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# PhI=NSes mediated aziridination of 11-pregnane derivatives: synthesis of an 11,12-aziridino analogue of neuroactive steroids

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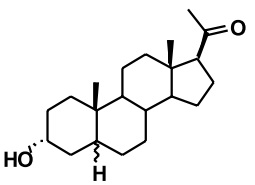
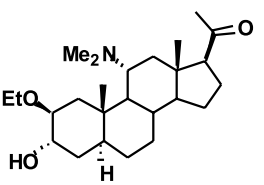
**Abstract**—Reaction of 11-pregnene-3,20-dione (**6**) or 3-α-acetoxy-11-pregnen-20-one (**12**) with trimethylsilylethanesulfonyl ('Ses') iminoiodinane **5** in the presence of copper (I) triflate gave the corresponding α,α-11,12-aziridino steroids **7** and **13** in 53 and 45% yields, respectively. The Ses group of each compound was removed using the TASF reagent and the resulting free aziridine NH was methylated to afford the 11α,12α-*N*-methyl aziridinosteroids **9** and **15**, respectively. The latter is a conformationally constrained analogue of the endogenous neurosteroid pregnanolone (**1**). 

Endogenously occurring steroids such as pregnanolone (**1**) and epiallopregnanolone (**2**) are known to interact with the neuroinhibitory $GABA_A$ receptor of the central nervous system.[1–3] Such neurosteroids and their synthetic analogues can, as a result, demonstrate sedative-hypnotic, anxiolytic or anticonvulsant activities in vivo. In the search for more active, selective or water-soluble steroid derivatives, several aminosteroids have been developed over the years. Thus, the 11α-(*N*,*N*-dimethylamino)pregnan-20-one, minaxolone (**3**)[4] and a 2-morpholinyl analogue of alfaxolone, Org 21465 (**4**)[5] are highly effective general anesthetics. Certain amino steroids have also been shown to demonstrate other activities such as enzyme inhibition.[6,7] An alternative way of obtaining more potent steroid derivatives is to synthesize conformationally restrained analogues. In this regard, the synthesis and biological activities of 3α-hydroxyandrostan-16,17-epoxides and oxetanes have recently been reported.[8]

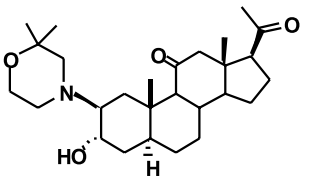
As a means of combining the presence of an apparently well-tolerated nitrogen atom at the 11 position of neurosteroids (i.e. as in minaxolone **3**) together with a certain level of conformational constraint to the steroid nucleus, we thought of preparing an 11,12-aziridino analogue of neurosteroids **1** or **2**. While a number of exocyclic aziridinosteroids have been described (i.e. in which the aziridine moiety shares one[9] or no[6,10] atoms with the steroid nucleus), there are only a few reported syntheses of fused aziridine-steroid derivatives[11,12] and none of aziridines fused at the 11,12-position. Such aziridino steroids have generally been prepared as epimeric mixtures by lithium aluminum hydride reduction of ketosteroid-derived oximes,[9,10,12] a method originally introduced by Tzikas and co-workers.[13] The aziridination of a bis-unsaturated steroid using $N_3CO_2Et$ under photolytic reaction conditions has also been reported.[11]




**1** Pregnanolone (5β–H)
**2** Epiallopregnanolone (5 α–H)




**3** Minaxolone




**4** Org 21465

A particularly attractive method for accessing such

*Keywords*: steroid; aziridine; Ses group; iminoiodinane.

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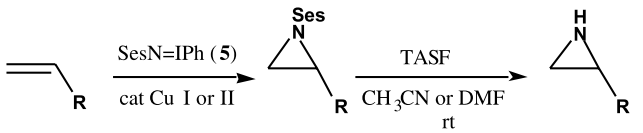


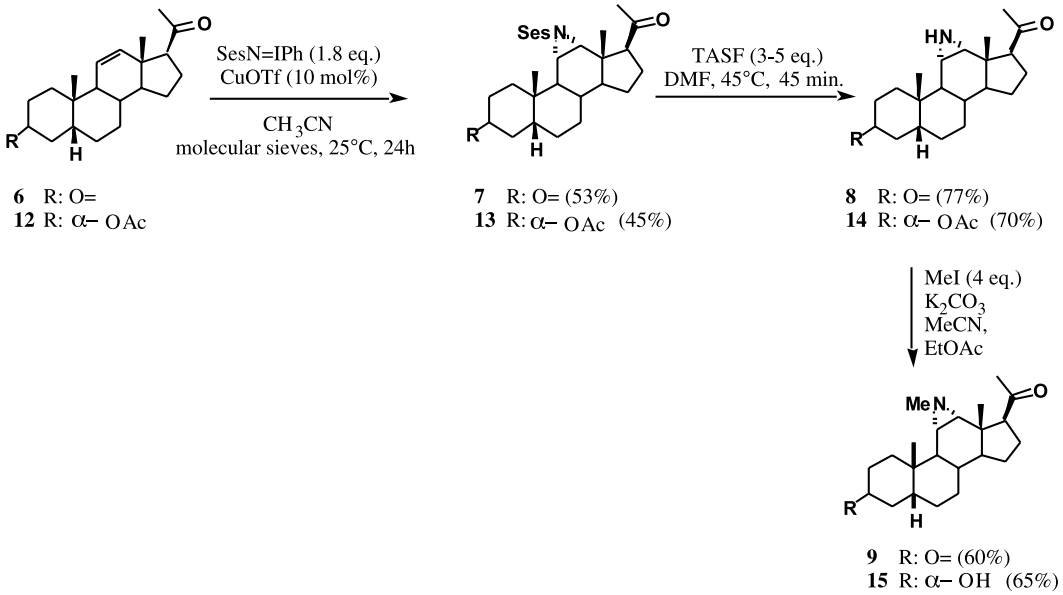

**Scheme 1.**

molecules would be application to an unsaturated steroid of an [*N*-(arylsulfonyl)imino]phenyliodinane-mediated aziridination. These hypervalent iodine reagents, in the presence of a copper catalyst, generate the nitrene species which adds to the olefin, forming an *N*-arylsulfonylaziridine.[14–16] Both electron-rich and electron-poor olefins can be aziridinated using this procedure. While the stereochemical outcome of the nitrene addition to a double bond can in some cases be controlled by addition of chiral catalysts to the reaction medium (e.g. bis-oxazolines),[14] use of a chiral substrate such as a steroid should in principle allow diastereoselective aziridination.

A disadvantage of this methodology, however, is the often troublesome removal of the stable *N*-arylsulfonyl group, both in the intact aziridine as well as in the products of nucleophilic aziridine ring opening.[17–19] It was for this reason that we developed as an alternative the trimethylsilylethanesulfonyl ('Ses') version of these reagents (i.e. **5**, Scheme 1) in order to allow facile removal of the alkylsulfonyl group using a source of fluoride anion.[20] In this paper, then, we describe the synthesis using the Ses iminoiodinane **5** of a minaxolone-type steroid in which the *N*,*N*-dimethylamino group at C-11 is replaced by an *N*-methyl 11,12-aziridino function.[21]

As a model study, it was initially decided to attempt aziridination of 11-pregnene-3,20-dione **6**. Thus, treatment of **6** in acetonitrile with Ses reagent **5** in the presence of 10 mol% of copper (I) triflate afforded, after 24 h at room temperature, the desired *N*-Ses aziridine derivative **7** in 53% yield (Scheme 2). The $^1$H NMR spectrum of **7** showed the aziridine hydrogens at 3.070 and 2.870 ppm (H-12 and H-11, respectively); the H-11 resonance appeared as a double doublet with a very small coupling (0.8 Hz) to H-9, indicative of the α orientation of the aziridine ring which corresponds to approach of the nitrene species from the less hindered face of the steroid. There was no evidence in the reaction mixture of any compound corresponding to the 11,12-β analogue of **7**. The stereochemistry of **7** was further confirmed by X-ray crystallography of the final product (see below). We have previously shown that it is possible to cleave the Ses group from the intact aziridine by use of excess tris(dimethylamino)sulfonium difluorotrimethylsilicate (TASF) under mild conditions (acetonitrile or DMF at room temperature).[20] In the case of compound **7**, heating in DMF with TASF (5 equiv.) at 45°C for 40 min was necessary to effect complete deprotection of the aziridine, giving **8** in 77% yield. The free amine was then methylated at room temperature using excess methyl iodide and potassium carbonate in acetonitrile/ethyl acetate (1:1), affording compound **9** in 60% yield. The NOESY spectrum of compound **9** showed strong correlations for the β-oriented aziridine hydrogens H-11 (1.37 ppm) and H-12 (1.65 ppm) with the angular methyl protons H-19 and H-18, respectively. The *N*-methyl group had strong NOE correlations with both aziridine hydrogens at positions 11β and 12β and a weak correlation with the 17α-H, consistent with an *exo* orientation. The structure of compound **9** and the orientation of the *N*-methyl group were confirmed by X-ray crystallography (Fig. 1), which clearly showed the α-configuration of the 11,12-aziridine ring and the flattening of the C-ring as a result of the presence of the fused aziridine; interestingly, the A-ring also shows a considerable distortion from its expected chairlike conformation, in the vicinity of C1 and C2.[22]

Having established that the transformation of the 11,12 double bond of steroid **6** to an *N*-methyl aziridine using the Ses-iminoiodinane **5** is a viable procedure, we then set about to prepare the 3-α-hydroxy analogue of **9** in order to target, by analogy with **1** and minaxolone **3**, a neuroactive steroid.




**Scheme 2.**

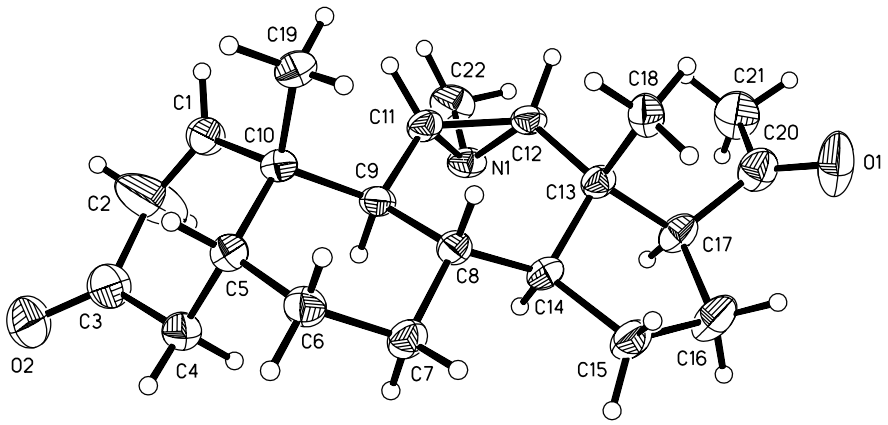



**Figure 1.** Displacement ellipsoid diagram of compound **9**[27] showing the numbering scheme used. Displacement ellipsoids drawn at a 40% probability level.

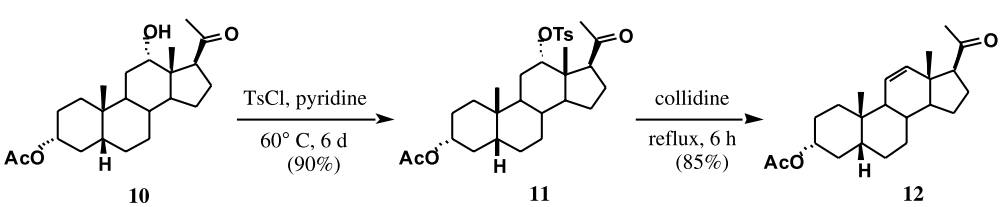
For this purpose, a more suitable starting material, the 3α-acetoxy-11-pregnene-20-one derivative **12**, was chosen. The latter was prepared as shown in Scheme 3. Thus, the 12α-hydroxy substrate **10** (prepared from deoxycholic acid as previously described)[23] was treated with tosyl chloride in anhydrous pyridine for 6 days at 60°C, yielding 90% of the tosyloxy derivative **11**, which could be purified by flash chromatography on silica gel. Refluxing of a solution of **11** in collidine for 6 h then provided the desired olefin **12** in 85% yield. Treatment of the latter with PhI=NSes and catalytic copper (I) triflate in acetonitrile produced the expected *N*-Ses aziridine derivative **13** in 45% yield (77% based on recovered starting material **12**). Again, only formation of the α-aziridine derivative was evident from the $^{1}$H NMR spectra. Finally, deprotection of the amine function of **13** with TASF in DMF gave the free amine **14**. Treatment of the latter with methyl iodide and potassium carbonate resulted in simultaneous *N*-methylation and O-deacetylation, thereby providing the desired *N*-methylaziridine-3α-hydroxy steroid derivative **15**, a direct structural analogue of **1** and **3**. It is interesting to note that, while this study was in progress, a report appeared[24] describing the allylic amidation of cholesteryl acetate by PhI=NTs catalyzed by a Ru(II)-salen complex. We observed no such amine insertion products in the reactions of steroids **6** and **12** with PhI=NSes and of **6** with PhI=NTs.[21]

In conclusion, use of PhI=NSes has allowed the efficient copper-catalyzed, diastereoselective aziridination of 11-pregnene derivatives **6** and **12** and facile conversion of the product of the latter, via TASF-mediated removal of the *N*-Ses blocking group, to the *N*-methyl-11,12-aziridino-3α-hydroxy-5β-pregnan-20-one (**15**). The pharmacological activity of compound **15**, a conformationally constrained analogue of the endogenous neurosteroid pregnanolone (**1**) and a structural analogue of the synthetic general anesthetic minaxolone (**3**), will be reported elsewhere.

## 1. Experimental

### 1.1. General

Mps were taken on a Fisher–Johns apparatus and are uncorrected. IR spectra were recorded in KBr pellets on a Nicolet Magna IR 550 FT-IR spectrometer. $^{1}$H and $^{13}$C NMR spectra were measured on a Bruker AC-200 (200.13 and 50.32 MHz) or AM-500 (500.13 and 125.72 MHz) NMR spectrometer for samples in deuteriochloroform (using tetramethylsilane as internal standard). *J* values are given in Hertz. Electron impact (EI) mass spectra were measured in a GC–MS Shimadzu QP-5000 mass spectrometer at 70 eV by direct inlet. Chemical ionization (CI) mass spectra were measured on a Kratos MS80 spectrometer. High resolution mass spectra were obtained with a VG ZAB BEQQ (EI), a Kratos MS80 (CI) or a Finnegan Navigator Aqua Thermoquest (ESI) mass spectrometer. Single crystal X-ray measurements were performed on a Bruker SMART CCD diffractometer, with graphite monochromated Mo Kα radiation. The structure was solved by direct methods with SHELXS97[25] and refined by full matrix least squares in $F^2$ using SHELXL97.[26] Hydrogen atoms were idealized at their expected positions (C–H: 0.93 Å) and allowed to ride. Molecular plots were drawn with XP, in the SHELXLTL-PC package.[27] All solvents used were reagent grade. Solvents were evaporated at 45°C under reduced pressure. Flash chromatography was performed on silica gel Merck 9385 (40–63μ). Homogeneity of all compounds was confirmed by TLC. Ketone **10** was synthesized in 8% yield from deoxycholic acid.[23]




**10** **11** **12**

**Scheme 3.**

11-Pregnene-3,20-dione was purchased from Sigma. Elemental analyses were performed at the ICSN, CNRS, Gif-sur-Yvette, France or at the UMYMFOR, CONICET-FCEN, Buenos Aires, Argentina.

**1.1.1. *N*-[2-(Trimethylsilyl)ethanesulfonyl]-11α12α-aziridino-5β-*H*-pregnane-3,20-dione (7).** PhI=NSes (448 mg, 1.17 mmol)[20] was added portionwise over a period of 5 h under argon to a mixture of 4 Å molecular sieves (185 mg), copper (I) triflate (14 mg, 0.065 mmol) and 11-pregnene-3,20-dione (**6**, 200 mg, 0.65 mmol) in acetonitrile (1.6 ml). The green reaction mixture was stirred at room temperature for 24 h and then purified directly by flash chromatography (heptane/ethyl acetate 8:2), aziridine **7** was first eluted (166 mg, 53% yield, 66% yield based on unreacted **6**), followed by unreacted starting material **6** (44 mg, 22%). The aziridine was obtained as an amorphous solid, mp 55–60°C; $[\alpha]_D^{20}$=+102.3° (*c*=0.1, $CHCl_3$); IR (KBr) 2952, 2361, 2342, 1707, 1321, 1251, 1144 $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$) δ 3.070 (d, *J*=6.4 Hz, 1H, 12-H), 3.060 (m, 2H, $SO_2CH_2$), 2.870 (dd, *J*≈0.8, 7.0 Hz, 1H, 11-H), 2.712 (t, *J*=9.8 Hz, 1H, 17-H), 2.569 (t, *J*=13.4 Hz, 1H, 4α-H), 2.429 (dt, *J*=13.6, 5.0 Hz, 1H, 2α-H), 2.225 (s, 3H, 21-H), 1.106 (s, 3H, 19-H), 0.816 (s, 3H, 18-H), 0.045 (s, 9H, Si–$CH_3$); $^{13}C$ NMR (125 MHz, $CDCl_3$) δ 211.68 (C-3), 209.69 (C-20), 58.68 (C-17), 48.59 (C–$SO_2$), 47.89 (C-12), 46.93 (C-14), 43.28 (C-13), 42.97 (C-5), 42.45 (C-4), 42.23 (C-9), 39.38 (C-11), 36.78 (C-2), 36.48 (C-1), 35.37 (C-10), 32.75 (C-8), 30.99 (C-21), 27.14 (C-15), 24.79 (C-6), 22.80 (C-19), 22.69 (C-16), 22.53 (C-7), 14.39 (C-18), 9.29 (Si–$CH_2$), −1.90 (Si–$CH_3$); MS (CI) 494 ($[M+H]^+$, 70), 330 (100), 315 (80), 297 (5), 166 (52); HRMS (CI) calcd for $C_{26}H_{44}NO_4SSi$ (M+1), 494.2760. Found 494.2789.

**1.1.2. 11α,12α-Aziridino-5β-*H*-pregnane-3,20-dione (8).** A solution of TASF (206 mg, 0.75 mmol) and *N*-Ses-aziridine **7** (126 mg, 0.25 mmol) in dry DMF (6 ml) was stirred at 45°C for 45 min. The solvent was evaporated under vacuum and the crude product was purified by flash chromatography on silica gel (ethyl acetate/methanol 95:5) yielding the deprotected aziridine **8** (64 mg, 77% yield), mp 184°C; $[\alpha]_D^{20}$=+92.5° (*c*=0.4, $CHCl_3$); IR (KBr) 3436, 2925, 2874, 1703, 1446, 1356, 1261, 1096 $cm^{-1}$; $^1H$ NMR (200 MHz, $CDCl_3$) δ 2.88 (t, *J*=9.2 Hz, 1H, 17-H), 2.63 (dt, *J*=13.3, 1.8 Hz, 1H, 4α-H), 2.52 (dt, *J*=14.5, 5.8 Hz, 1H, 2α-H), 2.39 (d, *J*=6.3 Hz, 1H, 12-H), 2.18 (s, 3H, 20-H), 2.13 (broad d, *J*=6.0 Hz, 1H, 11-H), 1.09 (s, 3H, 19-H), 0.78 (s, 3H, 18-H); $^{13}C$ NMR (50 MHz, $CDCl_3$) δ 212.6 (C-3), 209.6 (C-20), 59.1 (C-17), 46.5 (C-12), 44.1 (C-13), 43.5 (C-14), 43.3 (C-5), 42.7 (C-4), 39.7 (C-9), 37.2 (C-1), 36.9 (C-2), 35.6 (C-10), 33.2 (C-11), 31.2 (C-8), 30.3 (C-21), 27.4 (C-15), 25.0 (C-6), 23.0 (C-19), 22.7 (C-16), 22.4 (C-7), 15.2 (C-18); ESIMS *m/z* 659 ($2M+H^+$, 25), 330 ($M+H^+$, 100), 281 (2); Anal. calcd for $C_{21}H_{31}O_2N{\cdot}1/2H_2O$, C, 74.52; H, 9.52; N, 4.13. Found C, 74.56; H, 9.40; N, 3.82.

**1.1.3. *N*-Methyl-11α,12α-aziridino-5β-*H*-pregnane-3,20-dione (9).** Methyl iodide (12 μl, 0.18 mmol) was added to a solution of **8** (15 mg, 0.046 mmol) and $K_2CO_3$ (13 mg) in acetonitrile/ethyl acetate 1:1 (1 ml) and the mixture was stirred at room temperature under nitrogen for 18 h. After evaporation of the solvent, the crude product was purified by preparative chromatography (silica gel, ethyl acetate/methanol 99:1) giving the *N*-methyl aziridine **9** (9.9 mg, 60% yield) as a white, crystalline solid, mp 130–133°C; $[\alpha]_D^{20}$=+87.3° (*c*=0.1, $CH_2Cl_2$); IR (KBr) 2933, 2871, 1706, 1451, 1096 $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$) δ 2.889 (t, *J*=9.3 Hz, 1H, 17-H), 2.631 (t, *J*=13.0 Hz, 1H, 4α-H), 2.503 (dt, *J*=14.3, 5.0 Hz, 1H, 2α-H), 2.409 (s, 3H, N–$CH_3$), 2.204 (s, 3H, 21-H), 1.649 (d, *J*=6.6 Hz, 1H, 12-H), 1.372 (broad d, *J*=6.8 Hz, 1H, 11-H), 1.083 (s, 3H, 19-H), 0.723 (s, 3H, 18-H); $^{13}C$ NMR (125 MHz, $CDCl_3$) δ 212.40 (C-3), 209.12 (C-20), 59.15 (C-17), 50.61 (C-12), 48.18 (C-14), 47.60 (N–$CH_3$), 44.03 (C-13), 43.33 (C-5), 43.01 (C-9), 42.63 (C-4), 40.75 (C-11), 36.92 (C-2), 36.84 (C-1), 35.33 (C-10), 32.87 (C-8), 31.31 (C-21), 27.30 (C-15), 24.98 (C-6), 22.87 (C-19), 22.71 (C-7), 22.25 (C-16), 15.06 (C-18); EIMS *m/z* 343 ($M^+$, 12), 328 (10), 300 (23), 286 (6), 162 (8), 108 (12), 55 (32), 43 (100); HRMS (ESI) calcd for $C_{22}H_{33}O_2N+H^+$: 344.2589. Found 344.2588.

### 1.2. Crystallographic data and data collection parameters for compound 9

Colorless prismatic crystals recrystallized from acetone: mp 130–133°C. $C_{22}H_{33}NO_2$, *M*=342.49, monoclinic, space group $P2_1$ (No. 4); cell constants *a*=8.580(1) Å, *b*=12.678(2) Å, *c*=9.255(1) Å; β=102.20(1)°; *V*=984.0(3) $Å^3$, $D_c(Z=2)$=1.156 g $cm^{-3}$; crystal dimensions 0.38×0.28×0.22 $mm^3$, reflections measured: 5913, reflections unique: 3842, reflections observed ($I>2\sigma(I)$): 1339; *R*=0.047 and $R_w^2$=0.082.

**1.2.1. 3α-Acetoxy-12α-tosyloxy-5β-*H*-pregnan-20-one (11).** Tosyl chloride (771 mg, 3.5 mmol) was added to a stirred solution of **10** (437 mg, 1.16 mmol) in dry pyridine (3.3 ml) at 60°C under nitrogen. After 6 days the reaction mixture was cooled to room temperature, acidified with 1N HCl (pH ~3), transferred to a separatory funnel and extracted with dichloromethane (4×30 ml). The organic extracts were combined, washed with 5% aqueous $NaHCO_3$ and water, dried with $Na_2SO_4$ and the solvent was evaporated. The crude product was purified by flash chromatography (hexane/ethyl acetate 8:2) to give tosylate **11** (550 mg, 90% yield) as a white, crystalline solid, mp 157–158°C (hexane/ethyl acetate); IR (KBr) 3404, 2938, 2870, 1732, 1703, 1362, 1244, 1177, 1028, 897, 557 $cm^{-1}$; $^1H$ NMR (200 MHz, $CDCl_3$) δ 7.80 (d, *J*=8.4 Hz, 2H, Ph–$H_o$), 7.31 (d, *J*=8.4 Hz, 2H, Ph–$H_p$), 5.00 (t, *J*=2.6 Hz, 1H, 12-H), 4.64 (m, 1H, 3-H), 2.85 (t, *J*=9.9 Hz, 1H, 17-H), 2.43 (s, 3H, $CH_3$–Ph), 2.06 (s, 3H, 21-H), 2.02 (s, 3H, $CH_3COO$), 0.85 (s, 3H, 19-H), 0.75 (s, 3H, 18-H); $^{13}C$ NMR (50 MHz, $CDCl_3$) δ 208.6 (C-20), 170.4 (COO), 144.4 (C-1′), 134.6 (C-4′), 129.7 (C-3′), 127.6 (C-2′), 84.2 (C-12), 73.9 (C-3), 54.8 (C-17), 47.9 (C-14), 46.2 (C-13), 41.6 (C-5), 35.1 (C-1), 35.0 (C-4), 34.6 (C-10), 34.0 (C-8), 33.8 (C-9), 32.1 (C-21), 30.3 (C-2), 26.7 (C-6), 26.3 (C-7), 25.9 (C-11), 25.6 (C-15), 23.4 (C-19), 22.8 (C-16), 21.4 ($CH_3COO$), 21.3 ($CH_3Ph$), 13.5 (C-18); EIMS *m/z* 530 ($M^+$, 1%), 375 (1), 358 (10), 298 (31), 283 (7), 255 (25), 91 (23), 43 (100). Anal. calcd for $C_{30}H_{42}O_6S$: C, 67, 89; H, 7, 98. Found C, 68.22; H, 7.81.

**1.2.2. 3α-Acetoxy-5β-*H*-11-pregnen-20-one (12).** A solution of **11** (490 mg, 0.92 mmol) in dry collidine (27 ml) was

refluxed under nitrogen for 6 h. The reaction mixture was cooled to room temperature, acidified with 1N HCl and extracted with dichloromethane (4×20 ml). The organic extracts were combined, washed with 5% aqueous $NaHCO_3$ and water and dried with $Na_2SO_4$. The residue obtained after evaporation of the solvent was purified by flash chromatography (hexane/ethyl acetate 9:1) to give pregnene **12** (280 mg, 85% yield), mp 123–125°C (hexane); IR (KBr) 3397, 2936, 2868, 1736, 1705, 1449, 1362, 1242, 1028 $cm^{-1}$; EIMS *m/z* 358 ($M^+$, 2%), 315 (4), 298 (32), 255 (65), 228 (16), 213 (19), 43 (100); $^1H$ NMR (200 MHz, $CDCl_3$) $\delta$ 6.12 (dd, $J$=10.2, 2.9 Hz, 1H, 11-H), 5.52 (d, $J$=10.0 Hz, 1H, 12-H), 4.73 (m, 1H, 3-H), 2.68 (t, $J$=8.4 Hz, 1H, 17-H), 2.17 (s, 3H, 21-H), 2.02 (s, 3H, $CH_3COO$), 0.89 (s, 3H, 19-H), 0.67 (s, 3H, 18-H); $^{13}C$ NMR (50 MHz, $CDCl_3$) $\delta$ 208.8 (C-20), 170.4 (COO), 135.9 (C-12), 126.2 (C-11), 73.9 (C-3), 59.7 (C-17), 53.6 (C-14), 45.9 (C-13), 43.1 (C-5), 40.7 (C-9), 34.9 (C-10), 34.7 (C-1), 34.3 (C-8), 32.7 (C-4), 31.2 (C-21), 27.7 (C-2), 26.4 (C-6), 25.2 (C-7), 23.5 (C-19), 23.0 (C-15), 23.9 (C-16), 21.2 ($CH_3COO$), 17.8 (C-18). Anal. calcd for $C_{23}H_{34}O_3$: C, 77.05; H, 9.56. Found C, 76.85; H, 9.60.

**1.2.3. 3α-Acetoxy-*N*-[2-(trimethylsilyl)ethanesulfonyl]-11α,12α-aziridino-5β-*H*-pregnan-20-one (13).** Following the above procedure, pregnene **12** (80 mg, 0.22 mmol), PhI=NSes (153 mg, 0.40 mmol), 4 Å molecular sieves(185 mg) and copper (I) triflate (5 mg, 0.022 mmol) in acetonitrile(0.55 ml) gave after cromatography (silica gel, hexane/ethyl acetate 8:2) unreacted olefin **3** (34 mg, 45%) and aziridine **13** (53 mg, 45% yield, 77% yield based on unreacted **12**) as an amorphous solid, mp 50–54°C; $[\alpha]_D^{20}$=+68.3° ($c$=0.2, $CH_2Cl_2$); IR (KBr) 2951, 2872, 1736, 1705, 1323, 1248, 1144, 841 $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$) $\delta$ 4.743 (m, 1H, 3-H), 3.081 (m, 2H, $SO_2CH_2$), 3.057 (d, $J$=7.1 Hz, 1H, 12-H), 2.820 (t, $J$=9.3 Hz, 1H, 17-H), 2.765 (dd, $J$=0.9, 7.1 Hz, 1H, 11-H), 2.266 (s, 3H, 21-H), 2.002 (s, 3H, $CH_3COO$), 1.168 (m, 2H, $SiCH_2$), 1.027 (s, 3H, 19-H), 0.782 (s, 3H, 18-H), 0.076 (s, 9H, Si–$CH_3$); $^{13}C$ NMR (125 MHz, $CDCl_3$) $\delta$ 209.23 (C-20), 170.42 (COO), 73.33 (C-3), 58.67 (C-17), 48.78 ($SO_2CH_2$), 47.27 (C-12), 46.57 (C-14), 43.30 (C-13), 41.36 (C-5), 41.23 (C-9), 40.85 (C-11), 35.11 (C-10), 34.82 (C-1), 33.04 (C-8), 32.63 (C-4), 31.31 (C-21), 27.48 (C-15), 27.03 (C-2), 25.19 (C-6), 23.44 (C-19), 22.58 (C-16), 22.39 (C-7), 21.26 ($CH_3COO$), 14.55 (C-18), 9.29 (Si–$CH_2$), −2.05 (Si–$CH_3$); EIMS *m/z* 522 ($M^+$−15, 1), 372 (M−Ses, 84), 312 (35), 73 (97), 43 (100); HRMS (ESI) calcd for $C_{28}H_{47}O_5NSSiNa$: 560.2841. Found 560.2845.

**1.2.4. 3α-Acetoxy-11α,12α-aziridino-5β-*H*-pregnan-20-one (14).** Following the above procedure, a solution of TASF (123 mg, 0.445 mmol) and Ses-aziridine **13** (48 mg, 0.089 mmol) in dry DMF (2.5 ml) gave after flash chromatography on silica gel (ethyl acetate/methanol 95:5) the deprotected aziridine **14** (23 mg, 70% yield), mp 110–115°C (d); $[\alpha]_D^{20}$=+94.0° ($c$=1, $CH_2Cl_2$); IR (KBr) 3306, 2934, 2872, 1736, 1701, 1449, 1362, 1244, 1028 $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$) $\delta$ 4.730 (m, 1H, 3-H), 2.877 (t, $J$=9.4 Hz, 1H, 17-H), 2.319 (d, $J$=6.2 Hz, 1H, 12-H), 2.180 (s, 3H, 21-H), 2.076 (broad d, $J$=6.3 Hz, 1H, 11-H), 2.015 (s, 3H, $CH_3COO$), 1.011 (s, 3H, 19-H), 0.757 (s, 3H, 18-H); $^{13}C$ NMR (125 MHz, $CDCl_3$) $\delta$ 209.71 (C-20), 170.76 (COO), 73.87 (C-3), 59.18 (C-17), 46.73 (C-12), 44.14 (C-13), 42.55 (C-14), 41.18 (C-5), 39.59 (C-9), 35.33 (C-10), 35.17 (C-1), 33.41 (C-11), 32.60 (C-4), 31.18 (C-8), 30.53 (C-21), 27.67 (C-2), 26.65 (C-15), 25.41 (C-6), 23.58 (C-19), 22.66 (C-16), 22.31 (C-7), 21.42 ($CH_3COO$), 15.27 (C-18); EIMS *m/z* 373 ($M^+$, 1), 358 (2), 330 (3), 314 (1), 148 (4), 69 (26), 43 (100); HRMS (ESI) calcd for $C_{23}H_{35}O_3N+H^+$: 374.2695. Found 374.2688.

**1.2.5. 3α-Hydroxy-*N*-methyl-11α,12α-aziridino-5β-*H*-pregnan-20-one (15).** Methyl iodide (14 μl, 0.21 mmol) was added to a solution of **14** (20 mg, 0.054 mmol) and $K_2CO_3$ (15 mg, 0.11 mmol) in acetonitrile (1.5 ml) and the mixture was stirred at room temperature under nitrogen for 6 h. After evaporation of the solvent the residue was dissolved in a solution of $K_2CO_3$ (60 mg) in methanol/water (9:1, 4 ml), and stirred for 1 h at room temperature. The reaction mixture was concentrated to 1/2 of its volume, diluted with water and extracted with dichloromethane (4×2 ml). The combined organic phases were dried over $Na_2SO_4$ and evaporated. The crude product was purified by preparative chromatography (silica gel, ethyl acetate/methanol 95:5) to give the *N*-methyl aziridine **15** (12 mg, 65% yield) as an amorphous solid, mp 70°C; $[\alpha]_D^{20}$=+87.3° ($c$=0.1, $CH_2Cl_2$); IR (KBr) 3387, 2928, 2860, 1703, 1449, 1358, 1081, 1038 $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$) $\delta$ 3.636 (m, 1H, 3-H), 2.892 (t, $J$=9.4 Hz, 1H, 17-H), 2.387 (s, 3H, N–$CH_3$), 2.192 (s, 3H, 21-H), 1.557 (d, $J$=6.6 Hz, 12-H), 1.302 (broad d, $J$=6.6 Hz, 11-H), 0.981 (s, 3H, 19-H), 0.680 (s, 3H, 18-H); $^{13}C$ NMR (125 MHz, $CDCl_3$) $\delta$ 209.36 (C-20), 71.48 (C-3), 59.19 (C-17), 50.49 (C-12), 48.44 (C-14), 47.52 (N–$CH_3$), 44.11 (C-13), 42.23 (C-5), 41.37 (C-9), 40.97 (C-11), 36.97 (C-4), 35.60 (C-1), 35.01 (C-10), 33.21 (C-8), 31.33 (C-21), 30.48 (C-2), 27.79 (C-6), 25.49 (C-15), 23.54 (C-19), 22.72 (C-7), 22.16 (C-16), 15.07 (C-18); EIMS *m/z* 345 ($M^+$, 12), 330 (17), 302 (31), 286 (5), 246 (12), 162 (10), 108 (25), 43 (100); HRMS (ESI) calcd for $C_{22}H_{35}O_2N+H^+$: 346.2746. Found 346.2745.

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