

β -Alkoxy- α,β -unsaturated ketone systems in steroidal frameworks, and their conversion to 23,24-bisnorcholane lactones

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Abstract

The cleavage of the spiroketal side chain in 25*R* and 25*S* sapogenins by Ac₂O/BF₃·OEt₂, at room temperature, afforded compounds containing a β -alkoxy- α,β -unsaturated ketone system in their steroidal side chains. However, in (25*R*)-sapogenins, the ring E is cleaved regioselectively while the (25*S*)-sapogenin affords a mixture of products due to steric hindrance of the methyl group at C-25. The 23-acetyl-22,26-epoxycholest-22-enes (**2**, and **6**) were transformed into the 23-acetyl sapogenins (**12**, and **13**) under basic treatment. These 23-acetyl derivatives are useful intermediates for the preparation of 23,24-bisnorcholane lactones **10**, and **11**, in high yields.

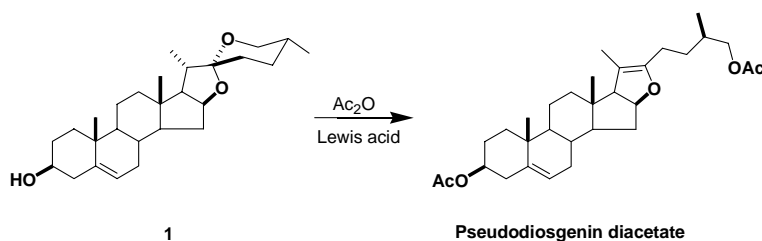
Keywords: Sapogenin, β -alkoxy- α,β -unsaturated ketone, 23,24-bisnorcholane lactones, BF₃·OEt₂

Introduction

Juaristi,¹ in the presentation of the special issue of Arkivoc dedicated to the development of Organic Chemistry in Mexico, described the massive production of sexual hormones carried out in Mexico to satisfy the huge demand around the world. Chemists working on the

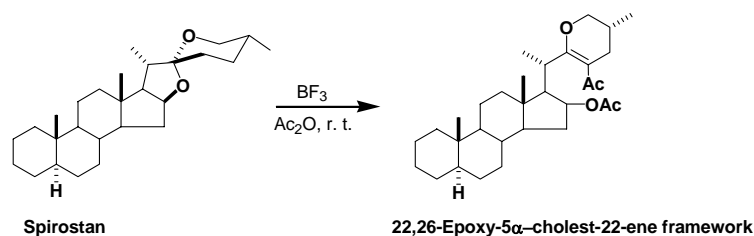
transformation of sapogenins gave a strong impetus to Organic Chemistry in Mexico. Since then, sapogenins became important steroidal starting material to obtain bio-active steroidal compounds.

The key step in the procedure developed by Marker² using diosgenin (**1**), the acetolysis of the F ring has been extensively investigated and great efforts have been directed to improve this isomerization of the spiroketal side-chain into furostenes (pseudosapogenins, see Scheme 1). The results have shown that adding Lewis acids as catalysts³ and/or cosolvents provides better yields.



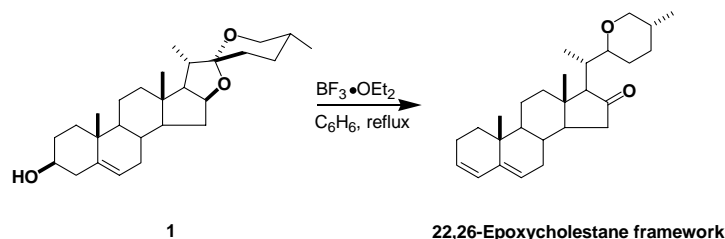
Scheme 1. Transformation of diosgenin into pseudodiosgenin diacetate.

For many years it was believed that cleavage of the spiroketal moiety occurs only at the F ring to produce furostenes derivatives. This misconception led to incorrect structural assignment in old as well as recent reports.⁴ The regioselective opening of ring E in a sapogenin skeleton was reported for the first time by Gonzalez⁵ in 1976, using BF_3 as Lewis acid (Scheme 2).



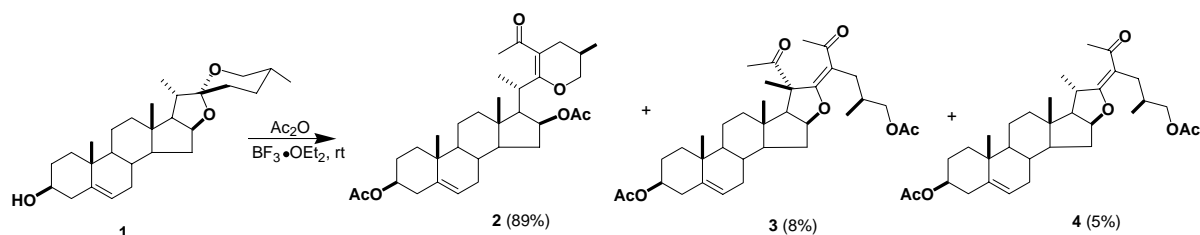
Scheme 2. Regioselective opening of the E ring of a spirostan.

In 1981 Dhar⁶ reported a different regioselective cleavage of ring E in diosgenin that provided a noteworthy 22,26-epoxycholestane framework in 63% yield (Scheme 3). However, in this case, the hydroxyl group at C-3 is eliminated generating a conjugated diene



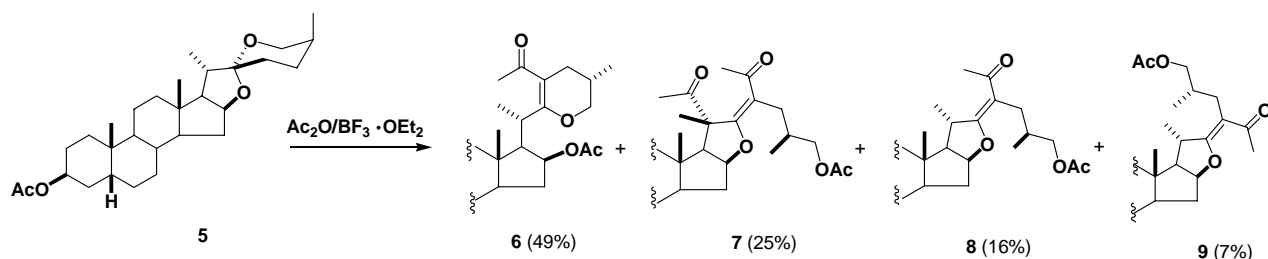
Scheme 3. 22,26-Epoxycholestane obtained from **1**.

Sandoval in 1999 reinvestigated treatment of **1** with $\text{Ac}_2\text{O}/\text{BF}_3\cdot\text{OEt}_2$, and found that, at room temperature, the reaction provides the 22,26-epoxycholest-22-ene⁷ structure **2** in high yields, retaining the hydroxyl group at C-3 (Scheme 4). Subsequent reinvestigation of the acetylation of diosgenin allowed isolating the corresponding furostene derivatives **3** and **4** in small quantities. We report in this paper their complete characterization.



Scheme 4. Transformation of diosgenin in 22,26-epoxycholest-22-ene **2**, and furostenes **3** and **4**.

A different behaviour was found in sarsasapogenin acetate (**5**)⁸ due to steric hindrance of the methyl group at C-25; nonetheless, a regioselective ring opening was also observed for ring E in a different ratio (Scheme 5).



Scheme 5. Compounds **6** - **9** obtained from the acetylation of sarsasapogenin.

Results and Discussion

In order to increase the selectivity for ring E cleavage in sarsasapogenin (25*S*), the use of two Lewis acids, ZnCl_2 and $\text{BF}_3\cdot\text{OEt}_2$ were compared. Different reaction conditions were investigated, observing that the best results were obtained when the reaction is carried out at room temperature for 10 min in the case of $\text{BF}_3\cdot\text{OEt}_2$ while 6 h are required in the case of ZnCl_2 . Similar results were obtained from diosgenin (25*R*), however, in this case, the *Z*-furostene, analogue of **9**, was not isolated.

Compounds **6**, **8**, and **9** presented very close structural features to **2** and **4**; for example, their UV spectra displayed the band for a β -alkoxy- α,β -unsaturated ketone system in the range of 274 - 285 nm. Also, the characteristic bands for the acetate appeared at $1731\text{-}1735\text{ cm}^{-1}$, and the

band for the conjugated ketone in the range 1650-1667 cm^{-1} . In all cases, the molecular ion was observed in the mass spectrum.

In the case of compounds **3**, and **7**, the presence of the additional acetyl group at C-20 was rapidly identified by their IR spectra from the band at 1702-1707 cm^{-1} and MS data.

It should be mentioned that the two distinct frameworks: the epoxy derivatives **2** and **6** and the furostenes **3**, **4**, **7**, **8**, and **9**, exhibit distinct signals in the ^1H NMR signal (Table 1) mainly for the diastereotopic protons at C-26.

Table 1. Selected ^1H Chemical shifts (δ in ppm) for epoxycholestenes and furostenes frameworks

	22,26-epoxycholestenes		20-acetyl-furost-22-ene		furost-22-enes		
	2	6 ⁸	3	7 ⁸	4	8 ⁸	9 ⁸
H-16	5.14	5.14	3.69	4.72	4.53	4.95	5.09
H-20	4.07	3.98	---	---	3.65	3.68	3.01
H-26	3.46	3.38	3.95	3.90	3.77	3.89	3.87
	4.00	4.05		3.96		3.95	3.92
CH ₃ -18	0.92	0.89	0.87	0.86	0.53	0.56	0.72
CH ₃ -19	1.03	0.98	1.01	0.97	0.95	0.97	0.98
CH ₃ -21	1.18	1.16	1.55	1.53	1.12	1.18	1.21
CH ₃ -27	0.97	0.96	0.95	0.94	0.85	0.88	0.86
CH ₃ -20 ²	---	---	2.31	2.31	---	---	---
CH ₃ -23 ²	2.20	2.20	2.18	2.19	2.15	2.21	2.35
AcO-16	1.84	1.82	---	---	---	---	---
AcO-26	---	---	2.06	2.05	1.99	2.06	2.05

In the 22,26-epoxycholest-22-ene derivatives **2** and **6**, the methylene group at C-26 appears between 3.98-4.05 and 3.38-3.45 ppm; having a $\Delta\delta$ of 0.60 ppm (AMX spin system). On the other hand, in all furostene derivatives, this signal appears as multiplet in the range between 3.82-3.95 ppm. Both protons are clearly differentiated in the case of epoxy compounds because they are placed in an axial or equatorial position in the tetrahydropyran ring; whereas in furostene there is free rotation.

The signals for the protons at C-16 for **2**, and **6** appear in 5.14 ppm, characteristic of a methyne containing an acetate group. On this basis, it was suggested that cleavage of tetrahydropyran E ring had generated the epoxy compounds.

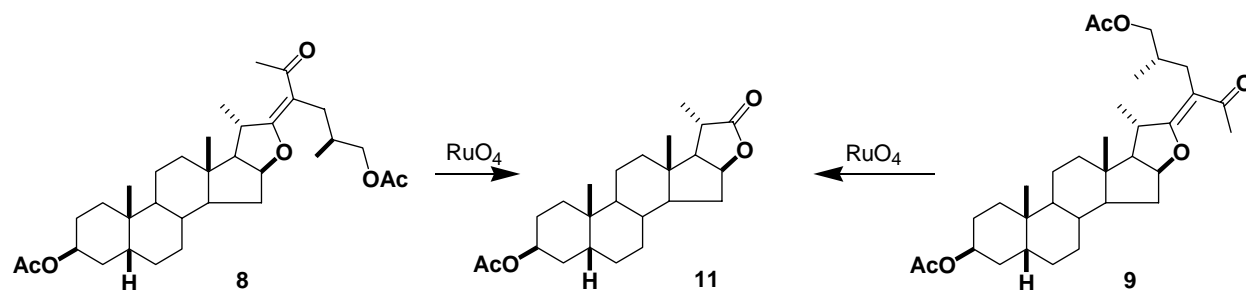
In the ^1H NMR spectra of **3** and **7**, C-21 appears as a singlet downshifted to 1.53-1.55 ppm (Table 2), evidencing the introduction of a new acetyl group at C-20. Crystallisation of **7** provided triclinic crystals suitable for X-ray diffraction analysis which permitted to corroborate the *E* configuration for the double bond in C-22 and the *S* configuration for C-20.^{9a}

Although the ^{13}C NMR chemical shifts for 22,26-epoxycholestenes **2** and **6**, are very similar to their corresponding (*E*)-23-acetylfurostenes **4** and **8**, (Table 2), spectral characterization can be easily achieved by comparing the chemical shift of C-16 and C-26, since C-16 in furostenes is shifted downfield with respect to epoxycholestenes (≈ 10 ppm), while the opposite effect is observed for C-26 (≈ 2.5 ppm).

Table 2. Selected ^{13}C chemical shifts (δ in ppm) for epoxycholestenes and furostenes

	22,26- epoxycholestenes		20-acetyl- furost-22-ene		furost-22-enes		
	2	6	3	7	4	8	9
C-11	20.7	20.9	20.3	20.3	20.3	20.3	20.4
C-12	39.6	40.2	39.7	40.0	38.0	38.3	38.6
C-13	42.1	42.7	42.9	43.1	41.3	41.6	41.8
C-14	54.2	54.3	56.6	56.4	55.4	55.3	55.4
C-15	34.8	34.8	36.8	31.9	33.3	33.3	33.8
C-16	74.9	75.1	85.0	84.6	86.1	86.0	88.3
C-17	55.8	55.8	63.8	63.9	62.3	62.4	61.8
C-18	12.8	13.1	15.2	15.1	13.1	13.1	14.2
C-19	19.1	23.8	19.3	23.6	19.3	23.6	23.7
C-20	32.7	33.2	62.3	62.2	38.1	38.0	37.9
C-21	19.3	18.6	15.6	15.5	19.8	19.7	20.0
C-22	171.1	171.5	174.0	173.7	179.0	178.7	175.3
C-23	106.8	107.5	110.2	110.0	108.0	107.2	108.4
C-24	31.5	31.5	36.4	31.6	31.2	31.0	31.8
C-25	26.4	26.3	31.2	32.9	31.3	32.9	32.1
C-26	71.4	71.8	68.6	69.0	68.8	69.2	69.6
C-27	16.7	16.8	17.3	16.3	17.3	16.3	17.1
C-20 ¹	---	---	207.2	207.2	---	---	---
C-20 ²	---	---	26.4	26.2	---	---	---
C-23 ¹	197.9	198.2	199.4	199.3	198.6	198.3	198.8

The diastereoisomeric relationship between **8** and **9** was established through fission of their double bond at C-22; the oxidation reaction in both cases led to the bisnorcholanolic lactone **11** (Scheme 6). Careful crystallisation of **8** provided monoclinic crystals suitable for X-ray diffraction analysis which permitted to corroborate the *E* configuration for the double bond in C-22 and the *S* configuration for C-20.^{9b} In turn, oxidation of **4** afforded the bisnorcholanolic lactone **10**, analogue of **11**. This proves that under the acetolysis reaction conditions the configuration at C-20 and C-25 is retained.¹⁰



Scheme 6. Preparation of the 23,24-bisnorcholanolic lactone **11**.

Bisnorcholanolic lactones **10**, and **11**, are important synthetic intermediates that have been used in the synthesis of sapogenins,¹¹ and brassinosteroid analogues.¹² Despite their usefulness no practical method has been developed to produce them in high quantities; only small quantities have been obtained by different reactions¹³ or by plant extraction.¹⁴ Herein we present a fast route to these 22C chiral synthons from furostenes **4**, **8** and **9** on gram scale.

In the ¹H-NMR spectrum, H-20 for **10** and **11** are shifted, about 1.1 ppm, upfield with respect to their starting material **8** and **4**, respectively. On the contrary, Me-18 in the lactones is shifted downfield approximately 0.2 ppm; Me-19, Me-21 and H-16 have similar δ values. Interestingly, H-15 β can be clearly observed in the lactones spectra, since it is separated from other protons signals (Table 3).

Table 3. Selected ¹H chemical shifts (δ in ppm) for lactones **10** and **11**

Lactone	H-15 β	H-16	H-20	CH ₃ -18	CH ₃ -19	CH ₃ -21
10	2.27	4.94	2.57	0.74	0.99	1.31
11	2.28	4.96	2.59	0.77	1.04	1.32

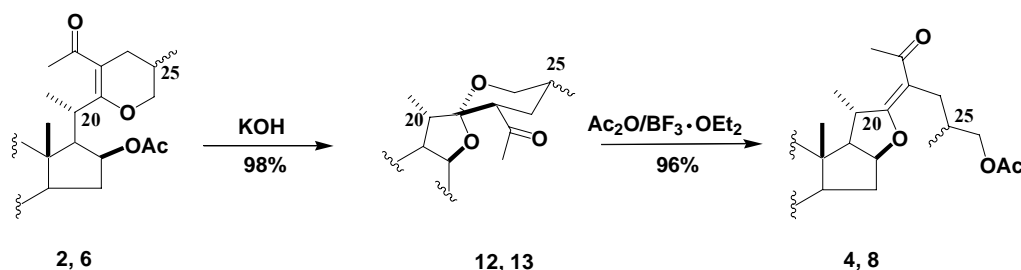
The transformation of furostenes **4** and **8** into lactones **10** and **11** generates a different π system on C-22 (C = C \rightarrow C = O), and as consequence, important shifts are observed in the ¹³C-NMR spectra for δ of C-16, C-17, C-20, and C-21 (Table 4).

Table 4. Selected ¹³C chemical shifts (δ in ppm) for lactones **10** and **11**

Lactone	C-14	C-15	C-16	C-17	C-18	C-19	C-20	C-21	C-22
10	54.7	33.1	82.9	59.2	13.9	23.8	36.1	18.0	181.4
11	54.7	33.1	82.7	58.9	13.8	19.4	36.1	18.1	181.0

A convenient method to obtain (*E*)-furostenes **4**, and **8** was developed by hydrolysis of epoxy compounds **2**, and **6** (Scheme 7) which afforded the corresponding 23-acetylated

sapogenins **12**, and **13**, followed by acetylation with Ac_2O in the presence of $\text{BF}_3 \cdot \text{OEt}_2$ affording the desired furostenes, in quantitative yield.



Scheme 7. Formation of 23-acetyl derivatives **12** and **13**.

The $^1\text{H-NMR}$ spectra for 23-acetyl sapogenins derivatives are very similar to those of the parent sapogenins; except for H-23ax which is strongly shifted downfield by the acetyl group (Table 5). The configuration of C-23 in **12** and **13** was assigned as *S* based on the observed coupling constants ($J_{23e-24a}=12-13$, $J_{23e-24e}=4.0-4.4$ Hz). The X-ray diffraction of **13** (a sarsasapogenin derivative) exhibited no epimerization for C-20 or C-25 and confirmed the equatorial position for the C-23 acetyl group.¹⁵

Table 5. Selected ^1H chemical shifts (δ in ppm) for sapogenins and their 23-acetylsapogenins

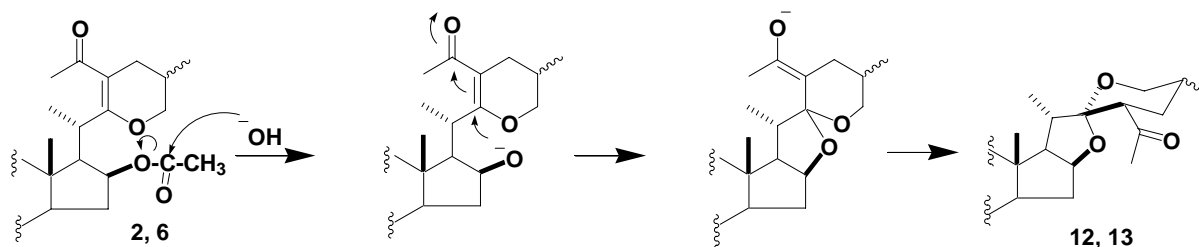
	Compounds			
	1	5	12	13
H-16	4.41	4.40	4.40	4.41
CH ₃ -18	0.79	0.76	0.66	0.64
CH ₃ -19	1.02	0.98	1.00	0.97
CH ₃ -21	0.97	0.99	0.98	1.00
H-23 _{ax}	1.81	1.87	2.51	2.84
H-26	3.46	3.94	3.48	3.99
	3.37	3.29	3.41	3.33
CH ₃ -27	0.79	1.07	0.86	1.08

In 25*R*-sapogenin the methyl group is placed in an equatorial position and in the 25*S*-serie this methyl is axial, this produces considerable differences in the $^{13}\text{C-NMR}$ spectrum for C-23, C-24, C-25, C-26, and C-27 (Table 6). For example, C-23 in 25*R*-serie is observed at 31.4 ppm and in the 25*S*-serie it is at 25.8 ppm. As expected in 23-acetyl sapogenins, C-23 is strongly shifted downfield, being observed now at 55.3 and 49.5 ppm, respectively.

Table 6. Selected ^{13}C Chemical shifts (δ in ppm) for sapogenins and their 23-acetylsapogenins

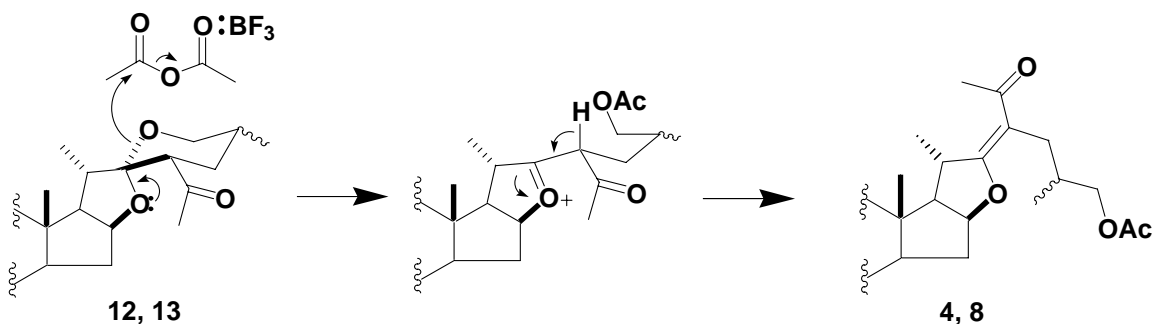
	Compounds			
	1	5	12	13
C-10	37.6	35.0	36.9	35.0
C-11	20.9	20.9	21.1	20.9
C-12	39.8	40.2	37.5	40.2
C-13	40.3	40.6	40.8	41.0
C-14	56.8	56.3	56.6	56.2
C-15	31.8	30.8	32.3	31.5
C-16	80.8	80.9	81.3	81.3
C-17	62.1	62.0	61.1	61.2
C-18	16.3	16.6	16.5	16.4
C-19	19.4	23.9	19.7	23.9
C-20	41.6	40.1	40.0	38.8
C-21	14.5	14.4	14.5	14.1
C-22	109.2	109.5	108.1	108.3
C-23	31.4	25.8	55.3	49.5
C-24	28.8	25.0	38.7	29.4
C-25	30.3	27.1	30.1	27.0
C-26	66.8	65.1	66.1	64.3
C-27	17.1	16.1	17.3	16.4
C-23 ¹	----	---	210.2	210.2
C-23 ²	---	---	28.6	28.7

A plausible mechanism for the formation of 23-acetylated sapogenins by alkaline treatment of the 22,26-epoxy compounds is depicted below (Scheme 9). It is noteworthy that the natural configuration at C-22 was regenerated in both 25*R* and 25*S* series.



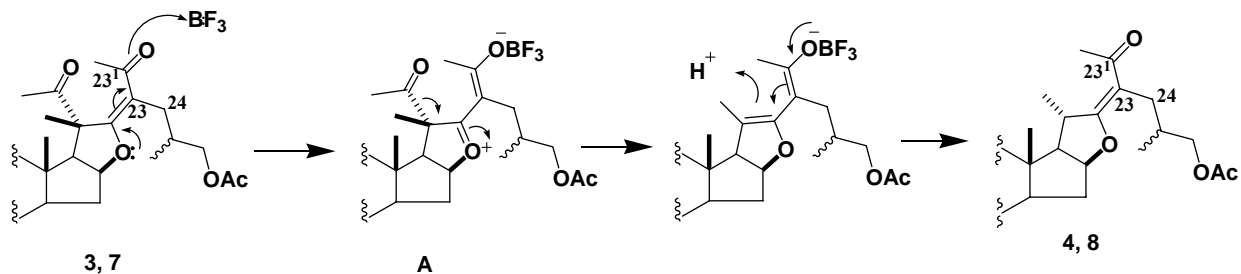
Scheme 9. Generation of 23-acetylsapogenins by basic treatment of epoxy compounds.

The subsequent ring opening reaction of the F ring using $\text{Ac}_2\text{O}/\text{BF}_3\cdot\text{OEt}_2$ at room temperature afforded compounds **4**, and **8**, in quantitative yields. A plausible mechanism is shown in Scheme 10, following the pathway reported for the acetolysis of the spiroketal moiety in sapogenin **2**.⁷



Scheme 10. Selective F ring opening in 23-acetylsapogenins in acidic medium.

An alternative pathway to obtain **4**, and **8**, was developed from the furostenes derivatives **3** and **7**. Treatment of compounds **3** and **7** with $\text{BF}_3\cdot\text{OEt}_2$ at 60 °C allows to selectively remove the acetyl group at C-20. A plausible mechanism for this reaction is shown in Scheme 11. The first step in this reaction leads to the intermediate **A** by the action of BF_3 over the oxygen atom at C-23¹; in this way a β -diketone-type intermediate is produced. The oxonium intermediate **A** acts as the driving force for deacetylation under a retro-Claisen type mechanism.



Scheme 11. Deacetylation of furostenes **3** and **7**.

In conclusion the formation of a number of useful intermediates obtained by treatment of sapogenins with Lewis acids is described. The reactions have been shown to be very sensitive to reaction conditions, the Lewis acid and even the work-up conditions. For derivatives of the 25*R* series (diosgenin) the acetolysis reaction is highly regioselective while sarsasapogenin (25*S*) leads to several products. Nonetheless, an alternative sequence of reactions has been developed to prepare either furostenes or epoxy derivatives in high yields. Some of these products are useful intermediates for the synthesis of 23-acetilsapogenins, bisnorcholanolic lactone and norbrassinosteroids analogues.

Experimental Section

General Procedures. Spectroscopy. UV spectra were determined on a Beckman DU-7500 spectrophotometer in ethanol solutions; wavelengths (λ) are expressed in nm. ^1H and ^{13}C NMR spectra were recorded on a Bruker DMX500 spectrometer (500 MHz for ^1H and 125 MHz for ^{13}C) and JEOL ECLIPSE NMR spectrometer (400 MHz for ^1H and 100 MHz for ^{13}C). Chemical shifts are stated in ppm (δ), and are referred to the residual ^1H signal ($\delta = 7.27$) or to the central ^{13}C triplet signal ($\delta = 77.0$) for CDCl_3 . Coupling constants (J) are quoted in Hz. IR spectra were acquired on a Nicolet Magna FT-IR 750 spectrophotometer using KBr pellets (ν , in cm^{-1}). Mass spectra were obtained on a HP 5989A spectrometer using electron impact ionization. Optical rotations were determined on a Perkin Elmer 241 polarimeter at 23 °C, using chloroform solutions. Melting points were obtained on a Gallenkamp MFB 595 apparatus and were not corrected. Analytical TLC were performed on silica gel ALUGRAM®SIL G/UV-252 plates and column chromatographies were carried out on silica gel Davisil™ grade 633 (200-425 mesh).

Chemistry: Acetolysis of sapogenins and their 23-acetyl derivatives. In a 10 mL round bottom flask was dissolved 1.0 mmol of sapogenin (**1**, **5**, **12**, or **13**) in 5 mL (52.6 mmol) of acetic anhydride and 1.0 mL (8.1 mmol) of $\text{BF}_3 \cdot \text{OEt}_2$ was added. The mixture was stirred at room temperature and monitored until complete disappearance of starting material (about 10 min). The reaction mixture was poured over ground ice (10 g) under vigorously shaking. The organic phase was extracted with CH_2Cl_2 (2x10 mL), neutralized with a saturated solution of NaHCO_3 , washed with brine and water, dried over anhydrous MgSO_4 and concentrated to dryness under vacuum. The crude product was chromatographed over silica gel using hexane/ AcOEt systems.

Selective deacetylation of 20,23-diacetylfurostenes **3 and **7**, to 23-acetylfurostenes **4** and **8**.** The procedure involved treatment of 20,23-diacetylfurostenes **3** or **7**, under the general conditions of the acetolysis process described above, but submitting the reactions to 60 °C during 5 min.

General procedure for oxidation of furostenes 4, 8 and 9

In a round bottom flask 0.9 mmol of furostenes **4**, **8** or **9** were dissolved in 6 mL of MeCN and added by a solution of 695 mg NaIO₄ in 1 mL of H₂O and a catalytic quantity of RuCl₃. The reaction was stirred under argon until no starting material was observed by TLC. The crude was filtered through a short silica gel column and eluted with 20 mL of CH₂Cl₂. The filtrate was washed with a NaHSO₃ soln (3x20 mL), followed by a NaCl saturated soln (3x20 mL) and water. The organic layer was dried with Na₂SO₄ and concentrated to dryness under vacuum.

Synthesis of 23-acetyl derivatives 12 and 13. In a round bottom flask 1.84 mmol of epoxycholestene (**2** or **6**) were dissolved with 20 mL of KOH/methanol (20%). The mixture was stirred for about 20 min at room temperature and monitored until complete disappearance of starting material. At the end of the reaction, the crude reaction mixture was pured into 30 mL of a saturated solution of NaCl. The organic phase was extracted with AcOEt (3x30 mL), washed with water (3x20 mL), dried with anhydrous Na₂SO₄, and concentrated to dryness under vacuum.

Compound characterization. (25R)-23-Acetyl-22,26-epoxycholesta-5,22-diene-3 β ,16 β -diyl diacetate (2). mp 95-96 °C (hexane). [α]_D -24 (*c* 0.65). UV: λ_{\max} (ϵ) 275 nm (10300); IR: 1732, 1660, 1566, 1366, 1248 cm⁻¹ ¹H NMR, δ (500 MHz): 5.35 (d, J_{6-7} = 4.5 Hz, H-6), 5.14 (ddd, $J_1 = J_2 = 7.5$ and $J_3 = 4.5$ Hz, H-16), 4.59 (m, H-3), 4.07 (m, H-20), 4.00 (dd, $J_{26\beta-25} = 3.5$ and $J_{26\beta-26\alpha} = 10.5$ Hz, H-26 β), 3.46 (dd, $J_{26\alpha-25} = J_{26\beta-26\alpha} = 10.5$ Hz, H-26 β), 2.20 (s, CH₃-23²), 2.02 (s, CH₃CO₂-3), 1.84 (s, CH₃CO₂-16), 1.18 (d, $J_{20-21} = 6.0$ Hz, CH₃-21), 1.03 (s, CH₃-19), 0.97 (d, $J_{25-27} = 6.0$ Hz, CH₃-27), 0.92 (s, CH₃-18). ¹³C NMR, δ (125 MHz): 197.9 (C-23¹), 171.1 (C-22), 170.4 (CH₃COO-3), 170.3 (CH₃COO-16), 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), 31.5 (C-7), 31.3 (C-8), 29.6 (C-23²), 27.6 (C-2), 26.4 (C-25), 21.2 (CH₃COO-3), 21.0 (CH₃COO-26), 20.7 (C-11), 19.3 (C-21), 19.1 (C-19), 16.7 (C-27), 12.8 (C-18). MS, *m/z* (%): 540 [M⁺] (13). Anal. calcd. for C₃₃H₄₈O₆: C, 73.30 ; H, 8.95; Found: C, 73.29 ; H, 9.28.

(E)-(20S,25R)-20,23-Diacetylfurosta-5,22-diene-3 β ,26-diyl diacetate (3). mp 135-137 °C. [α]_D -64 (*c* 1.0). UV λ_{\max} (ϵ): 285 (12200). IR: 1732, 1702, 1677, 1614, 1367, 1239 cm⁻¹; ¹H NMR δ (400 MHz): 5.36 (d, $J_{6-7} = 4.8$ Hz, H-6), 4.59 (m, H-3), 3.69 (m, H-16), 3.95 (m, H-26), 2.31 (s, CH₃-20²), 2.18 (s, CH₃-23²), 2.06 (s, CH₃COO-26), 2.03 (s, CH₃COO-3), 1.55 (s, CH₃-21), 1.01 (s, CH₃-19), 0.95 (d, $J_{27-25} = 7$ Hz, CH₃-27), 0.87 (s, CH₃-18). ¹³C NMR δ (100 MHz): 207.2 (C-20¹), 199.4 (C-23¹), 174.0 (C-22), 171.1 (CH₃COO-26), 170.5 (CH₃COO-3), 139.6 (C-5), 121.9 (C-6), 110.2 (C-23), 85.0 (C-16), 73.6 (C-3), 68.6 (C-26), 63.8 (C-17), 62.3 (C-20), 56.6 (C-14), 49.4 (C-9), 42.9 (C-13), 39.7 (C-12), 37.9 (C-10), 36.8 (C-15), 36.4 (C-24), 33.0 (C-8), 32.1 (C-7), 31.9 (C-4), 31.5 (C-1), 31.2 (C-25), 28.6 (C-23²), 27.5 (C-2), 26.4 (C-20²), 21.4 (CH₃COO-26), 20.9 (CH₃COO-3), 20.3 (C-11), 19.3 (C-19), 17.3 (C-27), 15.6 (C-21), 15.2 (C-18). MS, *m/z* (%): 582 [M⁺] (16). Anal. calcd for C₃₅H₅₂O₇: C 71.89, H 8.96, O 19.15, found: C 71.71, H 8.77, O 18.98.

(E)-(25R)-23-Acetylfurosta-5,22-diene-3 β ,26-diyl diacetate (4). mp 83-85 °C (heptane/AcOEt). [α]_D +4 (*c* 1.0). UV λ_{\max} (ϵ): 278 (12060). IR: 1733 1659 cm⁻¹. ¹H NMR δ

(400 MHz): 5.30 (br s, H-6), 4.91 (m, H-3), 4.53 (m, H-16) 3.77 (m, H-26), 3.65 (dq, $J_{20-17} = 11.1$, $J_{20-21} = 6.8$ Hz, H-20), 2.15 (s, $\text{CH}_3\text{-23}^2$), 1.99 (s, $\text{CH}_3\text{COO-26}$), 1.97 (s, $\text{CH}_3\text{COO-3}$), 1.12 (d, $J = 7.0$ Hz, $\text{CH}_3\text{-21}$), 0.95 (s, $\text{CH}_3\text{-19}$), 0.85 (d, $J_{27-25} = 6.5$ Hz, $\text{CH}_3\text{-27}$), 0.53 (s, $\text{CH}_3\text{-18}$). ^{13}C NMR δ (100 MHz): 198.6 (C-23¹), 179.0 (C-22), 171.2 ($\text{CH}_3\text{COO-26}$), 170.5 ($\text{CH}_3\text{COO-3}$), 139.8 (C-5), 122.0 (C-6), 108.0 (C-23), 86.1 (C-16), 73.8 (C-3), 68.8 (C-26), 62.3 (C-17), 55.4 (C-14), 50.0 (C-9), 41.3 (C-13), 38.1 (C-20), 38.0 (C-12), 36.9 (C-1), 36.6 (C-10), 33.6 (C-4), 33.3 (C-15), 31.9 (C-7), 31.3 (C-25), 31.2 (C-24), 31.0 (C-8), 29.2 (C-23²), 27.7 (C-2), 22.0 ($\text{CH}_3\text{COO-26}$), 21.4 ($\text{CH}_3\text{COO-3}$), 20.3 (C-11), 19.8 (C-21), 19.3 (C-19), 17.3 (C-27), 13.1 (C-18). MS, m/z (%): 540 [M^+] (32). Anal. calcd for $\text{C}_{33}\text{H}_{50}\text{O}_6$: C 73.03, H, 9.29, O 17.69, found: C 72.74, H 9.26, O 17.72

(20S)-3 β -Acetoxypregn-5-en-20,16 β -carbolactone (10). mp 213-215 °C. $[\alpha]_{\text{D}}$ -46 (*c* 1.0). IR: 1747, 1720, 1677 cm^{-1} . ^1H NMR, δ (400 MHz): δ 5.37 (d, $J_{6-7} = 4.5$ Hz H-6), 4.96 (m, H-16), 4.60 (m, H-3), 2.59 (dd, $J_{20-21} = J_{20-17} = 6.6$ Hz, H-20), 2.28 (m, H-15 β), 2.04 (s, $\text{CH}_3\text{CO}_2\text{-3}$), 1.32 (d, $J_{21,20} = 7.0$ Hz, $\text{CH}_3\text{-21}$), 1.04 (s, $\text{CH}_3\text{-19}$), 0.77 (s, $\text{CH}_3\text{-18}$). ^{13}C RMN, δ (CDCl_3 , 100 MHz): δ 181.0 (C-22), 170.3 ($\text{CH}_3\text{-COO-3}$), 139.6 (C-5), 121.8 (C-6), 82.7 (C-16), 73.7 (C-3), 58.9 (C-17), 54.7 (C-14), 50.0 (C-9), 41.5 (C-13), 38.2 (C-12), 38.1 (C-4), 36.2 (C-1), 36.1 (C-10), 36.1 (C-20), 33.1 (C-15), 31.9 (C-7), 31.2 (C-8), 27.2 (C-2), 21.5 ($\text{CH}_3\text{-COO-3}$), 20.4 (C-11), 19.4 (C-19), 18.1 (C-21), 13.8 (C-18).

(20S)-3 β -Acetoxy-5 β -pregnane-20,16 β -carbolactone (11). mp 183–185°C; $[\alpha]_{\text{D}}$ -31 (*c* 1.0). IR: 1768, 1757, 1734, 1254 cm^{-1} . ^1H NMR, δ (400 MHz): δ 5.07 (m, H-3), 4.94 (m, H-16), 2.57 (q, $J_{20-21} = 7.3$ Hz, H-20), 2.27 (m, H-15 β), 2.05 (s, $\text{CH}_3\text{CO}_2\text{-3}$), 1.31 (d, $J_{21,20} = 7.3$ Hz, $\text{CH}_3\text{-21}$), 0.99 (s, $\text{CH}_3\text{-19}$), 0.74 (s, $\text{CH}_3\text{-18}$). ^{13}C RMN, δ (CDCl_3 , 100 MHz): δ 181.4 (C-22), 170.8 ($\text{CH}_3\text{-COO-3}$), 82.9 (C-16), 70.5 (C-3), 59.2 (C-17), 54.7 (C-14), 41.9 (C-13), 40.1 (C-9), 38.6 (C-12), 37.2 (C-5), 36.1 (C-20), 35.1 (C-8), 35.0 (C-10), 33.1 (C-15), 30.8 (C-1), 30.6 (C-4), 26.4 (C-6), 26.3 (C-7), 25.0 (C-2), 23.8 (C-19), 21.6 ($\text{CH}_3\text{-COO-3}$), 20.4 (C-11), 18.0 (C-21), 13.9 (C-18). MS, m/z (%): 389 ($\text{M}^+ + 1$) (2). Anal. calcd. for $\text{C}_{24}\text{H}_{36}\text{O}_4$ C 74.19; H 9.34; O 16.47; found: C, 74.45; H, 9.41 O, 16.76.

23-Acetyldiosgenin (12). mp 181-183 °C (AcOEt); $[\alpha]_{\text{D}}$ -129 (*c* 0.24). IR: 3500, 1685 cm^{-1} . ^1H NMR δ (400 MHz): 5.32 (d, $J_{6-7} = 4.7$ Hz, H-6), 4.40 (ddd, $J = 7.0$ Hz, H-16), 3.50 (m, H-3), 3.48 (dd, $J = 11.0$ Hz H-26_a), 3.41 (dd, $J = 11.0$ Hz, H-26_b), 2.64 (dd, $J = 12.0$ Hz, H-23_a), 2.28 (ddd, $J_{24a-24e} = 13$, $J_{24a-23a} = 13$, $J_{24a-25e} = 5.0$ Hz, H-24_a), 1.00 (s, $\text{CH}_3\text{-19}$), 0.98 (d, $J_{21-20} = 6.0$ Hz, $\text{CH}_3\text{-21}$), 0.86 (d, $J_{27-25} = 6.0$ Hz, $\text{CH}_3\text{-27}$), 0.66 (s, $\text{CH}_3\text{-18}$). ^{13}C NMR δ (100 MHz): 210.2 (C-23¹), 108.1 (C-22), 140.9 (C-5), 121.3 (C-6), 81.3 (C-16), 71.9 (C-3), 66.1 (C-26), 61.1 (C-17), 56.6 (C-14), 55.3 (C-23), 50.2 (C-9), 42.5 (C-4), 40.8 (C-13), 40.0 (C-20), 38.7 (C-24), 37.5 (C-12), 36.9 (C-10), 32.3 (C-7), 32.3 (C-15), 31.9 (C-1), 31.9 (C-2), 31.5 (C-8), 30.1 (C-25), 28.6 (C-23²), 21.1 (C-11), 19.7 (C-19), 17.3 (C-27), 16.5 (C-18), 14.5 (C-21). MS, m/z (%): 456 [M^+] (25).

23-Acetylsarsasapogenin (13). mp 191-192 °C (methanol); $[\alpha]_{\text{D}}$ -93 (*c* 1.0). IR: 3383, 1695 cm^{-1} . ^1H NMR δ (400 MHz): 4.41 (ddd, $J = 7.0$ Hz, H-16), 4.15 (s, H-3), 3.99 (dd, $J = 11.0$ Hz, H-26_a), 3.33 (dd, $J = 11.0$ Hz, H-26_b), 2.84 (dd, $J = 13.0$ Hz, H-23_a), 2.37 (ddd, $J_{24a-24e}$

= 13.0 Hz, $J_{24a-23a} = 13.0$ Hz, $J_{24a-25e} = 5.0$ Hz, H-24_a), 2.20 (CH₃CO-23), 1.00 (d, $J_{21-20} = 6.0$ Hz, CH₃-21), 1.08 (d, $J_{27-25} = 6.0$ Hz, CH₃-27), 0.97 (s, CH₃-19), 0.64 (s, CH₃-18). ¹³C NMR δ (100 MHz): 210.2 (C-23¹), 108.3 (C-22), 81.3 (C-16), 67.0 (C-3), 64.3 (C-26), 61.2 (C-17), 56.2 (C-14), 49.5 (C-23), 41.0 (C-13), 40.2 (C-12), 38.8 (C-20), 39.8 (C-9), 36.5 (C-5), 35.1 (C-8), 35.0 (C-10), 33.5 (C-4), 31.5 (C-15), 29.9 (C-1), 29.4 (C-24), 28.7 (C-23²), 27.0 (C-25), 27.0 (C-2), 26.6 (C-7), 26.6 (C-6), 23.9 (C-19), 20.9 (C-11), 16.4 (C-18), 16.4 (C-27), 14.1 (C-21). MS, m/z (%): 458 [M⁺] (19).

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