate) of the residue yielded the aldehyde **101** (1.280 g, 88%) as a clear glass. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 9.69 (1H, d, *J*=2.2 Hz), 3.27 (3H, s), 2.72 (1H, dd, *J*=2.5, 2.5 Hz), 2.40 (1H, dd, *J*=15.7, 2.3 Hz), 2.10–0.70 (21H, m), 0.97 (3H, s), 0.96 (3H, d, *J*=5.9 Hz), 0.80 (3H, s), 0.60 (1H, dd, *J*=4.5, 4.5 Hz), 0.38 (1H, dd, *J*=7.9, 5.1 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 203.3, 82.3, 56.5, 56.4, 56.0, 50.9, 47.9, 43.3, 42.9, 40.1, 35.2, 35.0, 33.3, 31.6, 30.5, 28.5, 24.9, 24.1, 22.7, 21.4, 20.0, 19.2, 13.1, 12.2. FTIR (thin film): 2936, 2869, 2712, 1727, 1456, 1383, 1098 cm^{-1}. High-resolution MS (EI, *m*/*z*): 358.2869, calcd for $C_{24}H_{38}O_2$ 328.2872.

5.1.46. 3α,5-Cyclo-6β-methoxycholestan-23-one (77). To a stirring solution of the aldehyde **76** (1.151 g, 3.21 mmol) in diethyl ether (20 mL) at 0°C was added isobutylmagnesium bromide (2.0 M, 4.82 mL, 9.63 mmol) and the reaction was stirred for 1.5 h. The mixture was quenched with a saturated solution of ammonium chloride and extracted with ether (3×20 mL). The combined organic extracts were dried over magnesium sulfate, filtered, and concentrated under reduced pressure. Flash column chromatography (silica gel, 10:1 hexanes:ethyl acetate) of the residue provided a 1:1 mixture of the diastereomeric alcohols (1.060 g, 79%). To a stirring solution of the alcohols (976 mg, 2.342 mmol) in 2% pyridine:dichloromethane (50 mL) at 25°C was added pyridinium chlorochromate (1.509 g, 7.028 mmol) and the reaction mixture was stirred for 3 h. Ether (50 mL) was added followed by Celite (25 g) and the mixture was filtered. The filtrate was concentrated under reduced pressure and the crude oil was passed through a short column of silica gel, eluting with ether. Concentration yielded the ketone **77** (0.970 g, 100%) as a clear glass. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 3.25 (3H, s), 2.69 (1H, bdd, *J*=2.6, 2.6 Hz), 2.41 (1H, dd, *J*=15.5, 2.5 Hz), 2.24 (1H, d, *J*=6.9 Hz), 2.15–0.65 (23H, m), 1.02 (3H, s), 0.840 (6H, d, *J*=6.6 Hz), 0.829 (3H, d, *J*=6.6 Hz), 0.69 (3H, s), 0.57 (1H, dd, *J*=4.5, 4.5 Hz), 0.35 (1H, dd, *J*=7.9, 5.1 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 210.9, 82.3, 56.5 (2 carbons), 56.2, 52.4, 50.5, 47.9, 43.3, 42.8, 40.1, 35.2, 35.0, 33.3, 32.5, 30.4, 28.4, 24.9, 24.4, 24.1, 22.7, 22.6, 22.5, 21.4, 19.7, 19.2, 13.1, 12.2. FTIR (thin film): 2953, 2870, 1713, 1470, 1372, 1100 cm^{-1}. High-resolution MS (EI, *m*/*z*): 414.3496, calcd for $C_{28}H_{46}O_2$ 414.3498.

5.1.47. 3β-Hydroxycholest-5-en-23-one (78). To a stirring solution of the ketone **77** (950 mg, 2.29 mmol) in 30 mL of dioxane and 10 mL of water at 0°C was added toluenesulfonic acid monohydrate (50 mg) and the solution was refluxed for 3 h. The reaction mixture was allowed to cool to 25°C and saturated sodium bicarbonate was added and the mixture was extracted with ether (3×5 mL). The organic layers were combined, dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure to give a white solid. Flash column chromatography (silica gel, 3:1:0.5 hexanes:ethyl acetate:chloroform) of the crude solid gave the homoallylic alcohol **78** (860 mg, 94%) as a white solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 5.34 (1H, d, *J*=10.0 Hz), 3.51 (1H, m), 2.50–0.60 (26H, m), 2.41 (1H, dd, *J*=16.1, 2.6 Hz), 1.01 (3H, s), 0.917 (3H, d, *J*=6.2 Hz), 0.912 (3H, d, *J*=6.5 Hz), 0.901 (3H, d, *J*=6.5 Hz), 0.72 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 211.3, 140.9, 121.3, 71.5, 56.8, 56.0, 52.5, 50.4, 50.0, 42.4, 42.2, 39.6, 37.3, 36.4, 32.5, 31.8 (2 carbons), 31.5, 28.4, 24.5, 24.2, 22.6, 22.5, 21.0, 19.8, 19.4, 11.9. FTIR (thin film): 3351, 2936, 2870, 1709, 1468, 1368 cm^{-1}. High-resolution MS (EI, *m*/*z*): 400.3343, calcd for $C_{27}H_{44}O_2$ 400.3341.

5.1.48. 3α,5-Cyclo-23-(1,1-dimethylpropanoyloxy)-6β-methoxy-24-norcholane (79). To a stirring solution of the alcohol **75** (310 mg, 0.860 mmol) in pyridine (13 mL) at 25°C was added pivaloyl chloride (381 μL, 2.580 mmol) dropwise. The mixture was stirred for 24 h. Water was added and the mixture was extracted with hexanes (3×15 mL) and the combined extracts were washed with saturated sodium bicarbonate. The organic layer was dried over magnesium sulfate, filtered, and concentrated under reduced pressure. Flash column chromatography (silica gel, 10:1 hexanes:ether) of the residue provided the ester **79** (353 mg, 92%) as a clear glass. $[\alpha]_D^{25}=+49.4°$ (*c* 1.5, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 4.06 (2H, m), 3.28 (3H, s), 2.73 (1H, dd, *J*=2.6, 2.6 Hz), 2.00–0.70 (22H, m), 1.16 (9H, s), 0.99 (3H, s), 0.93 (3H, d, *J*=6.6 Hz), 0.68 (3H, s), 0.61 (1H, dd, *J*=4.3, 4.3 Hz), 0.39 (1H, dd, *J*=5.1, 8.0 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 178.6, 82.4, 62.5, 56.5, 56.5, 56.2, 48.0, 43.4, 42.8, 40.2, 38.7, 35.3, 35.0, 34.6, 33.3, 33.2, 30.4, 28.3, 27.2, 25.0, 24.1, 22.7, 21.5, 19.3, 18.8, 13.1, 12.1. FTIR (thin film): 2953, 2870, 1732, 1100 cm^{-1}. High-resolution MS (EI, *m*/*z*): 444.3594, calcd for $C_{29}H_{48}O_3$ 444.3603.

5.1.49. 23-(1,1-Dimethylpropanoyloxy)-24-norcholan-5-en-3β-ol (80). A mixture of the ether **79** (324 mg, 0.729 mmol) and toluenesulfonic acid monohydrate (30 mg, 0.073 mmol) was refluxed in dioxane:water (3:1, 15 mL) for 3 h. The solution was cooled to 25°C and saturated sodium bicarbonate was added followed by water. The mixture was extracted with ether (3×15 mL). The combined organic extracts were dried over magnesium sulfate, filtered, and concentrated under reduced pressure. Flash column chromatography of the residue (silica gel, 4:1:1 hexanes:ethyl acetate:chloroform) provided the homoallylic alcohol **80** (305 mg, 97%) as a white solid (mp 148°C). $[\alpha]_D^{25}=-38.0°$ (*c* 1.0, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 5.27 (1H, d, *J*=4.9 Hz), 4.02 (2H, m), 3.42 (1H, m), 2.64 (1H, s), 2.30–0.50 (23H, m), 1.12 (9H, s), 0.94 (3H, s), 0.91 (3H, d, *J*=6.2 Hz), 0.62 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 178.6, 140.9, 121.4, 77.4, 71.5, 62.6, 56.7, 56.0, 50.0, 42.4, 42.2, 39.7, 38.6, 37.3, 36.4, 34.5, 33.1, 31.8, 31.5, 28.2, 27.2, 24.2, 21.0, 19.4, 18.8, 11.7. FTIR (thin film): 3482, 2969, 2930, 2896, 2863, 2836, 1707, 1292, 1177, 1067 cm^{-1}. High-resolution MS (EI, *m*/*z*): 430.3444, calcd for $C_{28}H_{46}O_3$ 430.3447.

5.1.50. 23-(1,1-Dimethylpropanoyloxy)-3β-phenylmethoxy-24-norchol-5-ene (81). To a stirring solution of the alcohol

80 (278 mg, 0.646 mmol) in tetrahydrofuran (5 mL) at 25°C was added sodium hydride (104 mg, 2.584 mmol) and tetrabutylammonium iodide (48 mg, 0.130 mmol) followed by benzyl bromide (184 μL, 1.550 mmol). The reaction was stirred for 72 h. Water was added and the mixture was extracted with ether (3×5 mL). The combined organic layers were dried over magnesium sulfate, filtered, and concentrated under reduced pressure. Column chromatography (silica gel, 15:1 hexanes:ether) of the residue yielded the benzyl ether **81** (280 mg, 83%) as a white solid (mp 108°C). $[\alpha]_D^{25}=-23.9°$ (*c* 0.95, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.40–7.20 (5H, m), 5.36 (1H, d, *J*=5.2 Hz), 4.57 (2H, s), 4.11 (2H, m), 3.29 (1H, m), 2.45 (1H, m), 2.30 (1H, m), 2.10–0.50 (21H, m), 1.21 (9H, s), 1.03 (3H, s), 0.99 (3H, d, *J*=6.6 Hz), 0.70 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 178.6, 140.9, 139.1, 128.4, 127.6, 127.4, 121.6, 78.6, 70.0, 62.6, 56.8, 56.0, 50.2, 42.4, 39.8, 39.2, 38.7, 37.3, 36.9, 34.6, 33.2, 32.0, 31.9, 28.5, 28.3, 27.3, 24.3, 21.1, 19.4, 18.9, 11.8. FTIR (thin film): 2928, 1727 cm^{-1}.

5.1.51. 23-(1,1-Dimethylpropanoyloxy)-3β-phenylmethoxy-5α-24-norcholan-6α-ol (82). To a stirring solution of the olefin **81** (265 mg, 0.509 mmol) in 5 mL of THF cooled to 0°C was added borane–tetrahydrofuran complex (1.0 M, 1.018 mL, 1.018 mmol). The reaction mixture was stirred at 25°C for 12 h. The reaction mixture was cooled to 0°C and 1 mL of 10% NaOH was added dropwise followed by 1 mL of 30% hydrogen peroxide. The reaction was stirred vigorously for 1 h. Ether and water were added and the mixture was extracted with ether (3×10 mL). The organic layers were combined, dried over anhydrous magnesium sulfate and evaporated under reduced pressure to give a white solid. Flash column chromatography of the crude solid (silica gel, 20:1 hexanes:ether) gave the alcohol **82** (162 mg, 60%) as a white solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.40–7.20 (5H, m), 4.58 (1H, d, *J*=11.8 Hz), 4.52 (1H, d, *J*=11.8 Hz), 4.07 (2H, m), 3.34 (1H, m), 3.31 (1H, m), 2.40 (1H, m), 2.04 (1H, bs), 2.00–0.50 (23H, m), 1.14 (9H, s), 0.94 (3H, d, *J*=6.5 Hz), 0.79 (3H, s), 0.63 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 178.7, 139.1, 128.3, 127.6, 127.4, 78.1, 69.9, 69.3, 62.6, 56.2, 56.1, 53.8, 51.6, 42.6, 41.6, 39.8, 38.7, 37.3, 36.5, 34.6, 34.3, 33.2, 28.8, 28.2, 28.1, 27.2, 24.2, 21.1, 18.8, 13.4, 12.0. FTIR (thin film): 3422, 2938, 2870, 2851, 1727 cm^{-1}.

5.1.52. 6α-Acetyloxy-23-(1,1-dimethylpropanoyloxy)-3β-phenylmethoxy-5α-24-norcholane (83). To a stirring solution of the alcohol **82** (157 mg, 0.291 mmol) in 5 mL of pyridine at 25°C was added acetic anhydride (83 μL, 0.873 mmol) and the reaction was stirred overnight. Ice chips were added and the products were extracted with ether (3×10 mL). The organic layers were combined, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure to give a white solid. Flash column chromatography of the crude solid (silica gel, 6:1 hexanes: ethyl acetate) gave the acetate **83** (169 mg, 100%) as a white solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.35–7.20 (5H, m), 4.65 (1H, ddd, *J*=10.6, 10.6, 4.6 Hz), 4.56 (1H, d, *J*=11.8 Hz), 4.52 (1H, d, *J*=11.8 Hz), 4.20–3.90 (2H, m), 3.30 (1H, m), 2.02 (3H, s), 2.00–0.60 (24H, m), 1.18 (9H, s), 0.95 (3H, d, *J*=6.5 Hz), 0.86 (3H, s), 0.64 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 178.6, 170.7, 139.0, 128.4, 127.6, 127.4, 77.8, 72.6, 70.0, 62.5, 56.2, 56.0, 53.7, 48.6, 42.7, 39.7, 38.7, 37.7, 37.1, 36.9, 34.5, 34.1, 33.1, 29.1, 28.2, 27.8, 27.2, 24.0, 21.3, 21.1, 18.8, 13.3, 11.9. FTIR (thin film): 2942, 2869, 1736, 1242, 1159 cm^{-1}.

5.1.53. 6α-Acetyloxy-23-(1,1-dimethylpropanoyloxy)-5α-24-norcholan-3β-ol (84). To a stirring solution of the benzyl ether **83** (165 mg, 0.284 mmol) in ethanol (12 mL) at 25°C was added Pt (5 mg) and the flask was evacuated using a high-vacuum pump. The flask was back-filled with hydrogen gas from a balloon. This process of evacuating and back-filling was repeated two times and the reaction was stirred for 7 h. The solution was filtered through Celite and evaporated under reduced pressure to yield a crude oil. Flash column chromatography (silica gel, 1:1 hexanes: ethyl acetate) of the residue provided the alcohol **84** (134 mg, 96%) as a white solid (mp 148°C). ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 4.62 (1H, ddd, *J*=10.9, 10.9, 4.6 Hz), 4.04 (2H, m), 3.49 (1H, m), 2.10–0.50 (24H, m), 2.03 (1H, bs), 1.98 (3H, s), 1.14 (9H, s), 0.91 (3H, d, *J*=6.6 Hz), 0.82 (3H, s), 0.61 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 178.7, 170.8, 72.5, 70.8, 62.5, 56.2, 56.0, 53.6, 48.6, 42.7, 39.7, 38.7, 37.6, 37.2, 36.6, 34.5, 34.1, 33.1, 32.2, 31.1, 28.2, 27.2, 24.0, 21.2, 21.1, 18.7, 13.3, 11.9. FTIR (thin film): 3440, 2944, 2870, 1732 cm^{-1}.

5.1.54. 6α-Acetyloxy-3α-((4-benzoyl)phenylacetyloxy)-23-(1,1-dimethylpropanoyloxy)-5α-24-norcholane (85). To a stirring solution of the alcohol **84** (112 mg, 0.228 mmol) in THF (6 mL) at 25°C was added the carboxylic acid **16** (66 mg, 0.274 mmol), triphenylphosphine (120 mg, 0.456 mmol), and DEAD (72 μL, 0.456 mmol). After stirring for 1 h, the reaction was quenched with water and the mixture was extracted with ether (3×10 mL). The combined organic extracts were dried over magnesium sulfate, filtered, and concentrated under reduced pressure to yield a crude oil which was subjected to flash column chromatography (silica gel, 4:1 hexanes:ethyl acetate) to provide the ester **85** (145 mg, 90%) as a white solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.90–7.70 (4H, m), 7.55 (1H, m), 7.50–7.35 (4H, m), 5.05 (1H, m), 4.57 (1H, ddd, *J*=10.6, 10.6, 4.6 Hz), 4.06 (2H, m), 3.68 (2H, s), 2.00–0.50 (24H, m), 1.94 (3H, s), 1.16 (9H, s), 0.92 (3H, d, *J*= 6.5 Hz), 0.78 (3H, s), 0.60 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 195.9, 178.6, 170.8, 170.0, 139.4, 137.6, 136.2, 132.4, 129.9, 129.3, 128.3, 128.3, 72.4, 70.0, 62.5, 56.1, 56.0, 53.6, 44.0, 42.6, 42.0, 39.6, 38.7, 37.5, 36.7, 34.6, 33.9, 32.9, 28.2, 27.2, 27.1, 25.6, 24.05, 23.95, 21.2, 20.6, 18.8, 12.4, 11.9. FTIR (thin film): 2944, 2869, 1732, 1659, 1607 cm^{-1}.

5.1.55. 3α,6α,23-Tris[((1,1-dimethyl)ethyl)dimethylsilyloxy]-5α-24-norchol-14-ene (86). The benzophenone ester **85** (140 mg, 0.196 mmol) was dissolved in 200 mL of degassed, purified benzene. The solution was kept under argon at 25°C and irradiated with a 400 W mercury arc lamp for 10 h. The resulting solution was concentrated under reduced pressure. To the crude oil obtained was added 10 mL of KOH (10% aqueous):EtOH:THF (1:3:1) and the solution stirred overnight at 25°C and extracted thoroughly with ether (3×15 mL). The combined extracts were washed with 10% sodium bicarbonate solution, dried over magnesium sulfate, filtered, and concentrated under

reduced pressure to yield a white solid. The white solid obtained was dissolved in dichloromethane (10 mL) and cooled to 0°C. To the stirring solution was added 2,6-lutidine (83 μL, 0.714 mmol) followed by *tert*-butyldimethylsilyl triflate (123 μL, 0.536 mmol). The solution was quenched with water after 1 h and extracted with dichloromethane (3×10 mL). The combined dichloromethane extracts were dried over magnesium sulfate, filtered, and concentrated under reduced pressure. The crude oil was subjected to flash column chromatography on 20% silver nitrate-impregnated silica gel (6:1 hexanes:ethyl acetate) to yield the pure olefin **86** (66 mg, 48%) as a clear glass. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 5.17 (1H, s), 4.01 (1H, m), 3.65 (2H, m), 3.39 (1H, ddd, J=10.6, 10.6, 4.2 Hz), 2.33 (1H, ddd, J=15.3, 7.7, 2.3 Hz), 2.20–0.50 (20H, m), 0.93 (3H, d, J=6.4 Hz), 0.904 (3H, s), 0.895 (9H, s), 0.876 (9H, s), 0.867 (9H, s), 0.77 (3H, s), 0.05 (6H, s), 0.04 (3H, s), 0.02 (3H, s), 0.005 (3H, s), 0.003 (3H, s).

5.1.56. 3α,6α-Bis[((1,1-dimethyl)ethyl)dimethylsilyloxy]-5α-24-norchol-14-en-23-ol (87). The tris-silyl ether **86** (35 mg, 0.054 mmol) was stirred at 25°C for 24 h in 5.5 mL of AcOH:THF:water (4:6:1). The mixture was extracted with benzene (3×5 mL) and the combined organic layers were dried over magnesium sulfate, filtered, and concentrated under reduced pressure to provide a clear oil. Flash column chromatography (silica gel, 5:1 hexanes:ethyl acetate) of the oil provided the alcohol **87** (25 mg, 86%) as a clear glass. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 5.17 (1H, s), 4.01 (1H, m), 3.70 (2H, m), 3.39 (1H, ddd, J=10.6, 10.6, 4.2 Hz), 2.33 (1H, ddd, J=15.2, 7.8, 2.1 Hz), 0.50–2.20 (21H, m), 0.95 (3H, d, J=6.5 Hz), 0.91 (3H, s), 0.87 (9H, s), 0.86 (9H, s), 0.76 (3H, s), 0.03 (3H, s), 0.02 (3H, s), 0.003 (3H, s), 0.000 (3H, s).

5.1.57. 3α,6α-Bis[((1,1-dimethyl)ethyl)dimethylsilyloxy]-5α-24-norcholan-23-al (88). To a stirring solution of the alcohol **87** (23 mg, 0.039 mmol) in dichloromethane (4 mL) at 25°C was added pyridinium chlorochromate (13 mg, 0.059 mmol) and the reaction was allowed to stir for 5 h. Celite (13 mg) and ether (4 mL) were added and the solution was filtered through Celite and concentrated under reduced pressure. The resulting crude oil was subjected to flash column chromatography (silica gel, 15:1 hexanes:ether) to provide the aldehyde **88** (19 mg, 83%) as a clear glass. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 9.78 (1H, dd, J=1.5, 1.5 Hz), 5.15 (1H, s), 4.01 (1H, m), 3.39 (1H, ddd, J=10.6, 10.6, 4.3 Hz), 2.60–1.05 (21H, m), 1.02 (3H, d, J=6.2 Hz), 0.95 (3H, s), 0.87 (9H, s), 0.86 (9H, s), 0.77 (3H, s), 0.03 (3H, s), 0.017 (3H, s), 0.003 (3H, s), 0.001 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 203.4, 155.2, 116.6, 70.2, 66.4, 58.4, 52.9, 50.8, 47.1, 45.4, 42.2, 40.0, 36.8, 35.8, 33.9, 32.7, 31.0, 30.0, 29.5, 25.9, 25.8, 21.4, 20.3, 18.12, 18.07, 16.8, 12.3, −4.0, −4.6, −4.9, −5.0.

5.1.58. 3α,6α-Bis[((1,1-dimethyl)ethyl)dimethylsilyloxy]-5α-cholestane-15,23-dione (89a). A solution of the aldehyde **88** (18 mg, 0.031 mmol) in ether (3 mL) was added to a stirring solution of isobutylmagnesium bromide (2.0 M, 78 μL, 0.155 mmol) cooled to 0°C. The reaction was stirred for 0.5 h and then water was added and the mixture was extracted with ether (3×5 mL). The combined organic extracts were dried over magnesium sulfate, filtered, and concentrated under reduced pressure. Flash column chromatography (silica gel, 8:1 hexanes:ethyl acetate) provide an equal mixture of the diastereomeric alcohols (0.018 mg, 90%). To a stirring solution of the olefinic alcohols (0.017 mg, 0.026 mmol) in THF (3 mL) at 0°C was added borane–tetrahydrofuran complex (1.0 M, 78 μL, 0.078 mmol). The reaction mixture was stirred at 25°C for 12 h. The reaction mixture was cooled to 0°C and 0.5 mL of 10% NaOH was added dropwise followed by 0.5 mL of 30% hydrogen peroxide. The reaction was stirred vigorously for 1 h. Water was added and the aqueous layer was extracted with ether (3×10 mL). The organic layers were combined, dried over anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure to give the crude diol. To a stirring mixture of the crude diol in dichloromethane (4 mL) at 25°C was added pyridinium chlorochromate (26 mg, 0.120 mmol) and the reaction was stirred for 4 h. Celite (26 mg) was then added followed by ether and the mixture was filtered and concentrated under reduced pressure. Flash column chromatography (silica gel, 8:1 hexanes:ethyl acetate) of the residue provided the desired dione **89a** (12 mg, 71% for three steps) as a clear glass. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 4.01 (1H, m), 3.35 (1H, ddd, J=10.5, 10.5, 4.4 Hz), 2.87 (1H, ddd, J=12.6, 3.2, 3.2 Hz), 2.50–0.50 (24H, m), 0.98 (3H, d, J=6.4 Hz), 0.911 (3H, d, J=6.5 Hz), 0.900 (3H, d, J=6.5 Hz), 0.87 (9H, s), 0.86 (9H, s), 0.77 (3H, s), 0.75 (3H, s), 0.06 (3H, s), 0.02 (3H, s), 0.006 (6H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 214.6, 210.2, 69.8, 66.4, 65.6, 53.2, 52.7, 51.2, 49.9, 46.0, 42.4, 41.7, 40.2, 39.7, 36.6, 32.7, 31.8, 31.0, 30.5, 29.6, 25.94, 25.88, 24.5, 22.6, 22.5, 20.25, 20.19, 18.2, 18.1, 13.0, 12.5, −4.0, −4.7, −4.8, −4.9.

5.1.59. 7-Deoxyxestobergsterol A (1d). To a stirring solution of the diketone **89a** (8 mg, 0.012 mmol) in tetrahydrofuran (3 mL) was added 20% HCl (0.5 mL) and the reaction allowed to stir at 25°C for 48 h. Saturated sodium bicarbonate was added and the mixture was extracted with ether (3×5 mL). The combined organic extracts were dried over magnesium sulfate, filtered, and concentrated under reduced pressure to provide diol dione **90** (5 mg, 100%) as a white solid. To a stirring solution of the diol dione **90** (4 mg, 0.009 mmol) in ethanol (3.5 mL) was added 10% NaOH (0.5 mL) and the mixture was allowed to stir until the reaction was judged to be complete by TLC (24 h). Water was added and the mixture was extracted with ether (3×5 mL). The organic layers were dried over magnesium sulfate, filtered, and concentrated under reduced pressure to yield a white solid. The solid was subjected to flash column chromatography (silica gel, 13:1 chloroform:methanol) to provide the aldol product **1d** (5 mg, 100%) as a white solid. $[\alpha]_D^{25}=-23.8°$ (c 0.40, CH_2Cl_2). ^{1}H NMR (pyridine-d_5, 400 MHz) δ: 4.37 (1H, m), 3.65 (1H, ddd, J=10.8, 10.8, 4.4 Hz), 3.22 (1H, ddd, J=11.7, 11.7, 11.7 Hz), 2.81 (1H, bd, J=11.6), 2.67 (1H, d, J=10.0 Hz), 2.60 (1H, m), 2.56 (1H, bs), 2.33 (1H, m), 2.16 (1H, m), 2.09 (2H, m), 2.01 (1H, dd, J=14.2, 4.7 Hz), 2.00–0.90 (16H, m), 1.54 (1H, dd, J=14.3, 7.2 Hz), 1.16 (3H, s), 1.12 (3H, d, J=6.3 Hz), 1.01 (3H, d, J=6.5 Hz), 0.97 (3H, d, J=6.7 Hz), 0.84 (3H, s). ^{13}C NMR (pyridine-d_5, 100 MHz) δ: 217.0, 82.0, 69.6, 65.4, 62.8, 57.7, 56.5, 52.1, 51.7, 47.4, 46.4, 40.2, 38.70, 38.66,

37.2, 35.0, 33.2, 32.0, 31.5, 29.5, 25.2, 24.9, 24.7, 21.2, 20.9, 19.9, 12.5. FTIR (thin film): 3482, 3416, 3349, 2923, 2851, 1723 cm^{-1}. High-resolution MS (EI, *m/z*): 432.3233, calcd for $C_{27}H_{44}O_4$ 432.3240.

5.1.60. 3β-Acetyloxy-23-(1,1-dimethylpropanoyloxy)-24-norchol-5-ene (91). The methyl ether **79** (1.690 g, 0.380 mmol)) was dissolved in glacial acetic acid and heated to 90°C for 3 h. The solution was cooled and the volatile components were removed under reduced pressure to give the allylic acetate **91** (1.696 g, 94%) as a white solid. ^{1}H NMR (400 MHz) δ: 5.34 (1H, m), 4.56 (1H, m), 4.20–3.90 (2H, m), 2.40–0.50 (23H, m), 1.99 (3H, s), 1.16 (9H, s), 0.99 (3H, s), 0.94 (3H, d, *J*=6.5 Hz), 0.65 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 178.6, 170.4, 139.6, 122.5, 73.9, 62.5, 56.6, 56.0, 50.0, 42.4, 39.6, 38.7, 38.1, 37.0, 36.6, 34.6, 33.2, 31.8, 28.3, 27.7, 27.2, 24.2, 21.4, 21.0, 19.3, 18.8, 11.7. FTIR (thin film): 2973, 2965, 2940, 2822, 1732, 1478, 1466, 1368, 1157, 1040 cm^{-1}.

5.1.61. 3β-Acetyloxy-23-(1,1-dimethylpropanoyloxy)-24-norchol-5-en-7-one (92). A mixture of the olefin **91** (54 mg, 0.120 mmol) and ruthenium trichloride monohydrate (5 mg) was stirred at 25°C in 9:1 cyclohexane:water (32 mL). *tert*-Butyl hydroperoxide (70% aqueous, 5.53 mL) was added dropwise to the solution over 6 h and the mixture was stirred for an additional 18 h. Sodium sulfite (1.6 g) was added and the mixture allowed to stir for 1 h. Water was added and the mixture was extracted with ether (3×30 mL). The combined organic extracts were dried over magnesium sulfate, filtered, and concentrated under reduced pressure. Flash column chromatography (silica gel, 5:1:1 hexanes: ethyl acetate:chloroform) of the residue provided the enone **92** (1.111 g, 65%) as a white solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 5.66 (1H, d, *J*=1.6 Hz), 4.67 (1H, m), 4.03 (2H, m), 2.80–0.50 (21H, m), 2.01 (3H, s), 1.17 (3H, s), 1.15 (9H, s), 0.93 (3H, d, *J*=6.6 Hz), 0.65 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 201.7, 178.6, 170.2, 163.9, 126.6, 72.2, 62.5, 54.7, 49.9, 49.7, 45.3, 43.2, 38.7, 38.6, 38.3, 37.7, 36.0, 34.6, 33.1, 28.6, 27.3, 27.2, 26.2, 21.2, 21.1, 18.9, 17.2, 11.8. FTIR (thin film): 2950, 2870, 1732, 1671, 1638 cm^{-1}. High-resolution MS (EI, *m/z*): 486.3338, calcd for $C_{30}H_{46}O_5$ 486.3345.

5.1.62. 3β-Acetyloxy-23-(1,1-dimethylpropanoyloxy)-24-norchol-5-en-7β-ol (93). To a stirring solution of the enone **92** (1.087 g, 2.234 mmol) in dichloromethane: methanol (4:1, 50 mL) cooled to −78°C was added cerium trichloride heptahydrate (1.1664 g, 4.467 mmol) followed by sodium borohydride (0.169 g, 4.467 mmol). The solution was stirred and allowed to warm to 25°C slowly. The solution was acidified with 10% HCl and extracted with ether (3×100 mL). The combined organic layers were dried over magnesium sulfate, filtered, and concentrated under reduced pressure to yield the allylic alcohol **93** (1.060 g, 97%) as a white solid, which was used without further purification. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 5.27 (1H, d, *J*=1.6 Hz), 4.57 (1H, m), 4.20–3.90 (2H, m), 3.80 (1H, d, *J*=7.9 Hz), 2.50–0.50 (22H, m), 1.99 (3H, s), 1.15 (9H, s), 1.02 (3H, s), 0.93 (3H, d, *J*=6.6 Hz), 0.66 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 178.6, 170.4, 142.2, 126.5, 73.4, 73.0, 62.5, 55.9, 55.3, 48.1, 43.0, 40.6, 39.4, 38.7, 37.6, 36.6, 36.5, 34.6, 33.1, 28.6, 27.7, 27.2, 26.3, 21.4, 21.0, 19.0, 18.9, 11.7. FTIR (thin film): 3474, 2950, 2909, 2870, 2853, 1730, 1285, 1161, 1036 cm^{-1}.

5.1.63. 3β,7β-Diacetyloxy-23-(1,1-dimethylpropanoyloxy)-24-norchol-5-ene (94). To a stirring solution of the allylic alcohol **93** (1.000 g, 2.249 mmol) in pyridine (10 mL) at 25°C was added acetic anhydride (0.424 μL, 4.497 mmol) followed by DMAP (4 mg). The reaction was stirred overnight and then ice chips were added. Water was added and the mixture was extracted with ether (3×20 mL). The combined organic layers were dried over magnesium sulfate, filtered, and concentrated under reduced pressure. The excess pyridine was removed by a high-vacuum rotovaporator to provide the allylic acetate **94** (1.012 g, 92%) as a white solid, which was used without further purification. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 5.20 (1H, s), 4.98 (1H, d, *J*=8.6 Hz), 4.54 (1H, m), 4.05 (2H, m), 2.40–2.25 (2H, m), 2.10–0.80 (19H, m), 1.982 (3H, s), 1.975 (3H, s), 1.15 (9H, s), 1.04 (3H, s), 0.93 (3H, d, *J*=6.5 Hz), 0.66 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 178.5, 171.0, 170.2, 144.1, 122.2, 75.4, 73.2, 62.4, 55.4, 55.3, 48.0, 42.9, 39.2, 38.7, 37.5, 36.50, 36.46, 36.4, 34.6, 33.0, 28.4, 27.6, 27.2, 25.1, 21.6, 21.3, 21.0, 19.0, 18.8, 11.6. FTIR (thin film): 2950, 2872, 2911, 2855, 1734, 1373, 1240, 1161, 1032 cm^{-1}. High-resolution MS (EI, *m/z*): 529.3527, calcd for $C_{32}H_{49}O_6$ $(M-H)^+$ 529.3529.

5.1.64. 23-(1,1-Dimethylpropanoyloxy)-5α-24-norcholan-3β,6α,7β-triol (95). To a stirring solution of the olefin **94** (1.057 g, 1.992 mmol) in 20 mL of THF at 0°C was added borane–tetrahydrofuran complex (1.0 M, 6 mL, 5.976 mmol). The reaction mixture was stirred at 25°C for 12 h. The reaction mixture was cooled to 0°C and 5 mL of 10% NaOH was added dropwise followed by 2 mL of 30% hydrogen peroxide. The reaction was stirred vigorously for 1 h. Ether and water were added and the products were extracted with ether (3×20 mL). The organic layers were combined, dried over anhydrous magnesium sulfate, filtered, and evaporated under reduced pressure to give a white solid. Flash column chromatography (silica gel, 12:1 chloroform:methanol) of the crude solid gave the triol **95** (527 mg, 57%) as a white solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 4.09 (2H, m), 3.58 (1H, dddd, *J*=10.9, 10.9, 4.7, 4.7 Hz), 3.25 (1H, dd, *J*=10.5, 8.7 Hz), 3.11 (1H, dd, *J*=9.3, 8.7 Hz), 2.30–0.60 (25H, m), 1.19 (9H, s), 0.97 (3H, d, *J*=6.6 Hz), 0.86 (3H, s), 0.68 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 178.7, 80.2, 74.7, 70.8, 56.0, 55.3, 52.1, 47.9, 43.5, 40.9, 39.8, 38.7, 37.4, 35.6, 34.6, 33.0, 32.5, 32.5, 30.6, 28.6, 27.2, 26.9, 21.4, 18.9, 13.6, 12.2. FTIR (thin film): 3359, 2938, 2867, 1728, 1480, 1447, 1285, 1159, 1087, 735 cm^{-1}.

5.1.65. 3β,6α,7β-Triacetyloxy-23-(1,1-dimethylpropanoyloxy)-5α-24-norcholane (96). To a stirring solution of the triol **95** (261 mg, 0.562 mmol) in dichloromethane (7 mL) at 25°C was added acetic anhydride (239 μL, 2.528 mmol) followed by trimethylsilyl triflate (5 mL) and the reaction mixture was stirred for 30 min. Saturated sodium bicarbonate was added and the mixture was allowed to stir an additional 0.5 h. Water was added and the mixture was extracted with dichloromethane (3×10 mL). The combined organic extracts were dried over magnesium sulfate, filtered, and concentrated under reduced pressure.

Flash column chromatography of the residue (silica gel, 3:1 hexanes:ethyl acetate) yielded the triacetate **96** (316 mg, 95%) as a clear glass. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 4.76 (1H, dd, *J*=11.1, 9.2 Hz), 4.66 (1H, dd, *J*=9.9, 9.2 Hz), 4.53 (1H, dddd, *J*=11.3, 11.3, 5.0, 5.0 Hz), 4.20–3.80 (2H, m), 2.00–0.70 (22H, m), 1.92 (3H, s), 1.91 (3H, s), 1.87 (3H, s), 1.10 (9H, s), 0.88 (3H, s), 0.87 (3H, d, *J*=5.9 Hz), 0.59 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 178.5, 170.8, 170.7, 170.4, 76.9, 74.4, 72.6, 62.4, 55.0, 54.7, 51.7, 46.0, 43.6, 39.3, 39.0, 38.7, 36.7, 35.8, 34.6, 33.0, 28.5, 28.3, 27.2, 27.0, 24.8, 21.5, 21.4, 21.2, 20.9, 18.8, 13.3, 11.9. FTIR (thin film): 2955, 2870, 1744, 1375, 1248, 1161, 1036, 735 cm^{-1}.

5.1.66. 6α,7β-Diacetyloxy-23-(1,1-dimethylpropanoyl-oxy)-5α-24-norcholan-3β-ol (97). To a stirring solution of the triacetate **96** (296 mg, 0.501 mmol) in 1:1 THF: ethanol (10 mL) at 0°C was added 10% NaOH solution (0.5 mL) and the reaction mixture was stirred for 1 h. HCl (10% aqueous) was added and the mixture was extracted with ether (3×10 mL). The organic extracts were dried over magnesium sulfate, filtered, and concentrated under reduced pressure. Flash column chromatography (silica gel, 1.5:1 hexanes:ethyl acetate) of the residue yielded the alcohol **97** (244 mg, 89%) as a white solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 4.84 (1H, dd, *J*=11.2, 9.3 Hz), 4.66 (1H, dd, *J*=10.0, 9.3 Hz), 4.20–3.80 (2H, m), 3.52 (1H, dddd, *J*=11.3, 11.3, 5.0, 5.0 Hz), 2.00–0.70 (23H, m), 1.99 (3H, s), 1.95 (3H, s), 1.17 (9H, s), 0.95 (3H, d, *J*=5.9 Hz), 0.93 (3H, s), 0.66 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 178.6, 170.9, 170.7, 78.0, 74.5, 70.7, 62.4, 55.0, 54.8, 51.8, 46.2, 43.6, 39.4, 39.1, 38.7, 37.0, 35.8, 34.5, 32.9, 32.1, 31.0, 28.5, 27.2, 24.8, 21.5, 21.3, 20.8, 18.8, 13.4, 11.9. FTIR (thin film): 3441, 2950, 2940, 2870, 1746, 1728, 1480, 1460, 1246, 1161 cm^{-1}.

5.1.67. 6α,7α-Diacetyloxy-3α-((4-benzoyl)phenylacetyl-oxy)-23-(1,1-dimethylpropanoyl-oxy)-5α-24-norcholane (98). To a stirring solution of the alcohol **97** (240 mg, 0.437 mmol) in THF (7 mL) at 25°C was added triphenylphosphine (229 mg, 0.875 mmol) and the carboxylic acid **16** (126 mg, 0.524 mmol) followed by the dropwise addition of DEAD (138 μL, 0.875 mmol) and the solution was stirred for 0.5 h. The reaction mixture was concentrated under reduced pressure to give a pale orange oil. Flash column chromatography of the crude oil (silica gel, 3:1 hexanes: ethyl acetate) gave the ester **98** (313 mg, 93%) as a white solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.85–7.65 (4H, m), 7.53 (1H, dd, *J*=7.4 Hz), 7.43 (2H, dd, *J*=7.7, 7.4 Hz), 7.37 (2H, d, *J*=8.1 Hz), 5.02 (1H, m), 4.76 (1H, dd, *J*=11.2, 9.2 Hz), 4.68 (1H, dd, *J*=9.7, 9.3 Hz), 4.20–3.70 (2H, m), 3.66 (2H, s), 1.93 (3H, s), 1.91 (3H, s), 1.85–0.50 (22H, m), 1.14 (9H, s), 0.90 (3H, d, *J*=6.5 Hz), 0.85 (3H, s), 0.61 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 196.0, 178.6, 170.8, 170.8, 170.0, 139.1, 137.6, 136.4, 132.4, 130.5, 130.0, 129.3, 128.3, 77.8, 74.6, 69.6, 62.4, 55.0, 54.8, 52.0, 43.6, 41.8, 41.6, 39.3, 39.0, 38.7, 36.0, 34.6, 33.0, 32.8, 28.5, 27.3, 27.2, 25.5, 24.8, 21.5, 20.9, 20.8, 18.9, 12.5, 11.9. FTIR (thin film): 3061, 2955, 2872, 1740, 1661, 1607, 1366, 1377, 1248, 1157 cm^{-1}.

5.1.68. 5α-24-Norchol-14-ene-3α,6α,7β,23-tetrol (99). The ester **98** (300 mg, 0.389 mmol) was photolyzed in benzene (389 mL) at 25°C for 10 h with a 450 W mercury arc lamp and a pyrex filter. The solution was concentrated under reduced pressure and the residue was subjected to flash column chromatography (silica gel, 3:1:1 hexanes:ethyl acetate:chloroform) to give the olefin (184 mg, 61%). To a stirring solution of the olefin (175 mg, 0.227 mmol) at 25°C in dichloromethane (7 mL) was added pyridinium chlorochromate (98 mg, 0.454 mmol) and the reaction was stirred for 2 h. Celite (100 mg) and ether (7 mL) were added and the mixture was filtered through Celite. Concentration under reduced pressure gave the crude olefin, which was subjected to flash column chromatography (silica gel, 3:1 hexanes: ethyl acetate) to give the pure olefin (152 mg, 87%). To a stirring solution of the ester (142 mg, 0.185 mmol) in THF (5 mL) cooled to 0°C was added lithium aluminum hydride in portions (70 mg, 1.850 mmol). The mixture was stirred at 25°C overnight. Water (100 mL) was added, followed by 10% NaOH (100 mL), followed by 3 mL of water. The mixture was warmed to 25°C and stirred for 15 min. Magnesium sulfate was added and the reaction stirred for an additional 15 min. The solution was filtered and washed thoroughly with methanol. Concentration under reduced pressure and flash column chromatography of the resulting crude solid (silica gel, 9:1 chloroform:methanol) provided the tetrol **99** (55 mg, 79%) as a white solid. ^{1}H NMR (CD_3OD, 400 MHz) δ: 5.57 (1H, s), 4.04 (1H, m), 3.75–3.50 (2H, m), 3.41 (1H, dd, *J*=9.6, 8.6 Hz), 2.29 (1H, dd, *J*=11.2, 8.6 Hz), 2.35 (1H, ddd, *J*=14.9, 7.9, 2.3 Hz), 2.15–0.50 (22H, m), 0.98 (3H, d, *J*=6.5 Hz), 0.96 (3H, s), 0.85 (3H, s). ^{13}C NMR (CD_3OD, 100 MHz) δ: 152.6, 120.4, 78.3, 76.0, 66.6, 60.9, 60.2, 53.7, 48.8, 44.2, 43.0, 42.9, 39.9, 37.3, 37.0, 33.7, 32.4, 31.1, 29.2, 23.2, 19.8, 17.3, 12.8. FTIR (thin film): 3316, 2928, 1437, 1368, 1094, 1016 cm^{-1}.

5.1.69. 23-(1,1-Dimethylpropanoyloxy)-5α-24-norchol-14-ene-3α,6α,7β-triol (100). To a stirring solution of the tetrol **99** (48 mg, 0.127 mmol) in pyridine (3 mL) cooled to 0°C was added pivaloyl chloride (19 μL, 0.152 mmol). The mixture was stirred at 25°C overnight. Water was added and the mixture was thoroughly extracted with ethyl acetate (3×10 mL). The combined organic phases were dried over magnesium sulfate, filtered, and concentrated under reduced pressure. The excess pyridine was removed by high-vacuum rotovaporator. Flash column chromatography of the residue (silica gel, 17:1 chloroform:methanol) provided the triol ester **100** (49 mg, 83%) as a white solid. ^{1}H NMR (CD_3OD, 400 MHz) δ: 5.59 (1H, s), 4.30–4.09 (2H, m), 4.06 (1H, m), 3.42 (1H, dd, *J*=9.7, 8.7 Hz), 2.35 (1H, ddd, *J*=15.1, 7.8, 2.1 Hz), 2.29 (1H, dd, *J*=11.1, 8.6 Hz), 2.20–0.70 (21H, m), 1.20 (9H, s), 1.02 (3H, d, *J*=6.4 Hz), 0.97 (3H, s), 0.87 (3H, s). ^{13}C NMR (CD_3OD, 100 MHz) δ: 180.2, 152.6, 120.3, 78.2, 76.0, 66.6, 63.8, 59.8, 53.7, 48.8, 44.2, 42.93, 42.91, 39.9, 37.3, 37.0, 35.8, 33.6, 32.7, 31.1, 29.2, 27.7, 23.2, 19.7, 17.3, 12.8. IR (thin film): 3339, 2957, 2932, 2870, 2826, 1732, 1285, 1159, 1019 cm^{-1}.

5.1.70. 23-Acetyloxy-3α,5-cyclo-6β-methoxy-24-norcholane (101). To a stirring solution of the alcohol **75** (3.590 g, 9.956 mmol) in pyridine (40 mL) at 25°C was added acetic anhydride (1.13 mL, 11.95 mmol) dropwise and the mixture was stirred for 24 h. Water was added and the mixture was extracted with hexanes (3×15 mL). The organic layers were combined and dried over magnesium

sulfate, filtered, and concentrated under reduced pressure. Flash column chromatography (silica gel, 8:1 hexanes: ether) of the residue provided the ester **101** (3.990 mg, 100%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 4.20–3.85 (2H, m), 3.29 (3H, s), 2.74 (1H, dd, *J*=2.6, 2.6 Hz), 2.00–0.70 (22H, m), 2.01 (3H, s), 0.99 (3H, s), 0.93 (3H, d, *J*=6.6 Hz), 0.70 (3H, s), 0.62 (1H, dd, *J*=4.3, 4.3 Hz), 0.39 (1H, dd, *J*=5.1, 8.0 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 171.1, 82.3, 62.7, 56.5, 56.4, 56.1, 47.9, 43.3, 42.8, 40.2, 35.2, 35.0, 34.5, 33.3, 33.1, 30.4, 28.2, 24.9, 24.1, 22.7, 21.4, 21.0, 19.2, 18.7, 13.0, 12.1. FTIR (thin film): 2938, 2913, 2849, 2869, 1742, 1242, 1100 cm^{-1}.

5.1.71. 3β,23-Diacetyloxy-24-norchol-5-ene (102). The ether **101** (3.800 g, 9.439 mmol) was dissolved in glacial acetic acid (90 mL) and heated to 90°C for 3 h. The solution was cooled to 25°C and the acetic acid was removed under reduced pressure to provide the homoallylic acetate **102** (3.950 g, 97%) as a white solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 5.33 (1H, d, *J*=4.8 Hz), 4.57 (1H, m), 4.20–3.90 (2H, m), 2.40–2.20 (2H, m), 2.15–0.80 (21H, m), 2.01 (3H, s), 1.99 (3H, s), 0.99 (3H, s), 0.93 (3H, d, *J*=6.5 Hz), 0.66 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 171.1, 170.4, 139.5, 122.4, 73.8, 62.7, 56.5, 55.9, 49.9, 42.3, 39.6, 38.0, 36.9, 36.5, 34.5, 33.1, 31.74, 31.73, 28.1, 27.6, 24.1, 21.3, 21.0, 20.9, 19.2, 18.7, 11.7. FTIR (thin film): 2963, 2938, 2892, 2867, 1732, 1460, 1439, 1368, 1375, 1246 cm^{-1}.

5.1.72. 3β,23-Diacetyloxy-24-norchol-5-en-7-one (103). A mixture of the olefin **102** (2.900 g, 6.735 mmol) and ruthenium trichloride monohydrate (9 mg) was stirred at 25°C in 1,2-dichloroethane (34 mL) and water (7 mL). *tert*-Butyl hydroperoxide (70% aqueous, 8.76 mL) was added dropwise over 6 h and the mixture was allowed to stir for an additional 18 h. Sodium sulfite (2.9 g) was added and the mixture allowed to stir for 1 h. Water was added and the mixture was extracted with ether (3×30 mL). The combined organic extracts were dried over magnesium sulfate, filtered, and concentrated under reduced pressure. Flash column chromatography (silica gel, 5:1:2 hexanes:ethyl acetate:chloroform) of the residue provided the enone **103** (1.940 g, 65%) as a white solid. $[\alpha]_D^{25}=-106.4°$ (*c* 1.1, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 5.57 (1H, s), 4.58 (1H, dddd, *J*=11.4, 11.4, 4.4, 4.4 Hz), 4.20–3.80 (2H, m), 2.60–0.50 (21H, m), 1.93 (3H, s), 1.92 (3H, s), 1.10 (3H, s), 0.85 (3H, d, *J*=6.5 Hz), 0.58 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 201.4, 171.0, 170.0, 163.8, 126.5, 72.1, 62.6, 54.6, 49.9, 49.6, 45.2, 43.1, 38.5, 38.2, 37.6, 35.9, 34.5, 33.0, 28.5, 27.2, 26.2, 21.2, 21.05, 20.97, 18.9, 17.2, 11.8. FTIR (thin film): 2950, 2894, 2874, 2857, 1732, 1673, 1636, 1466, 1368, 1246 cm^{-1}. High-resolution MS (EI, *m/z*): 444.2873, calcd for $C_{27}H_{40}O_5$ 444.2876.

5.1.73. 3β,23-Diacetyloxy-24-norchol-5-en-7β-ol (104). To a stirring solution of the enone **103** (1.909 g, 4.294 mmol) in dichloromethane:methanol (4:1, 100 mL) cooled to −78°C was added cerium trichloride heptahydrate (3.200 g, 8.588 mmol) followed by sodium borohydride (0.325 g, 8.588 mmol). The solution was stirred and allowed to warm to 25°C slowly. The solution was acidified with 10% HCl and extracted with ether (3×100 mL). The combined organic extracts were dried over magnesium sulfate, filtered, and concentrated under reduced pressure to yield the allylic alcohol **104** (1.879 g, 98%) as a white solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 5.26 (1H, s), 4.56 (1H, dddd, *J*=11.4, 11.4, 4.4, 4.4 Hz), 4.20–3.90 (2H, m), 3.79 (1H, d, *J*=7.9 Hz), 2.50–0.50 (22H, m), 1.993 (3H, s), 1.986 (3H, s), 1.01 (3H, s), 0.92 (3H, d, *J*=6.5 Hz), 0.66 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 171.1, 170.3, 142.0, 126.4, 73.3, 72.9, 62.6, 55.8, 55.2, 48.0, 42.8, 40.5, 39.3, 37.4, 36.5, 36.3, 34.4, 33.0, 28.4, 27.6, 26.2, 21.2, 20.9, 20.8, 18.9, 18.7, 11.6. FTIR (thin film): 3455, 2907, 2948, 2872, 2853, 1736, 1468, 1439, 1366, 1246 cm^{-1}.

5.1.74. 3β,7β,23-Triacetyloxy-24-norchol-5-ene (105). To a stirring solution of the allylic alcohol **104** (1.861 g, 4.17 mmol) in pyridine (20 mL) at 25°C was added acetic anhydride (0.590 mL, 6.25 mmol) followed by 4-(dimethylamino)pyridine (10 mg). The reaction was stirred overnight and then ice chips were added. Water was added and the mixture was extracted with ether (3×40 mL). The combined organic extracts were dried over magnesium sulfate, filtered, and concentrated under reduced pressure. The excess pyridine was removed by high-vacuum rotovaporator. Flash column chromatography of the residue (silica gel, 4:1 hexanes:ethyl acetate) provided the allylic acetate **105** (1.968 g, 97%) as a white solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 5.19 (1H, s), 4.97 (1H, d, *J*=8.6 Hz), 4.54 (1H, dddd, *J*=11.4, 11.4, 4.4, 4.4 Hz), 4.20–3.90 (2H, m), 2.50–0.50 (21H, m), 1.986 (3H, s), 1.974 (3H, s), 1.967 (3H, s), 1.03 (3H, s), 0.91 (3H, d, *J*=6.5 Hz), 0.65 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 171.0, 170.9, 170.1, 144.0, 122.1, 75.3, 73.0, 62.6, 55.3, 55.2, 47.9, 42.8, 39.1, 37.4, 36.4, 36.33, 36.30, 34.4, 33.0, 28.2, 27.5, 24.9, 21.5, 21.2, 20.9, 20.9, 18.8, 18.7, 11.6. FTIR (thin film): 2950, 2815, 2874, 2855, 1736, 1368, 1240, 1032 cm^{-1}.

5.1.75. 5α-24-Norcholane-3β,6α,7β,23-tetrol (106). To a stirring solution of the triacetate **105** (1.933 g, 3.956 mmol) in THF (20 mL) cooled to 0°C was added borane–tetrahydrofuran complex (1.0 M, 12 mL, 11.867 mmol) dropwise and the reaction was stirred overnight at 25°C. The reaction was cooled to 0°C and sodium hydroxide (10% aqueous, 12 mL) was added very slowly followed by hydrogen peroxide (30% aqueous, 12 mL) and the mixture was stirred vigorously for 1 h. The mixture was acidified with HCl (10% aqueous) and extracted thoroughly with ethyl acetate (3×100 mL). The combined organic layers were dried over magnesium sulfate, filtered, and concentrated under reduced pressure to yield the tetrol **106** (0.750 g, 50%) as a white solid, which was used without further purification. ^{1}H NMR (CD_3OD, 400 MHz) δ: 3.70–3.40 (2H, m), 3.10 (1H, dd, *J*=10.4, 8.6 Hz), 2.96 (1H, dd, *J*=9.3, 8.9 Hz), 2.20–0.50 (27H, m), 0.94 (3H, d, *J*=6.5 Hz), 0.85 (3H, s), 0.71 (3H, s). ^{13}C NMR (CH_3OD, 100 MHz) δ: 80.0, 74.6, 70.4, 59.4, 56.3, 55.7, 52.3, 48.0, 43.4, 40.9, 40.0, 38.6, 37.3, 35.3, 32.8, 31.8, 30.5, 28.5, 26.5, 21.3, 18.3, 12.7, 11.5. FTIR (thin film): 3386, 2938, 2863, 1642, 1051 cm^{-1}.

5.1.76. 3β,6α,7β,23-Tetraacetyloxy-5α-24-norcholane (107). To a stirring solution of the tetrol **106** (20 mg, 0.053 mmol) in dichloromethane (1 mL) at 25°C was added acetic anhydride (30 mL, 0.315 mmol) followed by trimethylsilyl triflate (1 drop) and the mixture was stirred for 1 h. Saturated sodium bicarbonate was added and the

mixture was extracted with dichloromethane (3×2 mL). The combined organic extracts were dried over magnesium sulfate, filtered, and concentrated under reduced pressure to yield the tetraacetate **107** (28 mg, 97%) as a clear glass. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 4.82 (1H, dd, J=11.2, 9.1 Hz), 4.72 (1H, dd, J=10.0, 9.2 Hz), 4.59 (1H, dddd, J=11.1, 11.1, 4.7, 4.7 Hz), 4.20–3.90 (2H, m), 2.10–0.50 (22H, m), 2.00 (3H, s), 1.98 (3H, s), 1.97 (3H, s), 1.92 (3H, s), 0.93 (3H, s), 0.92 (3H, d, J=6.7 Hz), 0.65 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 171.2, 170.85, 170.75, 170.5, 77.8, 74.4, 72.6, 62.7, 55.0, 54.7, 51.6, 46.0, 43.6, 39.3, 39.0, 36.7, 35.8, 34.5, 33.0, 28.4, 28.3, 26.9, 24.8, 21.5, 21.3, 21.2, 21.1, 20.8, 18.8, 13.2, 11.9. FTIR (thin film): 2955, 2870, 1744, 1474, 1437, 1370, 1248, 1240, 1034 cm^{-1}. High-resolution MS (EI, *m/z*): 549.3437, calcd for $C_{31}H_{49}O_8$ $(M+H)^+$ 549.3427.

5.1.77. 6α,7β-Diacetyloxy-5α-24-norcholane-3β,23-diol (108). To a stirring solution of the tetraacetate **107** (350 mg, 0.626 mmol) in THF:ethanol (1:1, 10 mL) cooled to 0°C was added 10% sodium hydroxide (1 mL) dropwise and the reaction was stirred for 1 h. HCl (10% aqueous) was added to make the solution neutral and the mixture was extracted with dichloromethane (3×10 mL). The combined organic layers were dried over magnesium sulfate, filtered, and concentrated under reduced pressure. Flash column chromatography of the residue (silica gel, 19:1 chloroform: methanol) yielded the diol **108** (276 mg, 95%) as a white solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 4.68 (1H, dd, J=10.5, 9.6 Hz), 4.58 (1H, dd, J=9.6, 9.3 Hz), 3.60–3.20 (3H, m), 2.98 (2H, bs), 2.20–0.50 (22H, m), 1.84 (3H, s), 1.81 (3H, s), 0.79 (3H, s), 0.78 (3H, d, J=6.5 Hz), 0.53 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 170.9, 170.8, 77.9, 74.6, 70.2, 60.2, 55.2, 54.7, 51.7, 46.1, 43.5, 39.3, 38.9, 38.6, 36.8, 35.7, 32.6, 31.8, 30.7, 28.4, 24.7, 21.1, 21.2, 20.7, 18.8, 13.2, 11.9. FTIR (thin film): 3370, 2946, 2870, 1744, 1377, 1260, 1246, 1046, 1028, 733 cm^{-1}. High-resolution MS (EI, *m/z*): 464.3131, calcd for $C_{27}H_{44}O_6$ 464.3138.

5.1.78. 6α,7β-Diacetyloxy-23-[tris(1-methylethyl)]silyloxy-5α-24-norcholan-3β-ol (134). To a stirring solution of the diol **133** (283 mg, 0.609 mmol) in DMF (5 mL) at 0°C was added triisopropylchlorosilane (143 μL, 0.670 mmol) dropwise and the reaction was stirred for 4 h. Water was added and the mixture was extracted with dichloromethane (3×10 mL). The combined organic extracts were dried over magnesium sulfate, filtered, and concentrated under reduced pressure. Flash column chromatography of the residue (silica gel, 2:1 hexanes:ethyl acetate) yielded the diol **134** (286 mg, 76%) as a white solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 4.78 (1H, dd, J=10.5, 9.6 Hz), 4.68 (1H, dd, J=9.6, 9.3 Hz), 3.67–3.52 (2H, m), 3.44 (1H, dddd, J=11.3, 11.3, 5.0, 5.0 Hz), 2.23 (1H, bs), 2.00–0.50 (25H, m), 1.93 (3H, s), 1.89 (3H, s), 0.99 (18H, m), 0.88 (3H, s), 0.86 (3H, d, J=6.6 Hz), 0.61 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 170.91, 170.73, 77.96, 74.58, 70.46, 61.24, 55.22, 54.77, 51.81, 46.14, 43.58, 39.37, 39.02, 38.95, 37.01, 35.76, 32.48, 32.04, 30.91, 28.42, 24.83, 21.49, 21.26, 20.79, 19.04, 18.01, 13.32, 11.96, 11.86. FTIR (thin film): 3401, 1944, 2890, 2867, 1746, 1464, 1377, 1244, 1100, 1046 cm^{-1}. High-resolution MS (EI, *m/z*): 621.4565, calcd for $C_{36}H_{65}O_6Si$ $(M+H)^+$ 621.4550.

5.1.79. 3α-((-4-Benzoyl)phenylacetyloxy)-6α,7β-diacetyloxy-23-[tris((1-methyl)ethyl)-silyloxy]-5α-24-norcholane (135). To a stirring solution of the alcohol **134** (284 mg, 0.457 mmol) in THF (10 mL) at 25°C was added triphenylphosphine (240 mg, 0.914 mmol) and the carboxylic acid **40** (132 mg, 0.548 mmol) followed by the dropwise addition of DEAD (144 μL, 0.914 mmol) and the reaction was stirred for 1 h. Water was added and the mixture was extracted with ether (3×10 mL). The combined organic extracts were dried over magnesium sulfate, filtered, and concentrated under reduced pressure. Flash column chromatography of the crude residue (silica gel, 4:1 hexanes:ethyl acetate) provided the benzophenone ester **135** (286 mg, 74%) as a clear glass. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.80–7.70 (4H, m), 7.60–7.48 (1H, m), 7.48–7.30 (4H, m), 5.03 (1H, m), 4.77 (1H, dd, J=9.3, 11.2 Hz), 4.70 (1H, dd, J=9.8, 9.3 Hz), 3.80–3.50 (2H, m), 3.68 (2H, s), 2.10–0.40 (25H, m), 1.94 (3H, s), 1.92 (3H, s), 1.03 (18H, m), 0.89 (3H, d, J=6.5 Hz), 0.86 (3H, s), 0.62 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 195.80, 170.67, 170.57, 169.85, 138.90, 137.40, 136.18, 132.20, 130.26, 129.82, 129.12, 128.11, 77.63, 74.46, 69.36, 61.14, 55.06, 54.61, 51.87, 43.43, 41.61, 39.17, 38.86, 35.77, 32.62, 32.35, 28.30, 27.02, 25.30, 24.73, 21.36, 20.68, 20.57, 18.91, 17.90, 12.31, 11.84, 11.74. FTIR (thin film): 2944, 2892, 2867, 1744, 1661, 1607, 1464, 1447, 1377, 1277 cm^{-1}.

5.1.80. 3α,6α,7β-Tris(methoxymethoxy)-23-[tris((1-methyl)ethyl)silyl]oxy-5α-24-norchol-14-ene (137). The benzophenone ester **135** (286 mg, 0.339 mmol) was dissolved in purified, degassed benzene and photolyzed using a 450 W mercury arc lamp with a pyrex filter at 25°C for 10 h. The solvent was removed under reduced pressure and the solid subjected to flash column chromatography (silica gel, 3:1:1 hexanes:ethyl acetate:chloroform) to give the epimeric alcohols (137 mg, 48%). To a stirring solution of the epimeric alcohols (137 mg, 0.163 mmol) in dichloromethane (7 mL) at 25°C was added pyridinium chlorochromate (70 mg, 0.325 mmol) and the mixture was stirred for 2 h. Ether (10 mL) and Celite (100 mg) were added and the mixture was filtered through Celite and concentrated under reduced pressure to give the benzophenone olefin (86 mg, 63%). To a stirring solution of the benzophenone olefin (81 mg, 0.096 mmol) in THF (2 mL) at 25°C was added lithium aluminum hydride (37 mg, 0.963 mmol) and the reaction was stirred for several hours. The mixture was cooled to 0°C and water (100 mL) was added followed by 10% NaOH (100 mL), which was followed by the addition of water (300 mL) again. The mixture was warmed to 25°C and stirred for 15 min. Magnesium sulfate was added and the mixture was filtered and concentrated under reduced pressure. Flash column chromatography (silica gel, 20:1 chloroform:methanol) of the crude solid gave the olefinic triol **136** (44 mg, 85%) as a white solid. To a stirring solution of the triol **136** (32 mg, 0.060 mmol) in 1,2-dimethoxyethane (3 mL) was added diisopropylamine (470 μL, 2.700 mmol) and chloromethyl methyl ether (68 μL, 0.900 mmol) followed by sodium iodide (0.027 mg, 0.180 mmol) and the mixture was refluxed for 12 h. The mixture was allowed to cool and saturated sodium carbonate and water were added and the mixture was extracted with ether (3×5 mL). The combined

organic phases were dried over magnesium sulfate, filtered, and concentrated under reduced pressure. Flash column chromatography of the residue (silica gel, 5:1 hexanes:ethyl acetate) provided the ether **137** (32 mg, 80%) as a clear glass. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 5.63 (1H, m), 4.88 (1H, d, *J*=6.6 Hz), 4.80 (1H, d, *J*=6.6 Hz), 4.80 (1H, d, *J*=6.6 Hz), 4.65 (1H, d, *J*=6.6 Hz), 4.64 (1H, d, *J*=6.8 Hz), 4.61 (1H, d, *J*=6.8 Hz), 3.90 (1H, m), 3.85–3.60 (3H, m), 3.40–3.30 (1H, m), 3.41 (3H, s), 3.35 (3H, s), 3.30 (3H, s), 2.36 (1H, ddd, *J*=17.9, 8.0, 2.4 Hz), 2.28 (1H, dd, *J*=11.9, 10.3 Hz), 2.20–0.80 (29H, m), 1.05 (9H, m), 0.93 (3H, d, *J*=6.4 Hz), 0.92 (3H, s), 0.83 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 150.42, 118.84, 98.70, 35.95, 94.48, 82.95, 81.72, 70.57, 61.49, 58.53, 56.49, 55.85, 55.21, 52.58, 47.84, 42.99, 41.60, 40.54, 38.83, 36.00, 35.96, 32.92, 31.03, 27.96, 26.10, 22.64, 19.41, 18.06, 16.56, 12.51, 12.03. IR (thin film): 2942, 2930, 2890, 2867, 1464, 1148, 1100, 1042 cm^{-1}.

5.1.81. 3α,6α,7β-Tris(methoxymethoxy)-5α-24-norchol-14-en-23-ol (138). To a stirring solution of the ether **137** (32 mg, 0.048 mmol) in tetrahydrofuran (3 mL) at 25°C was added tetrabutylammonium fluoride (1.0 M in THF, 144 μL, 0.144 mmol) and the reaction was stirred for 1 h. The volatile components were removed under reduced pressure and the crude oil subjected to flash column chromatography (silica gel, 1:1 hexanes:ethyl acetate) to provide the alcohol **138** (22 mg, 92%) as a clear glass. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 5.53 (1H, bs), 4.88 (1H, d, *J*=6.6 Hz), 4.80 (1H, d, *J*=6.6 Hz), 4.80 (1H, d, *J*=6.6 Hz), 4.65 (1H, d, *J*=6.6 Hz), 4.64 (1H, d, *J*=6.8 Hz), 4.61 (1H, d, *J*=6.8 Hz), 3.90 (1H, m), 3.85–3.60 (3H, m), 3.40–3.30 (1H, m), 3.41 (3H, s), 3.35 (3H, s), 3.30 (3H, s), 2.36 (1H, ddd, *J*=17.9, 8.0, 2.4 Hz), 2.28 (1H, dd, *J*=11.9, 10.3 Hz), 2.20–0.80 (18H, m), 0.94 (3H, d, *J*=6.4 Hz), 0.92 (3H, s), 0.82 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 150.45, 118.72, 98.68, 95.95, 94.47, 82.94, 81.70, 70.55, 60.88, 58.56, 56.49, 55.85, 55.21, 52.53, 47.84, 43.00, 41.59, 40.54, 38.72, 36.04, 35.95, 32.91, 31.08, 27.94, 26.07, 22.62, 19.17, 16.61, 12.50. IR (thin film): 3443, 2932, 2890, 1466, 1443, 1372, 1148, 1100, 1040 cm^{-1}.

5.1.82. 3α,6α,7β-Tris(methoxymethoxy)-5α-24-norchol-14-en-23-al (139). To a stirring solution of the alcohol **138** (22 mg, 0.043 mmol) in dichloromethane (2 mL) at 25°C was added pyridinium chlorochromate (19 mg, 0.086 mmol) and the reaction was allowed to stir for 3 h. Celite (50 mg) and ether (4 mL) were added and the solution was filtered through Celite and concentrated under reduced pressure. The crude oil was subjected to flash column chromatography (silica gel, 2:1 hexanes:ethyl acetate) to provide the aldehyde **139** (18 mg, 82%) as a clear glass. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 9.78 (1H, dd, *J*=1.5, 1.5 Hz), 5.63 (1H, s), 4.88 (1H, d, *J*=6.7 Hz), 4.79 (1H, d, *J*=6.7 Hz), 4.78 (1H, d, *J*=6.6 Hz), 4.63 (1H, d, *J*=6.6 Hz), 4.63 (1H, d, *J*=6.8 Hz), 4.60 (1H, d, *J*=6.8 Hz), 3.89 (1H, m), 3.64 (1H, dd, *J*=10.0, 8.8 Hz), 3.41 (3H, s), 3.34 (3H, s), 3.33 (1H, dd, *J*=12.1, 8.0 Hz), 3.29 (3H, s), 2.60–1.05 (19H, m), 1.01 (3H, d, *J*=6.1 Hz), 0.96 (3H, s), 0.83 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 203.29, 150.56, 118.39, 98.65, 95.98, 94.44, 82.89, 81.62, 70.48, 57.88, 56.45, 55.81, 55.17, 52.44, 50.59, 47.79, 42.80, 41.56, 40.54, 36.17, 35.91, 32.87, 29.88, 27.90, 26.02, 22.52, 20.31, 16.55, 12.45. IR (thin film): 2930, 2894, 2822, 1725, 1466, 1443, 1372, 1148, 1908, 1040 cm^{-1}.

5.1.83. 3,6,7-Tris(methoxymethyl)xestobergsterol A (140). A solution of the aldehyde **139** (18 mg, 0.035 mmol) in ether (1 mL) at 0°C was added to a stirring solution of isobutyl magnesium bromide (2.0 M, 88 μL, 0.177 mmol) in ether (1 mL) at 0°C and the mixture was stirred for 20 min. Water was added and the mixture was extracted with ether (3×2 mL). The combined organic extracts were dried over magnesium sulfate, filtered, and concentrated under reduced pressure. Flash column chromatography (1.7:1 hexanes:ethyl acetate) of the crude product provided a 1:1 mixture of diastereomeric alcohols (16 mg, 80%). To a stirring solution of the diastereomeric alcohols (15 mg, 0.026 mmol) in THF (2 mL) at 0°C was added borane–tetrahydrofuran complex (1.0 M, 208 μL, 0.208 mmol) and the mixture was stirred for 6 h at 25°C. The solution was cooled to 0°C and 10% sodium hydroxide (200 μL) was added followed by 30 hydrogen peroxide (200 mL) and the reaction was stirred overnight. Water was added and the mixture was extracted with ether (3×2 mL). The combined organic extracts were dried over magnesium sulfate, filtered, and concentrated under reduced pressure to yield a mixture of alcohols which were used in the next step without further purification. To a stirring solution of the diastereomeric alcohols (15 mg, 0.026 mmol) in dichloromethane (2 mL) at 25°C was added pyridinium chlorochromate (22 mg, 0.104 mmol) and the reaction was stirred for 3 h. Celite (50 mg) and ether (4 mL) were added and the solution was filtered through Celite and concentrated under reduced pressure. The crude material was then dissolved in THF:ethanol (1:1, 3 mL) and 10% NaOH (0.5 mL) was added and the mixture stirred overnight. Water was added and the mixture extracted with ether (3×5 mL). The combined organic extracts were dried over magnesium sulfate, filtered, and concentrated under reduced pressure. Flash column chromatography of the residue (silica gel, 3:1 hexanes:ethyl acetate) yielded the hydroxyketone **140** (11 mg, 73% over three steps) as a clear glass. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 4.83 (1H, d, *J*=6.6 Hz), 4.79 (1H, d, *J*=6.1 Hz), 4.70 (1H, d, *J*=6.0 Hz), 4.63 (3H, d, *J*=6.5 Hz), 4.51 (1H, dd, *J*=10.7, 8.9 Hz), 3.15 (1H, dd, *J*=11.4, 8.9 Hz), 3.40 (3H, s), 3.35 (3H, s), 3.34 (3H, s), 2.70 (1H, m), 2.62 (1H, d, *J*=10.0 Hz), 2.60–1.05 (17H, m), 1.13 (3H, s), 1.09 (3H, d, *J*=6.3 Hz), 0.96 (3H, d, *J*=7.0 Hz), 0.94 (3H, d, *J*=6.6 Hz), 0.78 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 219.99, 99.39, 98.68, 94.43, 83.13, 82.55, 82.11, 70.55, 62.97, 57.49, 56.48, 56.35, 56.35, 55.23, 51.70, 51.68, 50.73, 46.17, 41.47, 38.35, 38.18, 38.05, 36.25, 34.57, 32.69, 27.75, 26.13, 24.82, 24.69, 24.47, 20.51, 19.72, 12.55. IR (thin film): 3476, 2930, 2857, 2822, 1724, 1468, 1148, 1130, 1098, 1032 cm^{-1}.

5.1.84. Xestobergsterol A (1a). To a stirring solution of the tris(methoxymethyl) ether **140** (3 mg, 0.005 mmol) in THF:ethanol (8:1, 1 mL) was added 50% HCl (200 μL) and the reaction allowed to stir at 25°C for 24 h. Saturated sodium bicarbonate was added and the mixture was extracted with ethyl acetate (3×5 mL). The combined organic extracts were dried over magnesium sulfate, filtered, and concentrated under reduced pressure. The

solid was subjected to flash column chromatography (silica gel, 9:1 chloroform:methanol) to provide xestobergsterol A **1a** (3 mg, 100%) as a white solid. $[\alpha]_D^{25}=-37.6°$ (*c* 0.25, $CHCl_3$). ^1H NMR (pyridine-d_5, 400 MHz) δ: 5.10 (1H, dd, *J*=10.0, 9.1 Hz), 4.37 (1H, m), 3.62 (1H, dd, *J*=10.7, 8.8 Hz), 3.49 (1H, m), 2.77 (1H, m), 2.70 (1H, d, *J*=9.9 Hz), 2.62 (1H, m), 2.42 (1H, m), 2.21 (1H, m), 2.09 (1H, dd, *J*=12.2, 5.4 Hz), 2.05–0.80 (19H, m), 1.19 (3H, s), 1.13 (3H, d, *J*=6.2 Hz), 1.07 (3H, d, *J*=6.7 Hz), 1.05 (3H, d, *J*=7.0 Hz), 0.91 (3H, s). ^{13}C NMR (pyridine-d_5, 100 MHz) δ: 217.20, 82.09, 75.83, 74.91, 65.23, 62.75, 57.91, 52.39, 51.94, 51.73, 46.48, 42.47, 39.15, 38.48, 38.37, 36.86, 34.80, 33.10, 31.46, 29.41, 25.24, 24.93, 24.85, 21.45, 20.82, 19.86, 12.80. FTIR (thin film): 3366, 2932, 2870, 1728, 1468, 1377, 1169, 1082, 1020, 988 cm^{-1}. High-resolution MS (EI, *m/z*): 449.3272, calcd for $C_{27}H_{45}O_5$ $(M+H)^+$ 449.3267.

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