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A new route for the preparation of the 22,23-dioxocholestane side chain from diosgenin and its application to the stereocontrolled construction of the 22*R*,23*S*-diol function

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Abstract—The new (22*R*,23*S*,25*R*)-3β,16β,26-triacetoxy-cholest-5-ene-22,23-diol (**11a**) was synthesized from diosgenin (**3**) through a synthetic route based on chemoselective RuO_4 oxidation of (25*R*)-3β,16β-diacetoxy-23-ethyl-23^1,26-epoxycholesta-5,23(23^1)-dien-22-one (**9**) that afforded (20*S*,25*R*)-3β,16β,26-triacetoxycholest-5-ene-22,23-dione (**10**) which was stereoselectively reduced using $NaBH_4$. Compound **9** was obtained from the known isomeric 22,26-epoxycholest-5-ene steroidal skeleton **8b** by treatment with *p*-TsOH in toluene, amberlyst-15 or directly from diosgenin by treatment with $BF_3 \cdot OEt_2/Ac_2O$. Chemoselective reduction of the 23-keto group of **10**, was attained using $NaBH_4/ZnCl_2$ at −70 °C to give 23*S*-**14**. The NMR spectra of all compounds were unambiguously assigned based on one and two dimensional experiments and the C-22 and C-23 stereochemistry in the diacetate derivative **11b**, as well as the structure of epoxycholestene **9** were further established by X-ray diffraction analyses. The new route for the functionalization of the side chain of diosgenin can find application in the synthesis of norbrassinosteroid analogues.

1. Introduction

In recent years there has been increasing interest in the selective functionalization and derivatization of spirostan sapogenins owing to their applications in the synthesis of potent anticancer agents such as OSW-1,[1] cephalostatins and ritterazines,[2] oxysterols[3] and steroidal natural products.[4] Since ring opening of the spiroketal is pivotal for the selective transformation of the side chain, a great variety of catalysts and reaction conditions have been explored providing a wide variety of products,[5] sometimes under similar reaction conditions.

For many years it was believed that cleavage of the spiroketal side chain always occurs at the F ring, leading to furostene derivatives.[6] This erroneous conception led to incorrect structural assignment in several old and recent reports. For example, although Zderic[7] obtained **8b** by treatment of diosgenin(**3**) with excess $BF_3 \cdot OEt_2/Ac_2O$, the structure was incorrectly assigned as (*E*)-(25*R*)-23-acetyl-furosta-5,22-diene-3β,16β-diyl diacetate (**4a**) (Fig. 1). Singh[8] described that under catalysis of the same Lewis acid (8 equiv, 1 h reflux), but in the absence of acetic acid, diosgenin undergoes regioselective cleavage of ring E, not F, to give a new derivative, the 22,26-epoxycholesta-3,5-diene-16-one (**5**). In a similar experiment, Tian[9] reported that the 20-epimeric furostenes **4a** and **4b**, as well as (*E*)-(20*S*,25*R*)-20,23-diacetylfurosta-5,22-diene-3β,16β-diyl diacetate (**6**) are obtained when an equivalent of the Lewis was added at 0 °C, and stirred for 3 h at room temperature. However, the same author[10] reinvestigated the reaction and corrected the structures proposed for the furostenes, which correspond to epoxycholestenes (25*R*)-23-acetyl-3β,16β-diacetoxy-22,26-epoxycholesta-5,22-diene (**8a**, **8b**). The regioselective opening of ring E in spirostan

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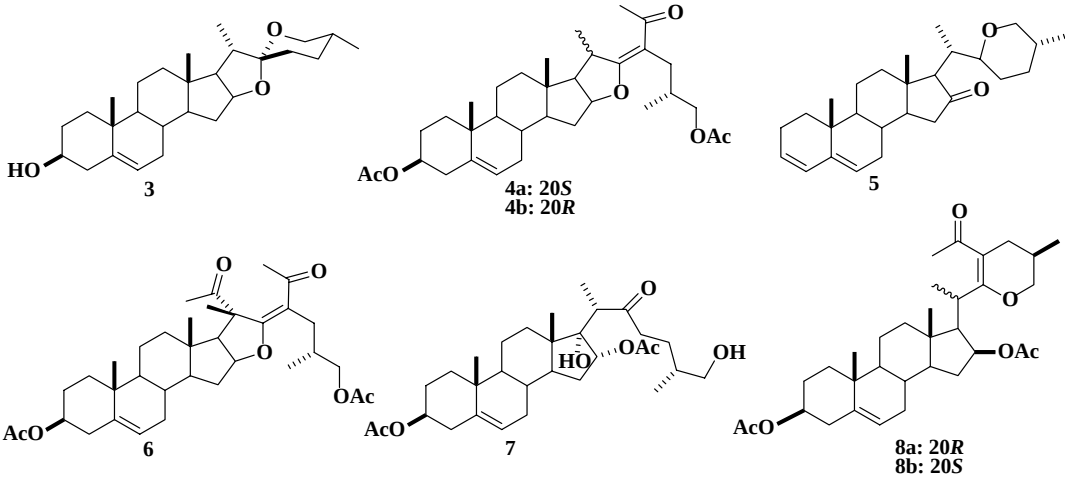


Figure 1. Products from $BF_3 \cdot OEt_2$ catalyzed transformations of sapogenins.

sapogenins to give an epoxy derivative analogous to **8a** has been described by González.[11] In turn, Strigina[12] reported that, with the same Lewis acid, 17α-hydroxydiosgenin (pennogenin) produced (20*S*,25*R*)-22-oxocholest-5-ene-3β,16α,17α,26-tetraol-3,16-diacetate (**7**) or a dimeric furostene, depending on the reaction conditions.

We have described the highly regioselective cleavage[13a] of ring E in sapogenins from the 25*R* serie whereby treatment of diosgenin (**3**) yielded 23-acetyl-3β,16β-diacetoxy-22,26-epoxycholesta-5,22-diene (**8b**) in 85%, as established by spectroscopic methods and X-ray diffraction analysis. In contrast, sarsasapogenin (25*S* serie), yields a mixture of furostenes and epoxy derivative due to steric hindrance of the methyl group at position 25.[13b,14] More recently, reduction of the vinylogous ester moiety in compound **8b** with 9-BBN provided steroidal derivatives[15] with vinyl substituents on C-23.

In continuation of our studies on the modification of the side chain of sapogenins we report the construction of a cholestane side chain supporting a *trans*-22,23-diol functionality from diosgenin, by stereoselective reduction of the corresponding 22,23-dioxocholestane. This functionality is analogous to the one present in plant growth hormones known as brassinosteroids where it has been recognized that the stereochemistry of the carbon atoms supporting the substituents on the side chain, plays an important role on the biological activity, thus all native brassinosteroids present a (22*R*,23*R*)-diol moiety.

Due to the high bioactivity of brassinosteroids, a variety of analogues have been prepared and tested, and great efforts have been devoted to the construction of the side chain that supports the (22*R*,23*R*)-diol function; for this reason, many synthetic pathways have been published.[16–20] In general, spectral characterization of the new native or synthetic derivatives is based on comparison with the reported NMR studies described for brassinolide (**1**) and 24-*epi*-brassinolide[21,22] (**2**) (Fig. 2).

The present work describes a new approach based on the construction of the 22,23-dioxocholestane from the intact side chain of diosgenin, an important raw materials for the synthesis of hormones and other biologically interesting steroids. It should be mentioned that diosgenin (**3**) has also been used for the preparation of brassinosteroids analogues with spirostanic or furostanic side chains.[23]

The structures of all compounds were established by detailed 1D and 2D NMR studies. Moreover, comparison of the data reported for a series of brassinosteroids derivatives revealed that assignment of the configuration of diol **11a** based solely on chemical shifts and coupling constants from the ^1H spectrum is not easy due to conformational changes [24–26] in the side chain. Thus, the configurations at the newly formed stereogenic centers were unambiguously established as 22*R*,23*S* by X-ray diffraction analysis of the diacetate derivative **11b**. Stereoselective formation of diol **11a** was attributed to steric hindrance at C-22 caused by Me-18, Me-21 and the acetate at C-16. This in turn allowed regioselective reduction of the carbonyl group at position 23.

The new methodology described herein could find application in the synthesis of brassinosteroids analogues and, to our knowledge, this constitutes the first report where the 22,23-functionality is constructed from the intact side chain of diosgenin. Moreover, stepwise reduction offers the possibility of stereoselective formation of specific 22,23-diol functions. Finally the new derivatives have potential for the preparation of labeled samples required in biosynthetic studies.

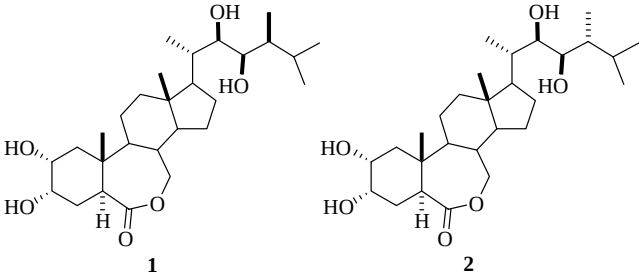
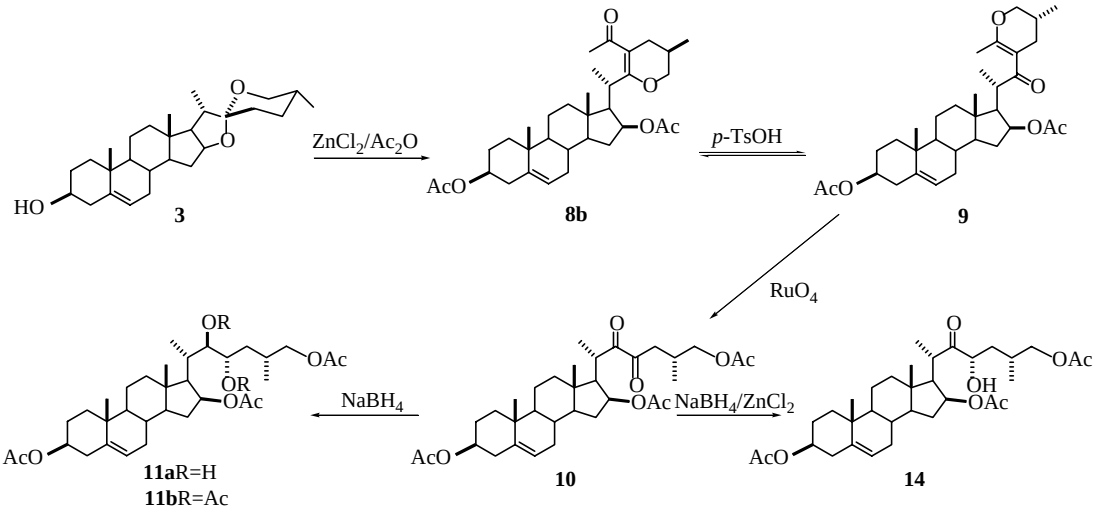


Figure 2. Native C-24 epimeric brassinolides.



Scheme 1. Synthetic route for the preparation of *trans*-diol **11a**.

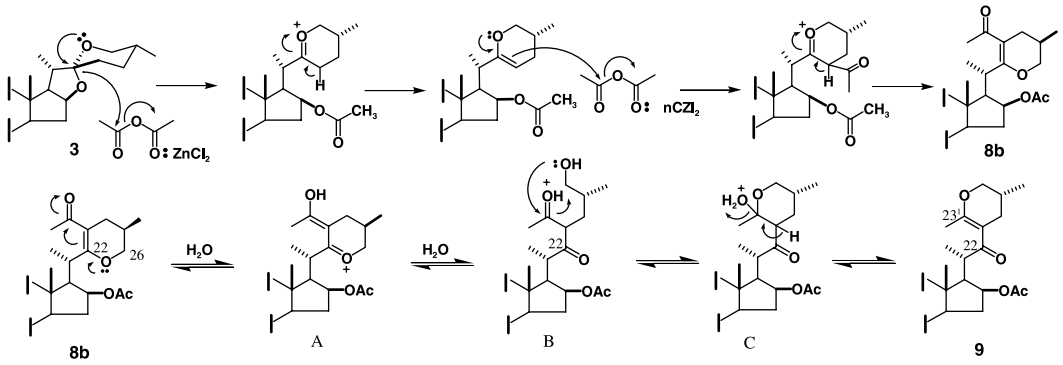
2. Results and discussion

In view of the synthetic value of **8b** for the construction of steroidal frameworks, the acetolysis reaction of diosgenin was reinvestigated using $ZnCl_2/Ac_2O$ instead of $BF_3\cdot OEt_2/Ac_2O$; this allowed to increase the yield to 95% (Scheme 1). The mechanism for the formation of **8b** (Scheme 2) is analogous to that described previously.[13a]

An important modification reported herein is the transformation of **8b** into the isomeric epoxycholesta-5,23(23[1])-dien-22-one (**9**). This reaction was carried out using different types of acids such as H_3PO_4, HCl, $BF_3\cdot OEt_2$, amberlyst-15 and *p*-TsOH (in hexane, acetone, benzene and toluene). The best results were obtained with *p*-TsOH acid in toluene or amberlyst-15 in water[27] which allowed to obtain the new β-alkoxy-α,β-unsaturated ketone **9** in 60% yield. The existence of an equilibrium between **8b** and **9** (4:6 ratio, determined by ^{1}H NMR) was confirmed by reacting epoxy **9** under the same conditions. Moreover, increasing the reaction times did not alter the product ratio and only reduced the yield. Alternatively, compound **9** could be obtained directly by treatment of diosgenin (**3**) with $BF_3\cdot OEt_2/Ac_2O$ provided quenching of the reaction is performed by slowly adding small portions of ice.

The acid catalyzed rearrangement of epoxycholestene **8b** can be explained through formation of oxonium ion **A** (Scheme 2), which is attacked by a molecule of H_2O giving a hemiketal, which tautomerizes to the β-diketone **B**. A new pyran ring is formed by nucleophilic attack of the hydroxyl group on C-26 to the carbonyl at C-23[1] (intermediate **C**). Protonation of the hemiketal followed by sequential elimination of water and proton gives the new product **9**. This mechanism is similar to the one proposed for the reaction of vinyl ethers with water in acidic solution.[28]

Compound **9** was obtained as colorless crystals, mp 255–256 °C; $[\alpha]_D^{20}$ −39, quite different from those of **8b**, mp 95–96 °C, and $[\alpha]_D^{20}$ −24. The mass spectrum of both **8b** and **9** showed the molecular ion at 540 amu with different fragmentation patterns. In the IR spectrum, characteristic carbonyl absorptions were observed at 1734 and 1671 for **9**, compared to 1732 and 1660 for **8b**. The ^{1}H NMR data for the isomeric derivatives **8b** and **9** showed similar chemical shifts for Me-21 (1.10 ppm in **9** and 1.19 ppm in **8b**), Me-18 (0.89 ppm in **9** and 0.92 in **8b**) and H-16α (5.02 in **9** and 5.14 in **8b**). However, the fact that the proton at C-20 is considerably shifted to low frequencies in **9** (3.20 ppm) compared to **8b** (4.08 ppm), could easily lead to the erroneous conclusion that the compounds are epimeric at



Scheme 2. Plausible mechanism for the formation of isomeric **8b** and **9**.

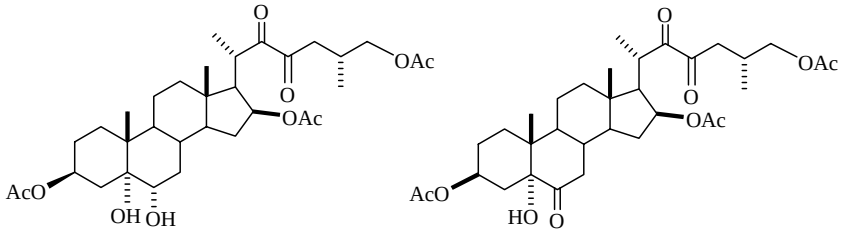


Figure 3. Δ^5 Oxidation of epoxy **9** with RuO_4.

C-20. Similarly, the ^{13}C NMR spectrum showed only slight chemical shifts differences except for the signals in the region from 160–175 ppm, which showed signals in 171.2, 170.4 and 170.3 for **8b**; 170.3, 169.6 and 164.2 for **9**, as well as C-20, which appears at 32.7 in **8b** and 38.6 in **9**.

Dione **10** was obtained by treatment of **9** with RuO_4 during 4 min at 0 °C in 63% yield[29d] (Scheme 1), together with recovered unreacted material. The chemoselectivity of the oxidation was confirmed by observation of the vinylic proton (H-6) at 5.36 ppm in the ^1H NMR spectrum. The diastereotopic protons at position 26 appear as dd at 4.03 and 3.88 ppm while the ones at position 24 are at 2.87 and 2.59 ppm. Conclusive evidence was obtained from the ^{13}C NMR spectrum that showed the presence of two carbonyl signals at 200.2 and 198.2 ppm and the double bond at 139.6 and 122.1 ppm.

The mass spectrum of **10** showed the pseudo molecular ion at 573 [$M^+ + 1$]. In the IR spectrum, carbonyl absorptions were observed at 1734 (C=O). The UV spectrum shows an absoption at 429 nm ($\varepsilon = 32$), characteristic of α-diketones.

When the epoxy derivative **9** was allowed to react with RuO_4 for 3 h other oxidation products were formed. In this way, 5,6-diol **12** and trione **13** were obtained, by further oxidation of the double bond in C-5 (Fig. 3). The ^1H NMR spectrum of 5,6-diol **12** showed the presence of a doublet of doublets for a proton geminal to an alcohol at 3.65 ppm, indicative of the oxidation of Δ^5. The corresponding ^{13}C NMR showed signals at 76.3 and 70.3 ppm for C-5 and C-6, respectively. The stereochemistry of the hydroxyl groups was established by a ROESY experiment, which showed correlation between H-6 and Me-19 that evidences a 6β disposition among them, therefore, the cis hydroxylation of the Δ^5 double bond occurs from the alpha side.[29] The UV spectrum of **12** shows a band at 275 nm ($\varepsilon = 1734$) for the α-diketone and IR bands at 1736 cm^{-1} (C=O) and 3480 cm^{-1} (OH). The mass spectrum shows the pseudo molecular ion at 607.

In the ^1H NMR spectrum of trione **13**, the new signal at 2.78 ppm (dd, $J_{7,8} = 12.7$ Hz), typical for a proton α to a carbonyl group, was assigned to H-7_{ax} while H-7_{eq} is shifted upfield and overlapped with other signals. The remaining signals had chemical shifts similar to those of dione **12**. Similarly, no vinylic signals were evident in the ^{13}C NMR spectrum, which shows three carbonyl signals at 211.5, 200.1 and 198.1 ppm. The high frequency signal was assigned to C-6 by comparison with the shift obtained for the corresponding carbons in dione **10**, while the remaining carbonyl groups at C-22 and C-23 were ascribed based on long range coupling constants from the HMBC experiment, which shows correlation between the carbonyl carbon at position 22 and Me-21. The signal at 80.1 ppm was assigned to the quaternary C-5.

The UV spectrum of **13** gives a band at 379 nm ($\varepsilon = 264$) characteristic of α-diketones. The carbonyl absorption appears at 1737 cm^{-1} and the hydroxyl groups at 3468 cm^{-1}, in the IR spectrum. The mass spectrum showed a pseudo molecular ion at $m/z = 605$.

The final step involved reduction of **10** with $NaBH_4$ in MeOH at room temperature, during 30 min, to give (22*R*,23*S*)-3β,16β,26-triacetoxycholest-5-ene-22,23-diol (**11a**). The proton NMR spectrum of **11a** showed multiplets for H-16 and H-3 at 5.27 and 4.60 ppm. The diastereotopic protons at C-26 showed the same pattern as in dione **10**, and their chemical shifts were also very similar (4.06 and 3.95 ppm). The broad dd at 3.66 ppm, was assigned to H-23 ($J_{22,23} = 8$ Hz) and the broad doublet ($J = 8$ Hz, $W_{1/2} = 7$ Hz) at 3.22 to H-22. The mass spectrum of **11a** showed the [$M^+ - 18$] ion at 558. In the IR spectrum, the hydroxyl band was observed at 3503 cm^{-1}. The UV spectrum shows an absorption at 269 nm ($\varepsilon = 413$).

In order to assign the configuration at C-22 and C-23, the coupling constant values reported for brassinosteroids and analogs (Fig. 4) were compared with those of diol **11a**, however, it is evident that these values are dependent on the configuration of C24, as well as the conformation of the side chain.[24–26] Evidence for the stereochemistry of the new stereogenic centers was obtained from a NOESY experiment, which showed through space interaction between H-22 and H-16, thus suggesting a (22*R*) configuration.

The ROESY spectrum for **11a** showed correlation between H-22 and H-16; H-22 and H-17, therefore H-22 is on the same side as H-16 and H-17. Also, an interaction between H-23 and H-20 was observed; since H-20 is beta, this suggests that H-23 is on the same face. This allowed to propose a (22*R*,23*S*) stereochemistry for **11a**, which is in agreement with the couplings constants reported for (23*S*,24*R*)-diepiteasterone, (22*S*,24*R*)-diepiteasterone and brassinolide (**1**) (Fig. 4).

In order to unambiguously establish the stereochemistry at C22 and C23, several diol derivatives, which include the boronic ester, acetonide and diacetate **11b** were prepared, the latter provided adequate crystals for X-ray analysis. Thus, the absolute configuration of the carbons at positions

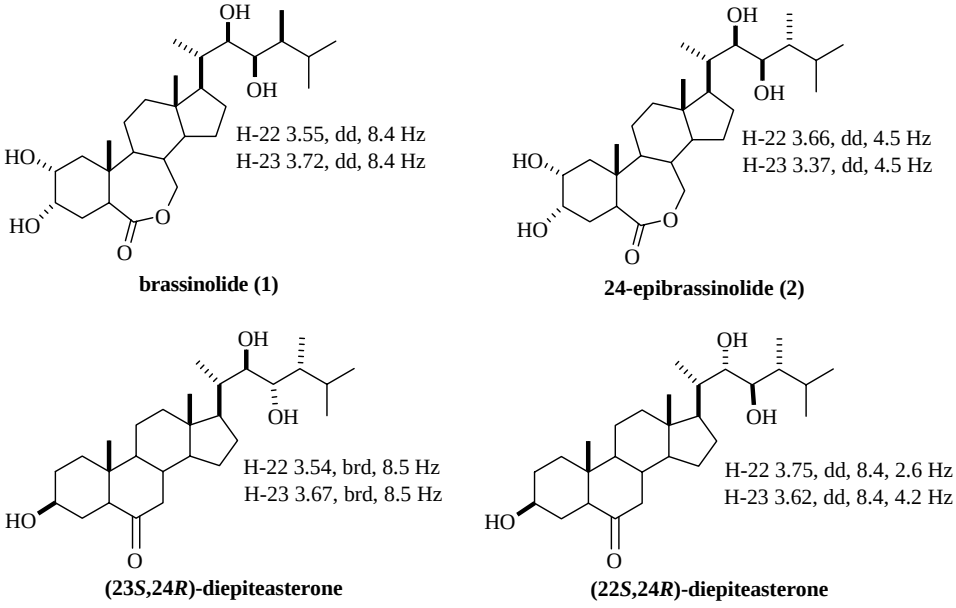


Figure 4. Chemical shifts and coupling constants for 22,23-dihydroxylated brassinosteroids.[24]

22 and 23 were established as *R* and *S*, respectively, confirming our previous assignments base on NMR studies.

The X-ray crystal structure analyses of compounds **9** and **11b** showed that the stereochemistry at C20 and C25 (*S*,*R* configuration, respectively) is retained (Fig. 5). In both compounds, the steroid nucleus shows that rings A and C adopt chair conformations. The C5–C6 (Csp^2–Csp^2) distance of 1.32 (4) Å confirms the position of the double bond, and ring B adopts a half-chair conformation. The cyclopentane ring D adopts an envelope conformation with torsion angles of 23.3° for the C15–C16–C17–C13 fragment. Bond lengths and angles for C-22 and C-23 unambiguously stand for sp^2 hybridized atoms in the case of **9**, while a sp^3 hybridization is observed in the case of **11b**. The dihedral angle for the H22–C22–C23–H23 fragment is 166.4° indicating a quasi *anti* conformation for the 22,23-diol.

Regioselective reduction of the carbonyl group at C-23 was attained by treatment of **10** with $NaBH_4$ in the presence of $ZnCl_2$, at −70 °C during 3 h, to give keto-ol **14**. The ^1H NMR spectrum showed the multiplets assigned to H-3 and H-16 at 4.57 and 4.78 ppm; the diastereotopic protons at C-26 are slightly downfield shifted (4.12 and 4.03 ppm) in comparison with those of the diol **11a** (4.06 and 3.95 ppm) or with respect to those in the diketone **10** (4.03 and 3.88 ppm). A dq at 3.02 ppm was assigned to H-20, the multiplet at 2.29 ppm to H-24 and the broad doublet at 4.23 ppm to H-23. The fact that H-20 (3.02 ppm) in **14** is shifted to high frequency with respect to diosgenin or the diol-**11a** evidences the presence of a carbonyl group at C-22; the same proton in dione-**10** is observed at 3.77 ppm. Moreover, the ^{13}C NMR spectrum of **14** showed only one carbonyl signal at 215.18 ppm and a new signal at 75.45 ppm for C-23. The results evidence that the stereoselectivity of the reduction of the carbonyl group at C-23 is due to a large steric hindrance caused by Me-18, and Me-21.

In conclusion, we have developed a new route for the preparation of 22,23-dioxocholestane frameworks via chemoselective oxidation of **9**. The sequence described provides a new route to norbrassinosteroid analogues by exploiting the intact skeleton of sapogenins. It is important to mention that there have been intensified efforts toward the synthesis of these phytohormones in view of their application for enhancement of crop yields.

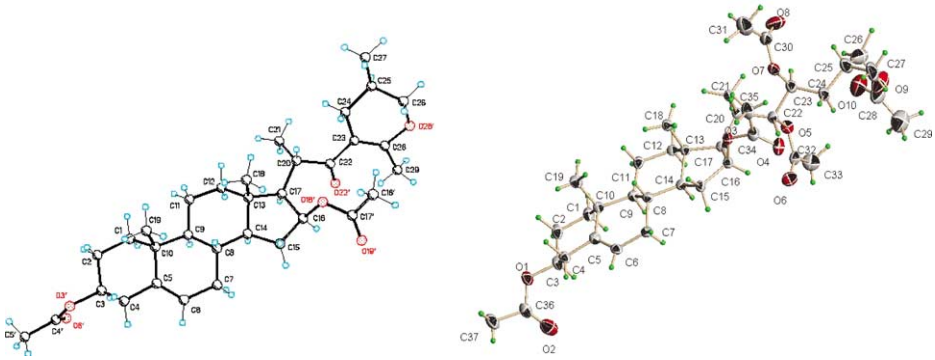


Figure 5. Perspective views of compounds **9** and **11b** (ellipsoids at 50% probability).

3. Experimental

3.1. General

1D and 2D ^{1}H and ^{13}C NMR spectra (DEPT, COSY, HMQC, HMBC, INADEQUATE) were recorded on Bruker DMX 500 and JEOL eclipse +400 spectrometers. Chemical shifts are stated in ppm (δ), and referred to the residual ^{1}H signal ($\delta=7.27$) or to the central ^{13}C triplet signal, ($\delta=77.0$) for $CDCl_3$. Infrared absorption spectra were obtained with Perkin Elmer 16F-PC-FT-IR and Perkin Elmer Spectrum GX spectrophotometers using KBr pellets. Mass spectra (EI) were obtained on a HP 5989A spectrometer adapted to a HP 6890A gas chromatograph.

Ultraviolet absorption spectra were determined on a Perkin Elmer Lambda 12 and Varian Cary UV–vis spectrophotometers; wavelengths (λ) are expressed in nm. Optical rotations were determined on a Perkin-Elmer 241 polarimeter at room temperature using chloroform solutions. Melting points were obtained on an Electrothermal 9200 apparatus. Elemental analyses were determined on a Thermofinnigan flash EA 1112. X-ray diffraction analyses were performed on Bruker P4 and Enraf-Nonius-Kappa CCD diffractometers with Mo Kα-radiation, $\lambda=0.71073$ Å. Column chromatography were carried out on silica gel grade 60 (230–400 mesh). Thin layer chromatography analyses were performed on silica gel $60F_{254}$ sheets using a 7:3 hexane/ethyl acetate mixture. High-resolution mass spectra were obtained on a Jeol JMS-SX102A using polyethylene glycol-600.

3.2. Reaction of diosgenin with $ZnCl_2/Ac_2O$

To a suspension of 1.00 g (2.4 mmol) of **3** in 10 mL (106.0 mmol) of Ac_2O were added 0.33 g (2.4 mmol) of anhydrous $ZnCl_2$. The reaction mixture was stirred 40 h at room temperature and quenched with ice. The organic phase was extracted with ethyl acetate, neutralized with a saturated $NaHCO_3$ solution, dried over anhydrous $MgSO_4$, and evaporated under vacuum to yield 1.23 g (95%, $R_f=0.50$) of **8b**.

3.2.1. (25*R*)-23-Acetyl-3β,16β-diacetoxy-22,26-epoxycholesta-5,22-diene (8b). Colorless crystals, mp 95–96 °C, lit. (95–96 °C) [11,13a] $[\alpha]_D^{20}$ −24 (*c* 0.65, $CHCl_3$); UV λ_{max} 275 nm (ε 10,300); IR $\bar{\nu}_{max}$: 1732 (OAc), 1660 and 1568 (C=C–C=O), 1248 (C–O) cm^{-1}; MS, *m/z* (%): 540 ([M$^{+\cdot}$], 3), 480 (9), 205 (100), 43 (91). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.36 (1H, d, $J=4.5$ Hz, H-6), 5.14 (1H, ddd, $J_{16-17\alpha}=J_{16-15\alpha}=7.5$ Hz, $J_{16-15\beta}=4.0$ Hz, H-16), 4.59 (1H, m, H-3), 4.08 (1H, dq, $J_{20-17}=11.0$ Hz, $J_{20-21}=7.0$ Hz, H-20), 4.01 (1H, ddd, $J_{gem}=10.5$ Hz, $J_{26eq-25ax}=3.5$ Hz, $J_{26eq-24eq}=2.0$ Hz, H-26$_{eq}$), 3.46 (1H, dd, $J_{gem}=J_{26ax-25ax}=10.5$ Hz, H-26$_{ax}$), 2.20 (3H, s, 23^2-$COCH_3$), 2.03 (3H, s, 3-OCOCH_3), 1.84 (3H, s, 16-OCOCH_3), 1.19 (3H, d, $J=7.0$ Hz, CH_3-21), 1.03 (3H, s, CH_3-19), 0.97 (3H, d, $J=6.5$ Hz, CH_3-27), 0.92 (3H, s, CH_3-18). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 197.9 (23^1-*CO*CH_3), 171.2 (C-22), 170.4 (16-O*CO*CH_3), 170.3 (3-O*CO*CH_3), 139.6 (C-5), 122.1 (C-6), 106.8 (C-23), 74.9 (C-16), 73.7 (C-3), 71.4 (C-26), 55.8 (C-17), 54.2 (C-14), 49.9 (C-9), 42.1 (C-13), 39.6 (C-12), 37.9 (C-4), 36.8 (C-1), 36.4 (C-10), 34.8 (C-15), 32.7 (C-20), 31.5 (C-24), 31.4 (C-7), 31.2 (C-8), 29.6 (23^2-$COCH_3$), 27.6 (C-2), 26.4 (C-25), 21.2 (3-OCO*C*H_3), 21.0 (16-OCO*C*H_3), 20.7 (C-11), 19.3 (C-21), 19.1 (C-19), 16.7 (C-27), 12.8 (C-18).

3.3. Reaction of diosgenin with $BF_3\cdot OEt_2/Ac_2O$

To a magnetically stirred suspension of 5.00 g (12.1 mmol) of **3** in 50 mL (531 mmol) of Ac_2O were added 10 mL (72.6 mmol) of $BF_3\cdot OEt_2$, at room temperature. The reaction mixture was stirred for 10 min and quenched by adding slowly small portions of ice over a period of 20 min (CARE most be taken because the reaction is highly exothermic) The organic phase was extracted with ethyl acetate, neutralized with saturated $NaHCO_3$ solution, dried over anhydrous $MgSO_4$ and evaporated under vacuum. The crude product (5.30 g) was chromatographed over silica gel using hexane/EtOAc 90:10 to give 1.00 g of **8b** (17% yield, $R_f=0.5$), 2.50 g of **9** (42% yield, $R_f=0.38$) contaminated with traces of furostene **4b** ($R_f=0.38$) pf 83–85 °C. All R_f are referenced to a hexane–ethyl acetate (7/3) mixture as mobile phase.

3.3.1. (25*R*)-3β,16β-Diacetoxy-23-ethyl-23^1,26-epoxycholesta-5,23(23^1)-dien-22-one (9). White crystals, mp 255–256 °C; $[\alpha]_D^{20}$ −39 (*c* 1.0, $CHCl_3$); UV λ_{max} 269 nm (ε 11,583); IR $\bar{\nu}_{max}$ (KBr) 2967 (CH), 1734 (OAc), 1671 (CO), 1576 (C=C), 1249 (C–O) cm^{-1}; MS, *m/z* (%): 540 ([M$^{+\cdot}$] 0.1), 139 (100). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.36 (1H, d, $J=5.2$ Hz, H-6), 5.02 (1H, m, H-16), 4.59 (1H, m, H-3), 4.06 (1H, ddd, $J_{gem}=10.4$ Hz, $J_{26eq-25ax}=3.0$ Hz, $J_{26eq-24eq}=1.9$ Hz, H-26$_{eq}$), 3.43 (1H, dd, $J_{gem}=J_{26ax-25ax}=10.4$ Hz, H-26$_{ax}$), 3.20 (1H, dq, $J_{20,17}=10.7$ Hz, $J_{20-21}=7.0$ Hz, H-20), 2.13 (3H, s, 23^2CH_3), 2.03 (3H, s, 3-OCOCH_3), 1.90 (3H, s, 16-OCOCH_3), 1.10 (3H, d, $J=7$ Hz, CH_3-21), 1.03 (3H, d, $J=6.4$ Hz, CH_3-27), 1.03 (3H, s, CH_3-19), 0.89 (3H, s, CH_3-18). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 203.8 (22-*CO*), 170.3 (3-O*CO*CH_3), 169.6 (16-O*CO*CH_3), 164.2 (C-23^1), 139.6 (C-5), 122.2 (C-6), 107.6 (C-23), 75.6 (C-16), 73.8 (C-3), 71.6 (C-26), 55.9 (C-17), 54.0 (C-14), 49.7 (C-9), 41.8 (C-13), 39.6 (C-12), 38.6 (C-20), 38.0 (C-4), 36.8 (C-1), 36.5 (C-10), 34.6 (C-15), 31.6 (C-7), 31.2 (C-8), 30.7 (C-24), 27.6 (C-2), 26.6 (C-25), 21.3 (3-OCO*C*H_3), 21.0 (16-OCO*C*H_3), 20.7 (C-11), 20.6 (C-23^2), 19.2 (C-19), 17.1 (C-21), 17.0 (C-27), 13.4 (C-18). Anal. Calcd for $C_{33}H_{48}O_6$: C 73.30, H 8.95, O 17.75. Found: C 73.26, H 9.03.

3.4. Acid catalyzed equilibration of 8b and 9

Method A. In a pressure tube were placed 2.00 g (3.70 mmol) of **8b** in 5 mL of toluene and 200 mg (1.05 mmol) *p*-toluenesulfonic acid and the mixture was heated at 120 °C for 30 min with vigorous stirring. The solvent was evaporated under vacuum and the organic phase extracted with ethyl acetate–water, neutralized with $NaHCO_3$ and dried over Na_2SO_4 to give a mixture of **8b** and **9** in a 4:6 ratio, as determined by ^{1}H NMR. The products were separated by chromatography as described previously. The same ratio of products was obtained starting from epoxy **9**.

Method B. In a pressure tube were placed 1.00 g (1.85 mmol) of **8b**, 5 mL of water and 30 mg of Amberlyst-15 and the mixture was heated at 120 °C for

7 h with vigorous stirring. The catalyst was separated by filtration, the solution evaporated under vacuum and the organic phase extracted with ethyl acetate–water, dried over Na_2SO_4 and evaporated to dryness to give a mixture of **8b** and **9** in a 4:6 ratio as determined by ^{1}H NMR. The products were separated by chromatography as described previously.

3.4.1. (20*S*,25*R*)-3β,16β,26-Triacetoxycholest-5-ene-22,23-dione (10). A solution of 0.27 g (0.50 mmol) of **9** in 7 mL of CH_2Cl_2, 3 mL of acetone, 3 mL of MeCN, was vigorously stirred at 5 °C and treated with half of a solution of RuO_4 prepared from 0.32 g of $NaIO_4$ (1.5 mmol), 0.018 g of $RuCl_3\cdot 3H_2O$ (0.085 mmol), in 1.2 mL of H_2O. The reaction mixture was stirred at 5 °C for 2 min, the remaining RuO_4 solution was added and the reaction mixture was stirred for 2 additional minutes after which it was quenched with 5 mL of a 20% solution of $Na_2S_2O_5$ and stirred for 5 min. All the solvents were evaporated under vacuum and the residue was extracted with CH_2Cl_2 (2×50 mL). The extracts were washed with H_2O, dried with anhydrous Na_2SO_4, and concentrated under vacuum to give 0.25 g of dione **10** containing traces of starting material (determined by NMR). Pure dione **10** was obtained by washing the crude product with MeOH (isolated yield 63%) since **9** is not soluble in this solvent. Attempts to purify the remaining mixture of dione **10** and epoxy **9** by column chromatography on silica gel led to extensive decomposition of dione **10**, thus the subsequent reduction was performed on the crude product.

Yellowish-green powder, mp 110–112 °C; $[\alpha]_D^{20}$ −21.2 (*c* 1.0, $CHCl_3$); UV ($CHCl_3$) λ_{max} 429 nm (ε=32); IR ν_{max} (KBr) 2937 (CH), 1734 (OAc), 1248 (C–O); MS, *m*/*z* (%): 573 ([$M^{+\cdot}$+1], 0.4), 387 (25), 327 (37), 253 (45), 101 (39), 43 (100). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.36 (1H, d, J=4.9 Hz, H-6), 4.99 (1H, ddd, $J_{16-17\alpha}$=7.7 Hz, $J_{16-15\alpha}$=7.5 Hz, $J_{16-15\beta}$=4.6 Hz, H-16), 4.60 (1H, m, H-3), 4.03 (1H, dd, J_{gem}=10.9 Hz, J_{26-25}=5.6 Hz, H-26), 3.88 (1H, dd, J_{gem}=10.9 Hz, J_{26-25}=6.5 Hz, H-26), 3.77 (1H, dq, J_{20-17}=11.3 Hz, J_{20-21}=7.2 Hz, H-20), 2.87 (1H, dd, J_{gem}=18.1 Hz, J_{24-25}=5.6 Hz, H-24), 2.59 (1H, dd, J_{gem}=18.1 Hz, J_{24-25}=7.7 Hz, H-24), 2.05 (3H, s, 26-OCOCH_3), 2.03 (3H, s, 3-OCOCH_3), 1.85 (3H, s, 16-OCOCH_3), 1.09 (1H, d, J_{21-20}=7.2 Hz, CH_3-21), 1.03 (3H, s, CH_3-19), 0.97 (3H, d, J_{27-25}=6.8 Hz, CH_3-27), 0.92 (3H, s, CH_3-18). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 200.2 (22-*C*=*O*), 198.2 (23-*C*=*O*), 170.9 (26-O*CO*CH_3), 170.4 (3-O*CO*CH_3), 170.0 (16-O*CO*CH_3), 139.6 (C-5), 122.1 (C-6), 74.7 (C-16), 73.7 (C-3), 68.1 (C-26), 54.6 (C-17), 54.0 (C-14), 49.7 (C-9), 42.1 (C-13), 39.9 (C-24), 39.5 (C-12), 38.0 (C-4), 36.8 (C-1), 36.6 (C-10), 35.0 (C-20), 34.2 (C-15), 31.8 (C-7), 31.5 (C-8), 28.1 (C-25), 27.6 (C-2), 21.3 (3-OCO*C*H_3), 20.8 (16-OCO*C*H_3), 20.7 (26-OCO*C*H_3), 20.6 (C-11), 19.2 (C-19), 16.7 (C-27), 15.8 (21), 13.0 (C-18). Anal. Calcd for $C_{33}H_{48}O_8$: C 69.28, H 8.45, O 22.35. Found: C 69.48, H 8.71.

3.4.2. (22*R*,23*S*,25*R*)-3β,16β,26-Triacetoxy-cholest-5-ene-22,23-diol (11a). A solution of 100 mg (0.18 mmol) of dione **10** in 10 mL MeOH was treated with 100 mg (2.60 mmol) of $NaBH_4$ and the solution was stirred 30 min at room temperature. The excess hydride was quenched with water, the methanolic suspension was concentrated and the organic phase was extracted twice with ethyl acetate, washed with water, dried over Na_2SO_4 and evaporated to dryness to give 60 mg (59% yield, R_f=0.38), the R_f was missing 19) of **11a**.

White powder, mp 194–195 °C ($CHCl_3$–CH_3OH); $[\alpha]_D^{20}$ −22.3 (*c* 0.2, $CHCl_3$); UV ($CHCl_3$) λ_{max} 269 nm (ε=413); IR $\bar{\nu}_{max}$ (KBr): 3503 (OH) 2930 (CH), 1732 (CO), 1252 (C–O); MS, *m*/*z* (%): 558 ([$M^{+\cdot}$−18], 0.1), 303 (27), 254 (30), 253 (100). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.36 (1H, d, J=4.9 Hz, H-6), 5.27 (1H, ddd, $J_{16-17ax}$=7.7 Hz, $J_{16-15eq}$=4.1 Hz, H-16), 4.60 (1H, m, H-3), 4.06 (1H, dd, J_{gem}=10.9 Hz, J_{26-25}=5.3 Hz, H-26), 3.95 (1H, dd, J_{gem}=10.9 Hz, J_{26-25}=6.2 Hz, H-26), 3.66 (1H, dd, J=8.0 Hz, H-23), 3.2 (1H, br d, J=8.0 Hz, H-22), 2.38 (1H, m, H-17), 2.30 (1H, m, H-4), 2.06 (3H, s, 3-OCO*C*H_3), 2.03 (3H, s, 16-OCO*C*H_3), 2.02 (3H, s, 26-OCO*C*H_3), 1.03 (1H, s, CH_3-19), 1.02 (3H, d, J=7.2 Hz, CH_3-27), 0.98 (3H, d, J=6.8 Hz, CH_3-21), 0.92 (3H, s, CH_3-18). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 171.4 (3-O*CO*CH_3), 170.9 (16-O*CO*CH_3), 170.5 (26-O*CO*CH_3), 139.7 (C-5), 122.1 (C-6), 76.7 (C-22), 75.2 (C-16), 74.7 (C-3), 70.0 (C-23), 68.7 (C-26), 55.6 (C-17), 54.6 (C-14), 49.8 (C-9), 42.4 (C-13), 39.5 (12), 38.1 (24), 38.0 (4), 36.9 (1), 36.5 (C-10), 34.8 (C-15), 31.5 (7), 31.4 (C-8), 30.7 (C-20), 29.4 (C-25), 27.6 (2), 21.3 (16-OCO*C*H_3), 21.3 (26-OCO*C*H_3), 20.9 (3-OCO*C*H_3), 20.6 (C-11), 19.2 (C-19), 18.5 (C-27), 12.5 (C-21), 11.4 (C-18).

HRMS: Calculated for $C_{33}H_{52}O_8$ $[M+H]^+$: 577.3737. Found 577.3740.

3.4.3. (22*R*,23*S*,25*R*)-3β,16β,22,23,26-Pentacetoxy-cholest-5-ene (11b). Diol **11a** (100 mg, 0.172 mmol) was dissolved in mL of 1 mL pyridine, 1.0 mL (10.6 mmol) of Ac_2O were added and the reaction was stirred for 5 h at room temperature. The reaction mixture was poured over iced water and the organic phase extracted with CH_2Cl_2/dilute HCl, neutralized with Na_2CO_3 and evaporated to dryness to give 100 mg (75% yield, R_f=0.31), the R_f was missing 20) of **11b**.

White powder, mp 152–153°C; $[\alpha]_D^{20}$ −25.8 (*c* 0.18, $CHCl_3$); IR $\bar{\nu}_{max}$ (KBr): 2970 (CH), 1737 (CO), 1241 (C–O); MS, *m*/*z* (%): 540 ([$M^{+\cdot}$−120], 4.0), 434 (2.0), 405 (10), 278 (5.0), 253 (100), 158 (10.0), 109 (5.0), 43 (6.0). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.34 (1H, d, J=4.9 Hz, H-6), 5.20 (1H, m, H-16), 5.16 (1H, dd, m, H-23), 4.87 (1H, d, J_{22-23}=7.6 Hz, H-22), 4.59 (1H, m, H-3), 3.94 (1H, dd, J_{gem}=11.0 Hz, J=5.4 Hz, H-26), 3.86 (1H, dd, J_{gem}=11.0 Hz, J=5.8 Hz, H-26), 2.08, 2.07, 2.06, 2.02 and 2.05 (3H each, s, 3-, 16-, 22-, 23-, 26-OCO*C*H_3), 0.99 (1H, s, CH_3-19), 0.98 (3H, d, J=7.2 Hz, CH_3-21), 0.94 (3H, d, J=6.8 Hz, CH_3-27), 0.85 (3H, s, CH_3-18). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 171.17, 170.58, 170.51, 170.18, 170.1 (3-, 16-, 22-, 23-, 26-O*CO*CH_3), 139.7 (C-5), 122.36 (C-6), 75.5 (C-16), 75.03 (C-22), 73.89 (C-3), 70.27 (C-23), 68.34 (C-26), 55.99 (C-17), 54.42 (C-14), 49.87 (C-9), 42.46 (C-13), 39.66 (C-12), 38.11 (C-4), 36.97 (C-24), 36.58 (C-10), 35.32 (C-1), 35.23 (C-15), 31.58 (C-7), 31.45 (C-25), 30.64 (C-8), 29.28 (C-20), 27.78 (C-2), 21.50, 21.50, 21.46, 21.22, 20.96 (3-, 16-, 22-, 23-, 26-O*CO*CH_3), 20.78 (C-11), 19.36 (C-19), 18.22 (C-27), 12.77 (C-21), 12.4 (C-18).

HRMS: Calculated for $C_{37}H_{57}O_{10}$ $[M+H]^+$: 661.3948. Found 661.3952.

3.4.4. (25*R*)-3β,16β,26-Triacetoxy-5,6α-dihydroxy-5α-cholestane-22,23-dione (12). Treatment of **9** as described previously, for 6 min gave 0.49 g of a mixture of dione **10** and 5,6-diol **12**, which were separated by column chromatography. Compound **10** (133 mg, 23%, $R_f=0.5$) eluted using a 9:1 mixture of hexane/ethyl acetate and **12** (230 mg, 40%, $R_f=0.33$) was eluted with an 8:2 mixture of the same solvents.

Yellow powder, mp 98–101 °C; $[\alpha]_D^{20}$ +6.59 (*c* 0.2, $CHCl_3$); UV ($CHCl_3$) λ_{max} 275 nm ($\varepsilon=1734$); IR $\bar{\nu}_{max}$ (KBr) 3480 (OH), 2941 (CH), 1736 (CO), 1244 (C–O); MS, *m/z* (%): 607 ([$M^{+\cdot}+1$] 0.6), 421 (76), 343 (83), 269 (100), 251 (44). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.10 (1H, dddd, $J_{3ax-2ax}=J_{3ax-4ax}=11.4$ Hz, $J_{3ax-2eq}=J_{3ax-4eq}=5.4$ Hz, H-3), 4.99 (1H, ddd, $J_{16-15ax}=J_{17-16}=8.0$ Hz, $J_{16-15eq}=4.9$ Hz, H-16), 4.02 (1H, dd, $J_{gem}=10.9$ Hz, $J_{26-25}=5.6$ Hz, H-26), 3.88 (1H, dd, $J_{gem}=10.9$ Hz, $J_{26-25}=6.5$ Hz, H-26), 3.76 (1H, dq, $J_{20-17}=11.2$ Hz, $J_{20-21}=7.1$ Hz, H-20), 3.65 (1H, dd, $J_{6ax-7ax}=11.3$ Hz, $J_{6ax-7eq}=5.1$ Hz, H-6), 2.86 (1H, dd, $J_{gem}=18.1$ Hz, $J_{24-25}=5.6$ Hz, H-24) 2.59 (1H, dd, $J_{gem}=18.1$ Hz, $J_{24-25}=7.7$ Hz, H-24), 2.04 (3H, s, 26-OCO*CH*$_3$), 2.02 (3H, s, 16-OCO*CH*$_3$), 1.84 (3H, s, 3-OCO*CH*$_3$), 1.07 (1H, d, $J_{21-20}=7.1$ Hz, CH_3-21), 0.97 (3H, s, CH_3-19), 0.96 (3H, d, $J_{27-25}=6.8$ Hz, CH_3-27), 0.88 (3H, s, CH_3-18). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 200.2 (22-*CO*), 198.2 (23-*CO*), 171.0 (3-O*CO*CH_3), 170.9 (16-O*CO*CH_3), 170.0 (26-O*CO*CH_3), 76.3 (C-5), 74.7 (C-16), 71.1 (C-3), 70.3 (C-6), 68.2 (C-26), 54.7 (C-17), 53.2 (C-14), 44.02 (C-9), 42.46 (C-13), 39.94 (C-24), 39.59 (C-4), 39.15 (C-10), 35.06 (C-20), 34.80 (C-7), 34.38 (C-1), 34.15 (C-15), 33.05 (C-8), 30.69 (C-2), 28.17 (C-25), 26.56 (C-12), 21.42 (3-OCO*CH*$_3$), 20.83 (16-OCO*CH*$_3$), 20.77 (26-OCO*CH*$_3$), 20.34 (C-11), 16.82 (C-27), 15.79 (C-21), 15.36 (C-19) 13.34 (C-18).

Anal. Calcd for: C 65.33, H 8.31, O 26.36. Found: C 65.03, H 8.39.

3.4.5. (25*R*)-3β,16β,26-Triacetoxy-5-hydroxy-5α-cholesta-6,22,23-trione (13). A solution of 0.54 g (1.0 mmol) of **9** in 18.4 mL of CH_2Cl_2, 8.1 mL of acetone, 8.1 mL of MeCN, was vigorously stirred at 5 °C and treated with a solution of RuO_4 at once prepared from 1.8 g of $NaIO_4$ (7.9 mmol), 0.49 g of $RuCl_3\cdot 3H_2O$ (2.3 mmol), in 10.8 mL of H_2O. The reaction mixture was stirred at 5 °C for 3 h, after which it was quenched with 13.2 mL of a 20% solution of $Na_2S_2O_5$ and stirred for 10 min. All the solvents were evaporated under vacuum and the residue was extracted with CH_2Cl_2 (2×50 mL). The extracts were washed with H_2O, dried with anhydrous Na_2SO_4, and concentrated under vacuum to give (0.52 g) of a mixture of the trione **13** and traces of 5,6-diol **12**, which were separated by column chromatography. Compound **13** (0.45 g, 74.5%, $R_f=0.53$) eluted using a 7:3 mixture of hexane acetate and **12** (0.12 g, 19.8%, $R_f=0.33$) eluted with an 5:5 mixture of the same solvents.

Yellow powder, mp 100–105 °C; $[\alpha]_D^{20}$ −33.7 (*c* 0.2, $CHCl_3$); UV ($CHCl_3$) λ_{max} 379 nm ($\varepsilon=264$); IR $\bar{\nu}_{max}$ (KBr) 3468 (OH), 2947 (CH), 1737 (–CO), 1243 (C–O); MS, *m/z* (%): 605 ([$M^{+\cdot}+1$] 0.4), 419 (51), 341 (66), 267 (100), 101 (47), 43 (95). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.03 (1H, dddd, $J_{3ax-2ax}=J_{3ax-4ax}=11.2$ Hz, $J_{3ax-2eq}=J_{3ax-4eq}=5.0$ Hz, H-3), 4.99 (1H, ddd, $J_{16-15ax}=J_{17-16}=8.0$ Hz, $J_{16-15eq}=5.2$ Hz, H-16), 4.02 (1H, dd, $J_{gem}=10.9$ Hz, $J_{26-25}=5.6$ Hz, H-26), 3.88 (1H, dd, $J_{gem}=10.9$ Hz, $J_{26-25}=6.5$ Hz, H-26), 3.77 (1H, dq, $J_{20-17}=11.3$ Hz, $J_{20-21}=7.1$ Hz, H-20), 2.86 (1H, dd, $J_{gem}=18.2$ Hz, $J_{24-25}=5.6$ Hz, H-24) 2.78 (1H, dd, $J_{gem}=J_{7ax-8ax}=12.7$ Hz, H-7), 2.60 (1H, dd, $J_{gem}=18.2$ Hz, $J_{24-25}=7.7$ Hz, H-24), 2.04 (3H, s, 26-OCO*CH*$_3$), 2.00 (3H, s, 16-OCO*CH*$_3$), 1.84 (3H, s, 3-OCO*CH*$_3$), 1.08 (1H, d, $J_{21-20}=7.1$ Hz, CH_3-21), 0.97 (3H, d, $J_{27-25}=6.8$ Hz, CH_3-27), 0.88 (3H, s, CH_3-18), 0.82 (3H, s, CH_3-19). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 211.5 (C-6), 200.1 (22-*C*O), 198.1 (23-*C*O), 171.0 (3-O*CO*CH_3), 170.1 (16-O*CO*CH_3), 170.0 (26-O*CO*CH_3), 80.1 (C-5), 74.3 (C-16), 70.6 (C-3), 68.2 (C-26), 54.6 (C-17), 53.6 (C-14), 44.1 (C-9), 42.8 (C-10), 42.4 (C-13), 41.3 (C-7), 39.9 (C-24), 39.4 (C-4), 36.5 (C-8), 35.0 (C-20), 33.9 (C-15), 32.3 (C-1), 29.4 (C-2), 28.1 (C-25), 26.2 (C-12), 21.3 (C-11), 21.0 (3-OCO*CH*$_3$), 20.9 (16-OCO*CH*$_3$), 20.9 (26-OCO*CH*$_3$), 16.8 (C-27), 15.7 (C-21), 13.8 (C-19) 13.3 (C-18).

HRMS: Calculated for $C_{33}H_{49}O_{10}$ $[M+H]^+$605.3326. Found 605.3329.

3.4.6. (23*S*,25*R*)-3β,16β,26-Triacetoxy-23-hydroxy-cholest-5-en-22-one (14). A solution of dione **10** (100 mg, 0.17 mmol) in 3 mL of methanol at −70 °C was treated with $ZnCl_2$ (48 mg, 0.35 mmol) and $NaBH_4$ (50 mg, 1.32 mmol) and the mixture was stirred for 3 h. The reaction was quenched with NH_4Cl and the organic layer was extracted with CH_2Cl_2, washed with water, dried with anhydrous $NaSO_4$ and concentrated under vacuum. The residue (93 mg) was purified by chromatography on silica gel (hexane/EtOAc 8:2) to yield (68 mg, 67.6%, $R_f=0.28$) of **14**.

White powder, mp 138–139°C ($CHCl_3$–CH_3OH); $[\alpha]_D^{20}$ +23.4 (*c* 0.2, $CHCl_3$); IR ν_{max} (KBr): 3461 (OH) 2938 (CH), 1735 (CO), 1245 (C–O); MS, *m/z* (%): 515 ([$M^{+\cdot}-59$], 0.3), 282 (32), 327 (14), 372 (16), 253 (100), 311 (16), 313 (67). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.33 (1H, d, $J=4.4$ Hz, H-6), 4.78 (1H, ddd, $J_{16-17ax}=8.1$ Hz, $J_{16-15eq}=3.3$ Hz, H-16), 4.57 (1H, m, H-3), 4.23 (1H, br d, $J=10.6$ Hz, H-23), 4.12 (1H, dd, $J_{gem}=11.0$ Hz, $J_{26-25}=6.2$ Hz, H-26), 4.03 (1H, dd, $J_{gem}=11.0$ Hz, $J_{26-25}=7.0$ Hz, H-26), 3.02 (1H, dq, $J_{17-20}=13.9$ Hz, $J_{20-21}=6.6$ Hz, H-20), 2.39 (1H, m, H-15), 2.29 (1H, m, H-24), 2.06 (3H, s, 3-OCO*CH*$_3$), 2.0 (3H, s, 16-OCO*CH*$_3$), 1.97 (3H, s, 26-OCO*CH*$_3$), 1.15 (3H, d, $J_{21-20}=6.6$ Hz, CH_3-21), 1.02 (1H, d, $J_{27-25}=6.6$ Hz, CH_3-27), 1.00 (3H, s, CH_3-19), 0.87 (3H, s, CH_3-18). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 215.18 (22-*C*O), 171.26 (3-O*CO*CH_3), 170.59 (16-O*CO*CH_3), 170.02 (26-O*CO*CH_3), 139.67 (C-5), 122.26 (C-6), 75.84 (C-16), 75.45 (C-23), 73.85 (C-3), 67.72 (C-26), 56.90 (C-17), 53.93 (C-14), 49.77 (C-9), 42.3 (C-13), 39.83 (C-12), 38.86 (C-20), 38.09 (C-4), 37.43 (C-24), 36.94 (C-1), 36.6 (C-10), 34.97 (C-15), 31.6 (C-7), 31.38 (C-8), 29.4 (C-25), 27.76 (C-2), 21.5 (16-OCO*CH*$_3$), 21.07 (26-OCO*CH*$_3$), 21 (3-OCO*CH*$_3$), 20.82 (C-11), 19.36 (C-19), 18.4 (C-27), 17.33 (C-21), 13.57 (C-18).

HRMS: Calculated for $C_{33}H_{50}O_8$ $[M+H]^+$ 575.3584. Found 575.3586.

3.5. X-ray data

Copy of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44 1223 336033) or e-mail: deposit@ccdc.cam.ac.uk No. 253082 for compound **9** and 269385 for **11b**.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tet.2005.12.036.

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