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New bisfuran derivative from sarsasapogenin An X-ray and NMR analysis

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ABSTRACT

The new bisfuran derivative, (22S,23S)-22,23-dihydroxy-23,26-epoxyfurostane (**5**), was obtained from the known oxidation of sarsasapogenin acetate with $NaNO_2/BF_3$ in 5% aqueous acetic acid. The structure of **5** was established using one and two-dimensional ^1H, ^{13}C experiments (DEPT, COSY, HETCOR and HMBC) and the configurations at the newly formed stereogenic centers were established as 22S,23S by an X-ray diffraction analysis. Addition of $TiCl_4$ to bisfuran **5** confirmed that this compound is an intermediate in the rearrangement to 22-oxo-23-spiroketals since it was transformed quantitatively into the latter product. The 23-nitroimino intermediate **2** was isolated from the same reaction and its structure established also by an X-ray diffraction analysis; this compound was further transformed into the 23-nitramine **7** which could find application in functionalization of position 24.

1. Introduction

Sapogenins are complex molecules containing a sugar bonded to a stereoidal or triterpenic nucleus, which are important sources for the syntheses of pharmacologically active steroids. Upon hydrolysis, these substances yield carbohydrates and an aglycone called sapogenin with cholestane, furostane or spirostane frameworks. Spirostane sapogenins are widely distributed in the plant kingdom and therefore are relatively cheap raw materials for the syntheses of other steroidal substances.

The main characteristic of spirostane sapogenins is a spiroketal system fused at the E/F rings of the side chain, thus spiroketal opening and functionalization constitutes one of the main strategies in the synthesis of other derivatives. Bisfuran derivatives, on the other hand, have not been isolated from plants and there are few reports concerning their synthesis, in spite of the fact that ditetrahydrofuran units are present in many natural products with remarkably diverse and important biological activity [1,2].

Suárez and co-workers in 1988 reported that treatment of steroidal spiroacetal methanesulfonate derivatives with DIBALH promotes a new rearrangement to the 2,2′-linked ditetrahydrofuran derivatives [3]. In turn, Morzycki and co-workers [4,5] described the formation of (22S,23R)-22-hydroxy-23,26-epoxyfurostanes by alkaline hydrolysis of (22S,23S)-23-bromosapogenins, as well as the reaction of (23S)-23-tosyloxyspirostanes and 23-tosylhydrazones (25R and 25S series) to give bisfuran products. In continuation of our studies on the transformation of the side chain of sapogenins [6–8] we describe herein the formation of the new bisfuran derivative **5** and 23-nitramine **7** from sarsasapogenin.

2. Experimental

2.1. General remarks

IR spectra were acquired on a FT-IR Perkin-Elmer Spectrum GX spectrophotometer using KBr pellets (υ, cm^{-1}). NMR spectra

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(^{1}H, ^{13}C, DEPT, HETCOR, COSY and HMBC) were determined with a JEOL eclipse +400, chemical shifts are stated in ppm (δ), and are referred to the residual ^{1}H signal ($\delta = 7.27$) or to the central ^{13}C triplet signal ($\delta = 77.0$) for $CDCl_3$. Mass spectra were obtained at 70 eV with a Hewlett Packard 5989A mass spectrometer. Optical rotations $[\alpha]_D^{25}$ were obtained at room temperature using chloroform solutions on a Perkin-Elmer 241 polarimeter. HRMS of **7** was obtained on a Jeol JMS-SX102A using polyethylene glycol (600) as internal reference. Elemental composition was calculated within an error of 10 ppb using the program installed in the system. Melting points were obtained on an Electrothermal 9200 apparatus and are not corrected. Elemental analyses were performed on a Thermo Finnigan Flash EA 1112 series apparatus. The products were separated by chromatography over (70–230 mesh) silica gel.

2.2. *Oxidation of sarsasapogenin acetate with $NaNO_2/BF_3{\cdot}Et_2O$*

2.2.1. *Experiment 1*

Treatment of sarsasapogenin acetate **1** with $NaNO_2/BF_3$ in glacial acetic acid, as previously described [9–13], afforded (25*S*)-3β-acetoxy-5β-spirostan-23-nitroimino (**2**), which hydrolyzes upon treatment with neutral Al_2O_3 (grade III) to give (25*S*)-3β-acetoxy-5β-spirostan-23-one (**3**) and a small quantity of (20*S*)-3β-acetoxy-5β-pregnan-20,16β-carbolactone (**4**).

2.2.2. *Experiment 2*

Treatment of sarsasapogenin acetate **1** (10.00 g, 21.83 mmol) with $NaNO_2/BF_3$ in acetic acid (100 ml, 5% aqueous solution) provided a mixture of compounds **3**–**5**. The products were chromatographed over silica gel with mixtures of hexane/EtOAc of increasing solvent polarity to give: 2.80 g (27% yield) of (25*S*)-3β-acetoxy-5β-spirostan-23-one (**3**), mp = 171–172 °C (literature [13], 171–173 °C) (hexane/EtOAc, 9:1); 3.10 g (37% yield) of (20*S*)-3β-acetoxy-5β-pregnan-20,16β-carbolactone (**4**), mp = 188 °C (literature [14], 184.5–185.5 °C) (hexane/EtOAc, 8:2); 0.70 g (7% yield) (rf = 1.3 hexane/EtOAc, 7:3) of (22*S*,23*S*)-22,23-dihydroxy-23,26-epoxyfurostane (**5**), mp = 178–179 °C (hexane/EtOAc, 7:3).

2.2.3. *Experiment 3*

Treatment of sarsasapogenin acetate **1** (8.00 g, 17.46 mmol) with $NaNO_2/BF_3$ in 80 ml glacial acetic acid provided **2** and **4**. The products were chromatographed over silica gel to give 3.30 g (37% yield) of (25*S*)-3β-acetoxy-5β-spirostan-23-nitroimino intermediate (**2**) [11,13] (hexane/EtOAc, 9:1) and 2.20 g (32% yield) of (20*S*)-3β-acetoxy-5β-pregnan-20,16β-carbolactone (**4**), mp = 188 °C (literature [14], 184.5–185.5 °C) (hexane/EtOAc, 8:2).

2.2.4. *(22S,23S)-22,23-Dihydroxy-23,26-epoxy-furostane (5)*

Compound **5**: white crystals, mp 178–179 °C (hexane/AcOEt); $[\alpha]_D^{25}$ −60° (c, 1.0, $CHCl_3$); IR_{max}: 3538 (OH), 3475 (OH), 2950 (CH), 1727 (OAc), 1452, 1377, 1252, 1145 cm^{-1}; MS, *m*/*z* (%): 490 (M^+, 1), 472 ($M^+ - 18$, 4), 444 (4), 389 (37), 329 (100), 315 (26), 255 (85), 130 (43); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 5.03 (1H, br, H-3), 4.60 (1H, td, $J = 7.7$ and 7.3 Hz, H-16), 4.18 (1H, t, $J = 8.2$ Hz, H-26), 3.39 (1H, br, OH), 3.35 (1H, t, $J = 8.2$, H-26), 3.13 (1H, br, OH), 2.65 (1H, m, H-20), 2.37 (1H, m, H-25), 2.01 (3H, s, 3-$OCOCH_3$), 1.04 (3H, d, $J = 7.0$ Hz, CH_3-27), 1.02 (3H, d, $J = 6.2$ Hz, CH_3-21), 0.95 (3H, s, CH_3-19), 0.76 (3H, s, CH_3-18); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 170.8 (3-$OCOCH_3$), 109.5 (C-22), 107.1 (C-23), 82.1 (C-16), 75.5 (C-26), 70.8 (C-3), 63.6 (C-17), 56.4 (C-14), 41.3 (C-13), 40.3 (C-12), 40.1 (C-15), 40.0 (C-9), 37.3 (C-5), 36.3 (C-25), 35.3 (C-8), 35.1 (C-10), 32.5 (C-20), 31.9 (C-4), 30.8 and 30.7 (C-1, C-2), 26.5 (C-6, C-7), 25.0 (C-24), 23.9 (C-19), 21.6 (3-$OCOCH_3$), 20.9 (C-11), 17.1 (C-21), 16.5 (C-18), 16.0 (C-27). Anal. calcd. for $C_{29}H_{46}O_6$: C 70.99, H 9.45, O 19.56; found: C 70.71, H 9.81, O 19.48.

2.3. *(23R,25S)-3β-Acetoxy-16β,23:23,26-diepoxy-5β-cholestan-22-one (6)*

To a solution of (22*S*,23*S*)-22,23-dihydroxy-23,26-epoxyfurostane (**5**) (13 mg, 0.03 mmol) in dry dichlorometane (4 ml), $TiCl_4$ was added (0.02 ml, 8 eq.). The reaction was stirred at room temperature overnight, poured over water and the organic layer extracted with dichlorometane (2 × 5 ml), dried over anhydrous $MgSO_4$ and evaporated under vacuum. The 22-oxo-23-spiroketal was obtained in quantitative yield (rf = 2.2, hexane/EtOAc, 7:3), mp = 168 °C (literature [19], 169–171 °C).

2.4. *(25S)-3β-Hydroxy-5β-spirostan-23-ene-23-nitramine (7)*

To a solution of (25*S*)-3β-acetoxy-5β-spirostan-23-nitroimino (**2**) (562 mg, 1.08 mmol) in ethylene glycol were added 17 ml of a 10% aqueous solution of NaOH. The reaction mixture was heated 22 h under reflux at 110–120 °C, cooled to room temperature and poured over water. The organic layer extracted with ethyl acetate (3 × 10 ml), dried over anhydrous $MgSO_4$ and evaporated under vacuum. The crude reaction product (0.56 g) was chromatographed over silica gel (hexane/EtOAc, 8:2) to give 350 mg (68% yield) (rf = 0.9, hexane/EtOAc, 7:3) of **7**.

Compound **7**: white powder, mp 154–156 °C; $[\alpha]_D^{25}$ −30° (c, 1.0, $CHCl_3$); IR_{max}: 3561, 2929 (CH), 1584, 1314 (NNO_2), 910 (N–O) cm^{-1}; MS, *m*/*z* (%): 474 (M^+, 3), 443 (6), 429 (28), 388 (6), 347 (41), 329 (40), 287 (42), 273 (84), 215 (15), 147 (46), 107 (61), 41 (100); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 9.26 (1H, br, NH), 6.44 (1H, d, $J = 7.0$ Hz, H-24), 4.53 (1H, q, $J = 8.0$ Hz, H-16), 4.11 (1H, br, H-3), 3.91 (1H, dd, $J = 3.3$ and 11.4 Hz, H-26), 3.51 (1H, d, $J = 11.4$ Hz, H-26), 2.27 (1H, m, H-25), 2.10 (1H, m, H-20), 1.20 (3H, d, $J = 7.0$ Hz, CH_3-27), 0.98 (3H, d, $J = 6.2$ Hz, CH_3-21), 0.97 (3H, s, CH_3-19), 0.82 (3H, s, CH_3-18); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 135.9 (C-24), 129.5 (C-23), 107.8 (C-22), 82.5 (C-16), 67.2 (C-3), 63.8 (C-26), 61.4 (C-17). 56.5 (C-14), 41.2 (C-13), 40.1 (C-12), 39.9 (C-9), 38.5 (C-20), 36.6 (C-5), 35.4 (C-10), 35.3 (C-8), 33.6 (C-4), 31.7 (C-15), 30.0 (C-1), 29.9 (C-25), 27.9 (C-2), 26.6 (C-6, C-7), 23.9 (C-19), 20.9 (C-11), 17.5 (C-27), 16.5 (C-18), 14.5 (C-21). HRMS calcd. *m*/*z* for $C_{27}H_{43}O_5N_2$ ($M^+ + 1$): 475.3172; found: 475.3159 error 2.6 ppm.

2.5. *Crystal structure determination*

Crystals of **2** and **5** suitable for X-ray analysis were obtained from a mixture of hexane–ethyl acetate (9:1) and (7:3), respectively, by slow evaporation of the solvent at room temperature. The X-ray measurement of (25*S*)-3β-acetoxy-5β-

spirostan-23-nitroimino (**2**) was performed at 293 K and that of (22*S*,23*S*)-22,23-dihydroxy-23,26-epoxyfurostane (**5**) at 198 K on an Enraf-Nonius-Kappa CCD diffractometer with Mo Kα radiation, λ = 0.71073 Å. The structures were solved by direct methods (SHELXS-86) [15] and refined using SHELXL-97 [16]. All non-hydrogen atoms were refined anisotropically, the H atoms were placed at calculated positions using a riding model. Crystallographic data have been deposited at the Cambridge Crystallographic Data Center as supplementary material Nos. 265697 (**2**) and 265698 (**5**). Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK. E-mail: deposit@ccdc.cam.ac.uk.

2.5.1. *Crystal data for compound* **2**

$C_{29}H_{44}N_2O_6$, colorless, 0.77 mm × 0.12 mm × 0.07 mm, formula weight $M = 516.66$, monoclinic, P 2_1, $a = 12.727(3)$ Å, $b = 7.2252(14)$ Å, $c = 16.811(3)$ Å, $\beta = 110.59(3)^\circ$, $V = 1447.1(5)$ Å^3, $Z = 2$, $D_x = 1.186$ Mg m^{-3}, $\mu = 0.082$ mm^{-1}, $F(000) = 560$. Collected reflections: 8713 within a 2θ range of 8.36–51.96° ($h = -15 \rightarrow 15$, $k = -8 \rightarrow 8$, $l = -20 \rightarrow 20$). Unique reflections: 5332 [$R_{int} = 0.1058$]. Observed reflections: 2381 with $F > 4\sigma(F)$, the absorption correction was no applied. Refinement: (Refinement on F^2), Final $R = 0.0763$, $wR_2 = 0.1472$, goodness-of-fit = 1.010, 2381 reflections, 335 parameters, absolute structure parameter 2(3), extinction coefficient: 0.029(5), maximum and minimum difference electron densities were 0.158*e* and −0.161*e* Å^{-3}, respectively.

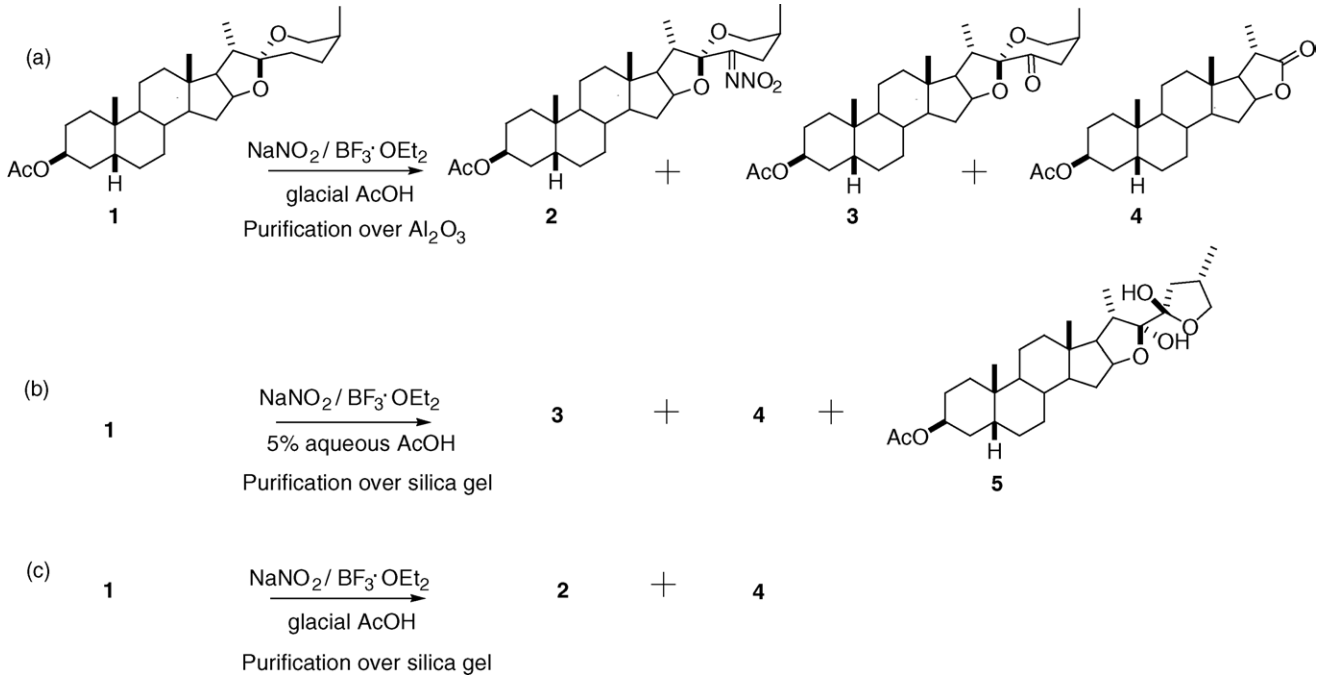
2.5.2. *Crystal data for compound* **5**

$C_{29}H_{46}O_6$, colorless, 0.50 mm × 0.22 mm × 0.17 mm, formula weight $M = 490.68$, monoclinic, P 2_1, $a = 10.8928(2)$ Å, $b = 6.08540(10)$ Å, $c = 20.3864(5)$ Å, $\beta = 99.9490(10)^\circ$, $V = 1331.03(5)$ Å^3, $Z = 2$, $D_x = 1.224$ Mg m^{-3}, $\mu = 0.084$ mm^{-1}, $F(000) = 536$. Collected reflections: 5359 within a θ range of 3.76–27.48° ($h = -12 \rightarrow 12$, $k = -7 \rightarrow 7$, $l = -26 \rightarrow 26$). Unique reflections: 5359 [$R_{int} = 0.0000$]. Observed reflections: 3972 with $F > 4\sigma(F)$, the absorption correction was no applied. Refinement: (Refinement on F^2), final $R = 0.0487$, $wR_2 = 0.1099$, goodness-of-fit = 1.008, 3972 reflections, 316 parameters, absolute structure parameter 0.1(14), extinction coefficient: 0.006(2), maximum and minimum difference electron densities were 0.296*e* and −0.294*e* Å^{-3}, respectively.

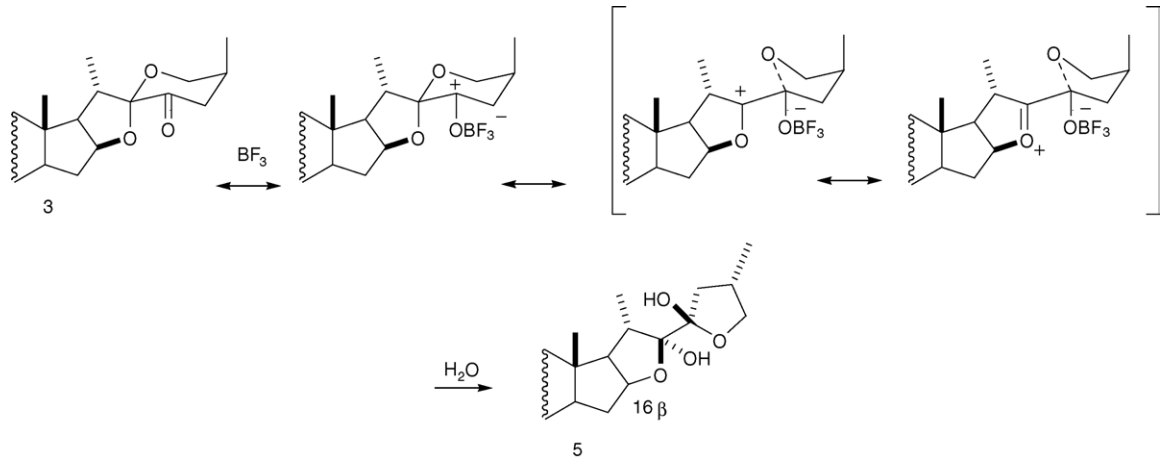
3. Results and discussion

It has been described previously [9–13] that oxidation of spirostane sapogenins of the 25*S* and 25*R* series with $NaNO_2/BF_3{\cdot}OEt_2$, in glacial acetic acid, gives small amounts of the steroidal C-22 lactone **4** and intermediate **2** which leads to the 23-oxosarsasapogenin acetate **3** upon treatment with neutral Al_2O_3 (grade III) (Scheme 1a).

In continuation of our studies on the transformation of sapogenins [6–8], we carried out the same oxidation using 5% aqueous acetic acid and the crude reaction mixture was chromatographed over silica gel. Under these conditions, 23-oxosarsasapogenin acetate **3**, the steroidal C-22 lactone **4** and the new bisfuran derivative **5** were obtained (Scheme 1b). The low yield for the bisfuran derivative **5** can be attributed to the fact that hemiketals are not very stable, and as a consequence they are difficult to isolate [17]. The fact that the 23-nitroimino intermediate **2** was not isolated is attributed due to facile transformation of these derivatives to carbonyl compounds in the presence of water [18]. In contrast, when the reaction is carried out in glacial acetic acid, as described in the literature [9–13] but the purification was carried out using silica gel,



Scheme 1 – (a) Products from the oxidation of sarsasapogenin 1 with $NaNO_2/BF_3{\cdot}OEt_2$ in glacial AcOH. (b) New bisfuran derivative 5 from the oxidation of sarsasapogenin with $NaNO_2/BF_3{\cdot}OEt_2$ in 5% aqueous AcOH. (c) Reaction conditions for the isolation of intermediate 2.



Scheme 2 – Proposed mechanism for the formation of bisfuran derivative 5.

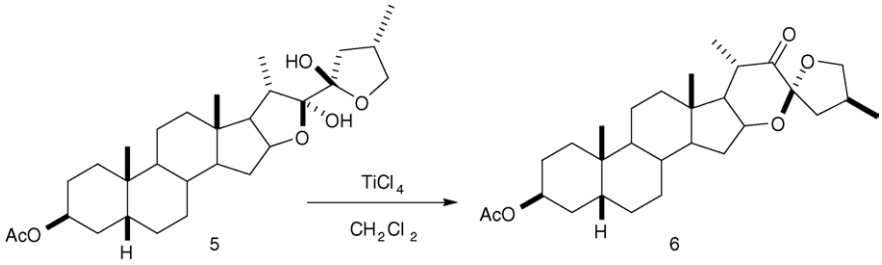
the 23-nitroimino **2** and C-22 lactone **4** were the sole products (Scheme 1c).

Suárez and co-workers [3] have proposed that rearrangement of steroidal spiroacetal methanesulfonate derivatives to bisfurans with DIBALH proceeds in two steps which involve: (1) coordination of the aluminum at the less hindered tetrahydropyranyl oxygen to cleave exclusively the C-22–O bond and (2) the C-26 alcoxy intermediate attacks C-23 to replace the methanesulfonyl substituent via an S_N2 reaction with inversion of configuration. Moreover, Morzycki and co-workers [4,5] proposed that the rearrangement of 23-spirostanyl bromides and tosylates to bisfuran derivatives containing a hydroxyl group at C-22, proceeds through neighboring-group participation of O-26 which facilitates the departure of a good leaving group at C-23. More recently, Cyrański et al. [19] proposed a mechanism for the formation of 22-oxo-23-spiroketals from the corresponding 23-oxosarsasapogenin acetate with $BF_3{\cdot}OEt_2$. The mechanism involves two 1,2-oxygen shifts from C-22 to C-23. They also considered migration of O-26 to the C-23 electrophilic center to give the bis-hemiketal provided aqueous conditions were used, however, this mechanism was discarded because it is thermodynamically disfavoured.

An alternative mechanism for the formation of bisfuran derivative **5** is shown in (Scheme 2). Coordination of $BF_3{\cdot}OEt_2$ to the carbonyl oxygen and subsequent migration of O-26 to the electrophilic center C-23 leads to the bisfuran carbocation shown which is attacked by the water present in the reaction medium.

In order to obtain evidence that bisfuran derivative **5** was an intermediate in the rearrangement to the 22-oxo-23-spiroketal, $TiCl_4$ was added at room temperature to give **6** in quantitative yield (Scheme 3) while the use of $BF_3{\cdot}OEt_2$ yielded **6** in complex mixture of products. Attempts to isolate the bisfuran derivative **5** by treatment of **3** with $BF_3{\cdot}OEt_2$/glacial acetic acid or $BF_3{\cdot}OEt_2$/5% aqueous acetic acid at room temperature did not provide **5**, instead compound **6** was obtained in low yields. Formation of the 22-oxo-23-spiroketal **6** from bisfuran derivative **5** was confirmed by comparison with the data reported by Cyrański et al. [19].

The mass spectrum of bisfuran derivative **5** showed the molecular ion at 490 amu, as well as the fragment corresponding to loss of a water molecule at $m/z = 472$ amu and an ion at 329 corresponding to the loss of the furan and acetate groups. In the IR spectrum, characteristic absorptions for the hydroxyl groups were observed at 3538 and 3475 cm^{-1}. The ^1H NMR spectrum shows a broad signal for H-3 (5.03 ppm), a doublet of triplets for H-16 (4.60 ppm), two triplets at 4.18 and 3.35 ppm for the diastereomeric protons at H-26, two broad signal for two hydroxyl groups at 3.39 and 3.13 ppm, the acetate group at 2.01 ppm, the characteristic singlets for CH_3-19 and CH_3-18 at 0.95 and 0.76 ppm and two doublets for CH_3-27 and CH_3-21 at 1.04 and 1.02 ppm, respectively. The ^{13}C NMR spectrum shows the two C-22 and C-23 hemiketal carbons at 109.5 and 107.1 ppm. The DEPT experiment of **5** shows 10 methylene signals, 9 methine carbons and 5 methyl carbons. Assignment of the signals was based on the HETCOR cross-peaks, thus the signal at 5.03 ppm (H-3) in the ^1H spectrum correlates with the



Scheme 3 – Rearrangement of bisfuran derivative 5 to 22-oxo-23-spiroketal 6.

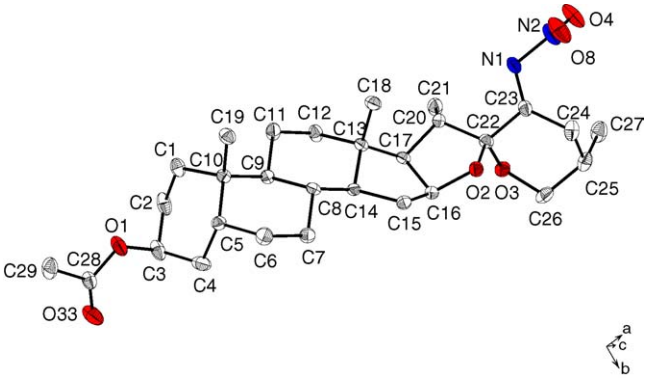


Fig. 1 – X-ray structure of (25*S*)-3β-acetoxy-5β-spirostan-23-nitroimino (2).

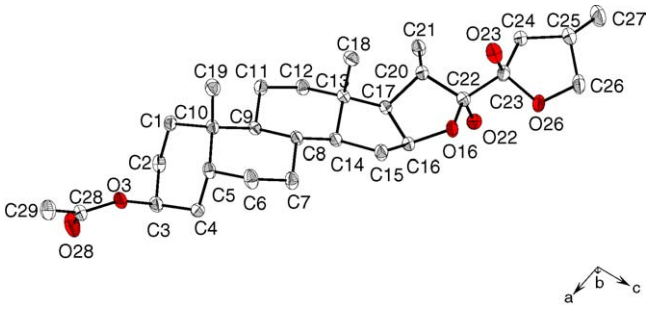


Fig. 2 – X-ray structure of (22*S*,23*S*)-22,23-dihydroxy-23,26-epoxyfurostane (5).

signal at 70.8 ppm, the one at 4.60 ppm (H-16) with the signal at 82.1 ppm, the protons at 4.18 and 3.35 ppm (H-26) correlate with the signal at 75.5 ppm, the methyls and acetate groups in 2.01, 1.04, 1.02, 0.95 and 0.76 ppm correlate with the signals at 21.6, 16.0, 17.1, 23.9 and 16.5 ppm, respectively. Specific assignment of the quaternary signal at 107.1 ppm to C-23 was based on the HMBC cross-peaks with CH_2-26 at 4.18 and 3.35 ppm, as well as with CH-25 at 2.37 ppm. The quaternary carbon at 41.3 ppm was assigned to C-13 based on correlation with the CH_3-18. Spectroscopic assignment of the steroidal framework was based on comparison with the data reported for sarsasapogenin [20].

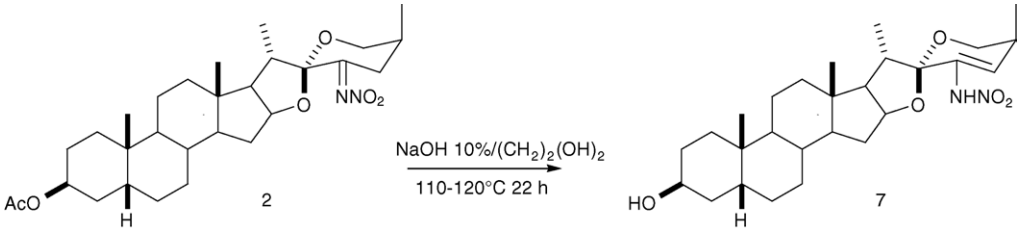
The X-ray diffraction analysis of 23-nitroimino **2** (Fig. 1) shows short contact distances of 2.618 Å between the *equatorial* proton H-12B with the carbonyl group of the ester at position 3 of another 23-nitroimino molecule, as well as H-27C···H-29B 2.182 Å. The conformation for ring F is *pseudo*-chair and the five-membered D and E rings present nearly envelope conformations with torsion angles of 5.5° for the C-15–C-16–C-17–C-13 fragment and 8.5° for C-16–C-17–C-20–C-22. The O-3 atom in the F ring occupies a *pseudo-axial* position with respect to the five-membered D ring and the O-2 is axial. The C-23–N-1 distance of 1.271(7) Å confirms the existence of a double bond at this position, other characteristic distances are: 1.437(7), 1.195(8) and 1.219(8) for the N-1–N-2, N-2–O-4 and N-2–O-8 bonds, respectively.

The X-ray diffraction analysis of bisfuran derivative **5** (Fig. 2) proved unequivocally the configurations at C-22 (*S*) and C-23 (*S*) which were assigned with reference to carbon atoms of known configuration. The structure shows retention of configuration at C-20 and C-25. The five-membered D ring has nearly pure envelope conformation with torsion angles of −2.3° for C-15–C-16–C-17–C-13, the furanose E rings presents a slightly distorted half-chair conformation with torsion angles of 19.3° for C-16–C-17–C-20–C-22 and 3.5° for O-16–C-16–C-17–C-20 while ring F has a conformation between an envelope and a half-chair with torsion angles of 9.3° for the C-25–C-26–O-26–C-23 fragment and 38.1° for C-23–C-24–C-25–C-26. The oxygen atoms in the furanose rings are approximately *gauche* with a torsion angle of 66.0° for the O-16–C-22–C-23–O-26 and the hydroxyl groups at C-22, C-23 are *trans* located with torsion angles −176.3° for O-22–C-22–C-23–O-23. Compound **5** has a chair conformation for rings A–C. Rings A and B are *cis* fused and the latter two are *trans*. The C-20 and C-25 methyl groups occupy *pseudo-equatorial* positions. The *pseudo-axial* proton at position 26 showed an intermolecular between O-16···H-26A 2.5903 Å, other intermolecular contacts observed are: O-22···O-26, 2.8212 Å; O-22···H-23, 2.5566 Å; O-23···H-22, 2.5106 Å.

Attempts to transform intermediate **2** to bisfuran derivative **5** using $BF_3{\cdot}OEt_2$/acetic acid at room temperature and *p*-Ts-OH in toluene under reflux for three days were unsuccessful.

Moreover, basic treatment of **2** yielded (25*S*)-3β-hydroxy-5β-spirostan-23-ene-23-nitramine (**7**), which allows to functionalize position 24 (Scheme 4).

In conclusion bisfuran derivative **5** was isolated and shown to be an intermediate in the formation of 22-oxo-23-spiroketals. The low yield is attributed to the absence of a good leaving group at C-23 and the fact that hemiketals are not very stable, the compound was obtained diastereoselectively. The diastereoselectivity observed in the formation **5** is attributed to steric interaction of the 27 methyl group at position 25 with the hydroxyl group attached to C-23 leading to an *anti*-disposition of the hydroxyl groups at C-22 and C-23, which, is the most stable based on steric effects. The 23-nitroimino intermediate **2** was isolated and further transformed into the corresponding 23-nitramine **7** which could find application in functionalization of position 24.



Scheme 4 – Preparation of 23-nitramine 7.

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