

## First Synthesis of a C-Homosteroid from Pregn-4-ene-3,11,20-trione

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(3 $\alpha$ ,5 $\alpha$ )-3-Hydroxy-C-homopregnane-11,20-dione (**3**) was prepared in eleven steps from the commercially available pregn-4-ene-3,11,20-trione (**4**) via the 11-oxo-13-formyl-12,13-secopregnane intermediate **11** (Scheme 2). Subjection of this secopregnane to an intramolecular aldol condensation afforded the  $\alpha,\beta$ -unsaturated key intermediate C-homopregn-12-en-11-one **12**.

**Introduction.** – Research over the past decade has shown that neurosteroids become an extensive and important class of biologically active compounds [1] no matter whether these are natural neurosteroids or their synthetic analogues (see **1** and **2** in the Fig.). They have been shown to possess hypnotic [2], anticonvulsant [3], anesthetic [4], or anxiolytic activities [5] *in vivo*. There is considerable current interest in the development of new analogues as pharmaceuticals having these activities.

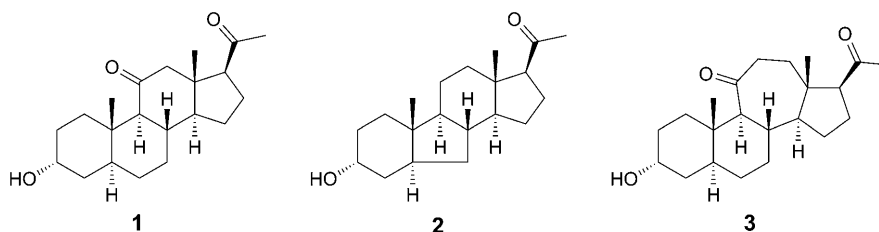


Figure. Known neurosteroid modulators **1** and **2** of GABA<sub>A</sub> receptors and the new potential modulator **3** prepared herein

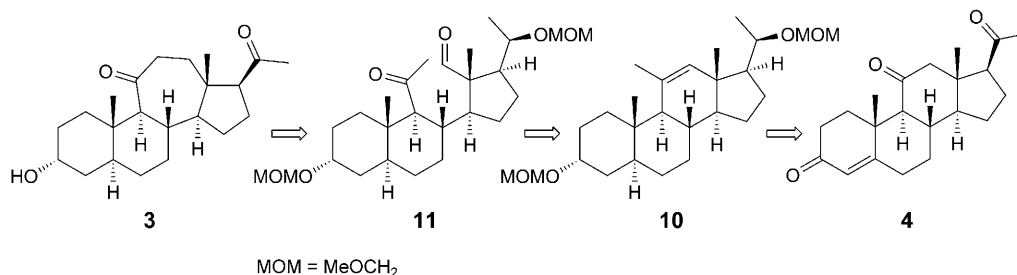
The structure–activity relationship (SAR) studies and pharmacological actions of neurosteroids are topics of widespread interest. Besides natural neurosteroids, many compounds were synthesized and evaluated such as 17 $\beta$ -CN [6][7], a series of benz[*e*]indene analogues [8][9], 6-thia-allopregnanolone [10], 6-oxa-allopregnanolone [11], 6-aza-allopregnanolone [12], 7-aza-allopregnanolone [13], 17a-aza-*D*-homosteroid analogues [14], 13,24-cyclo-18,21-dinorcholane analogues [15], O-bridged and 2,19-sulfamoyl analogs of allopregnanolone [16], as well as many modified steroids, including steroids substituted at the 3 $\beta$ ,5,6,7,10,11,17, or 21 position [17]. Recently, many studies showed that ring expansion or ring contraction of the steroid skeleton by a

ring elastic strength affects the chemical properties of the steroid and thus may play a critical role in changing biological activities, thus leading to new active pharmaceuticals. Kasal and co-workers [18] reported the partial synthesis of several *B*-nor analogues of allopregnanolone and pregnanolone, which have neuroactivity similar to that of allopregnanolone. *B*-Norallopregnanolone (= (3 $\alpha$ ,5 $\alpha$ )-3-hydroxy-7-norpregnan-20-one (**2**); *Fig.*) was found to be comparable to allopregnanolone when checked with labeled TBPS (*tert*-butyl [<sup>35</sup>S]bicyclophosphorothionate). Analogous results were obtained concerning their effect on neurons in culture: this time, (3 $\alpha$ ,5 $\alpha$ )-3-hydroxy-7-norpregnan-20-one (**2**), was found to stimulate [<sup>3</sup>H]flunitrazepam binding and GABA-induced <sup>36</sup>Cl<sup>−</sup> influx. These effects were inhibited by GABA<sub>A</sub> receptor antagonists.

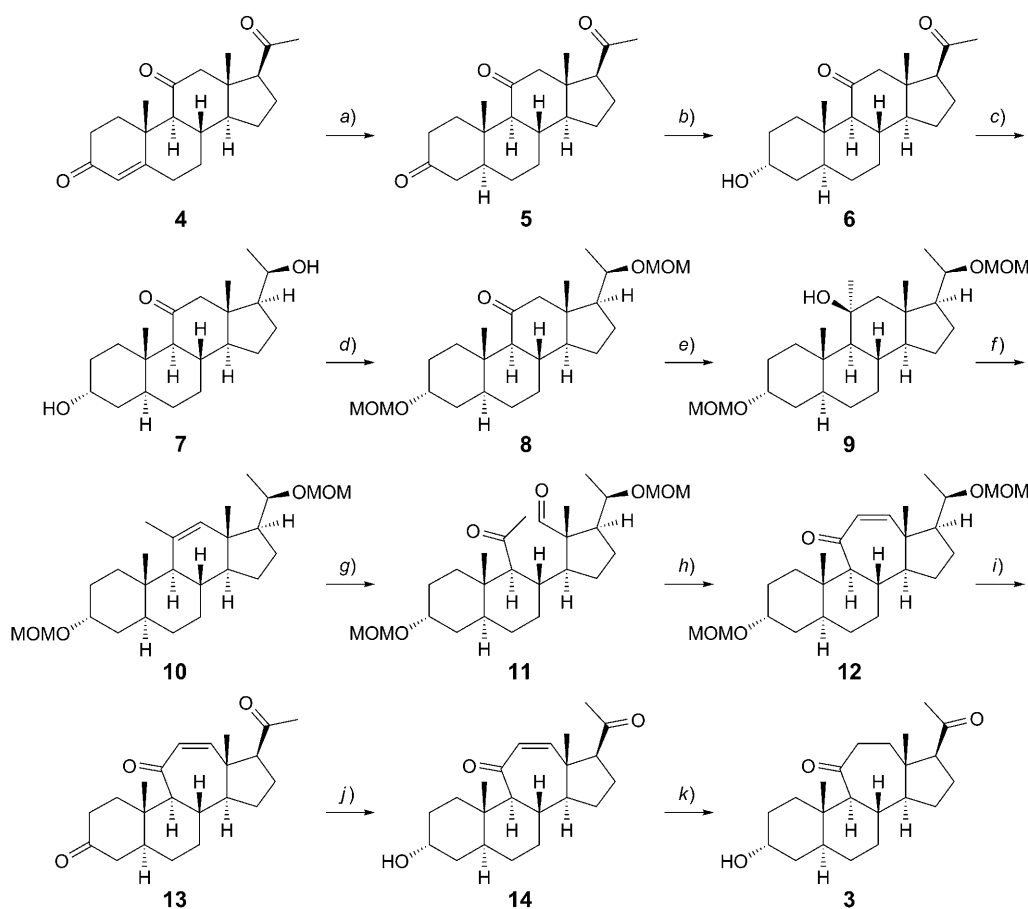
The actions of the (3 $\alpha$ ,5 $\alpha$ )-hydroxy-*C*-homopregnane-11,20-dione (**3**; *Fig.*) have not been described and, to the best of our knowledge, synthetic routes to **3** are not reported in the literature. To explore a new steroidal skeleton, we now report the synthesis of (3 $\alpha$ ,5 $\alpha$ )-3-hydroxy-*C*-homopregnane-11,20-dione as a new neurosteroid candidate, thus extending the range of potential neurosteroids with improved activity against GABA<sub>A</sub> receptors.

**Results and Discussion.** – The retrosynthetic analysis of the title compound utilizes keto aldehyde **11**, obtained from the ozonolysis of 11-methylpregn-11-ene **10** derived from the corresponding 11-methylpregnan-11-ol, as a precursor for the enone intermediate **12**. Ring closure *via* an aldol condensation gives the steroidal 12-en-11-one **12**, and Pd/C-catalyzed hydrogenation of the C=C bond yields the desired (3 $\alpha$ ,5 $\alpha$ )-3-hydroxy-*C*-homopregnane-11,20-dione (**3**; *Scheme 1*).

Scheme 1. Retrosynthetic Approach to (3 $\alpha$ ,5 $\alpha$ )-3-Hydroxy-*C*-homopregnane-11,20-dione (**3**)



Thus, the commercially available pregn-4-ene-3,11,20-trione (**4**) was converted into (5 $\alpha$ )-pregnane-3,11,20-trione (**5**) by a known methodology [19][20] (*Scheme 2*). Then, the 3-oxo group of **5** was selectively reduced with *K-Selectride* [21][17g] in dry THF at  $-78^{\circ}$  for 2 h to give the 3 $\alpha$ -hydroxy steroid **6** in 78% yield. The 20-oxo group of **6** was reduced with NaBH<sub>4</sub> in EtOH/H<sub>2</sub>O at room temperature within 5 min to give the 3 $\alpha$ ,20 $\beta$ -dihydroxy steroid **7** in 92% yield [22]. The OH groups at the 3,20-position of **7** were protected by the reaction with MeOCH<sub>2</sub>Cl and (i-Pr)<sub>2</sub>EtN in CH<sub>2</sub>Cl<sub>2</sub> to afford steroid **8** (93%) after 12 h at room temperature. Treatment of **8** with MeLi at room temperature overnight gave 11-hydroxy-11-methyl-substituted steroid **9** (86%). Subjection of **9** to standard *Chugaev* reaction conditions [23] with KH, CS<sub>2</sub>, and MeI in THF afforded 11-methylpregn-11-ene **10** in 63% yield. The structural assignment was

Scheme 2. Synthesis of (3 $\alpha$ ,5 $\alpha$ )-3-Hydroxy-C-homopregnane-11,20-dione (**3**) from Pregn-4-ene-3,11,20-trione (**4**) through a 12-Step Sequence

a) Liq. NH<sub>3</sub>/Li/THF, <sup>t</sup>BuOH, –78°, 2 h; 78%. b) *K-Selectride*, THF, –78°, 2 h; 78%. c) NaBH<sub>4</sub>, EtOH/H<sub>2</sub>O, r.t., 15 min; 92%. d) MeOCH<sub>2</sub>Cl, (i-Pr)<sub>2</sub>EtN, CH<sub>2</sub>Cl<sub>2</sub>, r.t., 12 h; 93%. e) 1.6M MeLi in Et<sub>2</sub>O, benzene/Et<sub>2</sub>O, N<sub>2</sub>, 12 h; 86%. f) KH, THF, reflux, 20 min, then CS<sub>2</sub>, MeI, r.t., 12 h; 63%. g) O<sub>3</sub>, AcOEt/MeOH, –78°, 1 h; 50%. h) 1M KOH in MeOH, THF, r.t., 24 h; 63%. i) 1. 3M HCl, THF, r.t., 12 h; 2. *Jones* reagent, acetone, r.t., 30 min; 92%. j) *K-Selectride*, THF, –78°, 2 h; 81%. k) H<sub>2</sub>, Pd/C, AcOEt, r.t., 4 h; 98%.

confirmed by NMR: among other signals, the <sup>1</sup>H-NMR spectrum shows an olefinic H-atom at  $\delta$ (H) 6.12 (s). Ozonolysis of the C(11)=C(12) bond gave keto aldehyde **11** (50%), which was cyclized to C-ring  $\alpha,\beta$ -unsaturated ketone **12** (63%) by treatment with KOH in EtOH at room temperature for 24 h. The 3,20-dihydroxy protecting groups of compound **12** were readily removed by using 3M HCl in THF at room temperature for 12 h to give, in quantitative yield, the corresponding 3,20-dihydroxy ketone. *Jones* oxidation [24] of the latter at room temperature in acetone yielded the

3,11,20-trione **13**. The 3-keto group of **13** was regio- and stereoselectively reduced with *K-Selectride* in THF at  $-78^{\circ}$  to afford the 3-hydroxy-12-ene-11,20-dione **14** in 81% yield. Finally, hydrogenation of the C=C bond of **14** in the presence of Pd/C in AcOEt gave compound **3** (98%) (*Scheme 2*).

In conclusion, the first synthesis of (3 $\alpha$ ,5 $\alpha$ )-3-hydroxy-*C*-homopregnane-11,20-dione was achieved *via* eleven steps from commercially available pregn-4-ene-3,11,20-trione, by using the *Chugaev* reaction of an 11-hydroxy-11-methyl-substituted steroid, ozonolysis of the formed C=C bond in ring *B*, and intramolecular aldol condensation as key steps. The biological activity of this *C*-homosteroid is currently investigated and will be reported in due course.

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### Experimental Part

*General.* Solvents were dried over standard drying agents and freshly distilled prior to use. The reagents were purchased from Aldrich and Acros and used without further purification unless otherwise stated. All moisture-sensitive reactions were carried out under N<sub>2</sub>. Column chromatography (CC): silica gel (SiO<sub>2</sub>; 60–120 mesh). M.p.: Yanaco melting-point apparatus; uncorrected. Optical rotations: Perkin-Elmer-343 polarimeter. IR Spectra: Nicolet-FT-IR-5DX spectrometer; KBr pellets;  $\tilde{\nu}$  in cm<sup>-1</sup>. <sup>1</sup>H- and <sup>13</sup>C-NMR Spectra: Bruker-ACF-300 spectrometer;  $\delta$  in ppm rel. to Me<sub>4</sub>Si as internal standard, *J* in Hz. Elemental analyses: Perkin-Elmer-240C instrument.

(3 $\alpha$ ,5 $\alpha$ ,20R)-3,20-Bis(methoxymethoxy)pregnan-11-one (**8**). To a mixture of compound **7** (1.67 g, 5.0 mmol), (i-Pr)<sub>2</sub>EtN (1.82 g, 14.0 mmol), and catalyst *N,N*-dimethylpyridin-4-amine (DMPA; 50 mg) in dry CH<sub>2</sub>Cl<sub>2</sub> (35 ml) was added MeOCH<sub>2</sub>Cl (1.12 g, 14.0 mmol) at r.t., and the resulting mixture was stirred for 30 min at r.t. until an orange color appeared. After dilution with CH<sub>2</sub>Cl<sub>2</sub> (20 ml), the mixture was washed with H<sub>2</sub>O and brine, dried (Na<sub>2</sub>SO<sub>4</sub>), and concentrated and the residue purified by CC (SiO<sub>2</sub>, AcOEt/hexanes 1:8): **8** (1.97 g, 93%). White solid. M.p. 68–70° (hexanes). IR: 2926, 1708, 1446, 1380, 1046, 915. <sup>1</sup>H-NMR (CDCl<sub>3</sub>): 4.71–4.68 (*m*, 4 H); 3.82 (*s*, 1 H); 3.55–3.53 (*m*, 1 H); 3.40 (*s*, 3 H); 3.36 (*s*, 3 H); 2.60 (*d*, *J* = 12.6, 1 H); 2.25–2.22 (*m*, 2 H); 1.12 (*d*, *J* = 6, 3 H); 1.02 (*s*, 3 H); 0.66 (*s*, 3 H). <sup>13</sup>C-NMR (CDCl<sub>3</sub>): 212.0; 95.3; 94.4; 75.8; 71.3; 64.1; 57.8; 56.2; 55.4; 55.3; 55.1; 46.4; 39.5; 36.8; 35.4; 33.2; 32.6; 31.4; 27.9; 25.9; 25.8; 23.6; 19.4; 13.1; 11.1. Anal. calc. for C<sub>25</sub>H<sub>42</sub>O<sub>5</sub> (422.60): C 71.05, H 10.02; found: C 71.00, H 10.16.

(3 $\alpha$ ,5 $\alpha$ ,11 $\beta$ ,20R)-3,20-Bis(methoxymethoxy)-11-methylpregnan-11-ol (**9**). To a soln. of **8** (1.27 g, 3.0 mmol) in dry benzene (20 ml) and dry Et<sub>2</sub>O (30 ml) was added (1.6M MeLi in Et<sub>2</sub>O (3 ml) at r.t., and the resultant mixture was stirred at r.t. for 12 h. Then the reaction was quenched by adding H<sub>2</sub>O (1 ml). The mixture was diluted with Et<sub>2</sub>O (30 ml), washed with H<sub>2</sub>O and brine, dried (Na<sub>2</sub>SO<sub>4</sub>), and concentrated, and the residue purified by CC (SiO<sub>2</sub>, AcOEt/hexanes 1:8): **9** (1.13 g, 86%). Oil.  $[\alpha]_D^{20} = +20.06$  (*c* = 0.5660, CHCl<sub>3</sub>). IR: 2926, 1622, 1452, 1440, 1371, 1097, 1045, 918. <sup>1</sup>H-NMR: 4.75–4.70 (*m*, 4 H); 3.80 (*s*, 1 H); 3.57–3.54 (*m*, 1 H); 3.42 (*s*, 3 H); 3.38 (*s*, 3 H); 1.43 (*s*, 3 H); 1.12 (*d*, *J* = 5.4, 3 H); 1.11 (*s*, 3 H); 0.89 (*s*, 3 H). <sup>13</sup>C-NMR: 95.6; 94.4; 76.0; 71.0; 61.3; 59.3; 57.8; 56.1; 56.0; 55.1; 41.5; 40.8; 39.4; 36.9; 36.8; 35.4; 33.8; 33.7; 33.0; 29.1; 26.5; 25.3; 25.0; 19.8; 14.3; 13.8. Anal. calc. for C<sub>26</sub>H<sub>46</sub>O<sub>5</sub> (438.64): C 71.19, H 10.57; found: C 71.22, H 10.76.

(3 $\alpha$ ,5 $\alpha$ ,20R)-3,20-Bis(methoxymethoxy)-11-methylpregn-11-ene (**10**). The suspension of **9** (1.10 g, 2.5 mmol) and KH (1.33 g, 10 mmol; 30% in mineral oil) in dry THF (35 ml) was refluxed for 1 h under N<sub>2</sub>. Then, the mixture was cooled to r.t., CS<sub>2</sub> (0.24 g, 3.13 mmol) was added, and the resulting mixture was stirred at r.t. for 1 h. Then, MeI (0.45 g, 3.13 mmol) was added, and the mixture stirred at r.t. overnight. The reaction was then quenched by adding MeOH. The mixture was extracted with AcOEt (2  $\times$  25 ml), the org. layer washed with H<sub>2</sub>O and brine, dried (Na<sub>2</sub>SO<sub>4</sub>), and concentrated, and the residue purified by CC (SiO<sub>2</sub>, AcOEt/hexanes 1:20): **10** (0.66 g, 63%). Oil.  $[\alpha]_D^{20} = +22.36$  (*c* = 0.5165, CHCl<sub>3</sub>). IR: 2926; 1622, 1452, 1440, 1371, 1097, 1045, 918. <sup>1</sup>H-NMR: 6.12 (*s*, 1 H); 4.68–4.65 (*m*, 4 H); 3.80 (*s*, 1 H); 3.61–

3.59 (*m*, 1 H); 3.42 (*s*, 3 H); 3.37 (*s*, 3 H); 1.97 (*d*, *J* = 10.8, 1 H); 1.78 (*s*, 3 H); 1.12 (*d*, *J* = 6, 3 H); 0.85 (*s*, 3 H); 0.75 (*s*, 3 H). <sup>13</sup>C-NMR: 138.9; 134.1; 95.3; 94.4; 76.7; 71.2; 59.9; 56.0; 55.0; 53.3; 52.3; 43.8; 40.2; 39.5; 35.1; 34.5 (2 C); 31.4; 30.4; 28.0; 26.8; 25.7; 23.6; 19.6; 16.2; 12.0. Anal. calc. for C<sub>26</sub>H<sub>44</sub>O<sub>4</sub> (420.63): C 74.24, H 10.54; found: C 74.22, H 10.78.

(1*S*,2*S*,5*S*)-2-[1*S*,2*S*,4*aS*,6*R*,8*aS*]-1-Acetyldecahydro-6-(methoxymethoxy)-8*a*-methylnaphthalen-2-yl]-5-[1*R*]-1-(methoxymethoxy)ethyl]-1-methylcyclopentanecarboxaldehyde (**11**). A soln. of **10** (210 mg, 0.50 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (35 ml) was cooled to –78°, and a slow stream of ozone was introduced into the soln. until it became blue. Excess ozone was removed by flushing the soln. with O<sub>2</sub>. Me<sub>2</sub>S (0.37 ml, 5 mmol) was then added, and the resulting mixture was stirred overnight from –78° to r.t. After evaporation, the residue was directly purified by CC (SiO<sub>2</sub>, AcOEt/hexanes 1:4): **11** (113.2 mg, 50%). Colorless oil.  $[\alpha]_D^{20}$  = +66.76 (*c* = 1.745, CHCl<sub>3</sub>). IR: 3429, 2928, 1724, 1704, 1449, 1372, 1146, 1097, 1040, 917. <sup>1</sup>H-NMR: 9.05 (*s*, 1 H); 4.65 (*s*, 2 H); 4.52–4.48 (*m*, 2 H); 3.82 (*s*, 1 H); 3.43–3.41 (*m*, 1 H); 3.37 (*s*, 3 H); 3.30 (*s*, 3 H); 2.37 (*d*, *J* = 11.7, 1 H); 2.13 (*s*, 3 H); 1.11 (*d*, *J* = 5.7, 3 H); 0.92 (*s*, 3 H); 0.84 (*s*, 3 H). <sup>13</sup>C-NMR: 212.9; 204.8; 114.8; 94.5; 81.9; 71.2; 57.8; 56.8; 55.1; 54.9; 52.8; 51.2; 48.8; 48.3; 41.0; 36.5; 33.6; 32.1; 30.8; 27.9; 26.3; 25.0; 23.6; 22.2; 13.8; 12.4. Anal. calc. for C<sub>26</sub>H<sub>44</sub>O<sub>6</sub> (452.62): C 68.99, H 9.80; found: C 68.82, H 9.78.

(3*a*,5*a*,20*R*)-3,20-Bis(methoxymethoxy)-C-homopregn-12-ene-11-one (= (3*aS*,4*S*,6*aS*,6*bS*,8*aS*,10*R*,12*aS*,12*bS*)-4,5,6,6*a*,6*b*,7,8,8*a*,9,10,11,12,12*a*,12*b*-Tetradecahydro-10-(methoxymethoxy)-4-[1*R*]-1-(methoxymethoxy)ethyl]-3*a*,12*a*-dimethylnaphth[2,1-*e*]azulen-1(3*aH*)-one; **12**). The mixture of **11** (45 mg, 0.1 mmol) and 1*M* KOH/MeOH (0.5 ml) in THF (10 ml) was stirred at r.t. for 24 h. After evaporation, the residue was diluted with H<sub>2</sub>O (1 ml) and extracted with AcOEt (2 × 15 ml), the org. layer washed with H<sub>2</sub>O and brine, and dried (Na<sub>2</sub>SO<sub>4</sub>), and evaporated, and the residue purified by CC (SiO<sub>2</sub>, AcOEt/hexanes 1:3): **12** (27.4 mg, 63%). Oil.  $[\alpha]_D^{20}$  = +26.33 (*c* = 0.5005, CHCl<sub>3</sub>). IR: 3390, 2928, 1693, 1444, 1376, 1097, 1043, 918. <sup>1</sup>H-NMR: 6.25 (*d*, *J* = 12.3, 1 H); 5.82 (*d*, *J* = 12.3, 1 H); 4.65–4.62 (*m*, 4 H); 3.82 (*s*, 1 H); 3.58–3.54 (*m*, 1 H); 3.43 (*s*, 3 H); 3.36 (*s*, 3 H); 2.29 (*d*, *J* = 10.5, 1 H); 1.18 (*d*, *J* = 5.7, 3 H); 0.95 (*s*, 3 H); 0.93 (*s*, 3 H). <sup>13</sup>C-NMR: 213.5; 100.0; 94.4; 79.1; 75.3; 71.1; 71.0; 57.7; 56.8; 55.2; 51.4; 51.2; 47.9; 39.6; 37.4; 33.2; 33.0; 31.1; 30.7; 29.2; 26.2; 25.7; 24.8; 18.8; 12.5; 7.47. Anal. calc. for C<sub>26</sub>H<sub>42</sub>O<sub>5</sub> (434.61): C 71.85, H 9.74; found: C 71.82, H 9.78.

(5*a*)-C-Homopregn-12-ene-3,11,20-trione (= (3*aS*,4*S*,6*aS*,6*bS*,8*aS*,12*aS*,12*bS*)-4-Acetyl-3*a*,4,5,6,6*a*,6*b*,7,8,8*a*,9,11,12,12*a*,12*b*-tetradecahydro-3*a*,12*a*-dimethylnaphth[2,1-*e*]azulene-1,10-dione; **13**). The mixture of **12** (44 mg, 0.10 mmol) and 3*M* HCl (0.5 ml) in THF (5 ml) was stirred at r.t. for 48 h. After evaporation, the residue was diluted with AcOEt (15 ml), the soln. washed with 10% aq. NaHCO<sub>3</sub> soln., H<sub>2</sub>O, and brine, dried (Na<sub>2</sub>SO<sub>4</sub>), and concentrated, and the residue dissolved in acetone (10 ml). To the soln. was added Jones reagent at r.t. until appearance of an orange color, and then the reaction was quenched by adding some *i*-PrOH. After evaporation, the residue was diluted with H<sub>2</sub>O (10 ml) and extracted with CH<sub>2</sub>Cl<sub>2</sub> (2 × 10 ml), the combined org. phase washed with H<sub>2</sub>O and brine, dried (Na<sub>2</sub>SO<sub>4</sub>), and evaporated, and the residue purified by CC (SiO<sub>2</sub>, AcOEt/hexanes 1:2): **13** (31.5 mg, 92%). White solid. M.p. 150–152° (AcOEt/hexanes).  $[\alpha]_D^{20}$  = +16.18 (*c* = 0.7602, CHCl<sub>3</sub>). IR: 3390, 2928, 1710, 1693, 1444, 1376, 1097, 1043, 918. <sup>1</sup>H-NMR: 6.34 (*d*, *J* = 12.3, 1 H); 5.84 (*d*, *J* = 12.3, 1 H); 2.63 (*t*, *J* = 6.3, 1 H); 2.40–2.20 (*m*, 5 H); 2.15 (*s*, 3 H); 1.09 (*s*, 3 H); 0.94 (*s*, 3 H). <sup>13</sup>C-NMR: 210.9; 208.6; 207.6; 144.8; 129.5; 69.9; 60.8; 52.3; 50.9; 46.1; 44.0; 37.9; 37.6 (2 C); 31.4; 31.3; 30.1; 29.3; 24.2; 22.7; 15.2; 12.6. Anal. calc. for C<sub>22</sub>H<sub>30</sub>O<sub>3</sub> (342.47): C 77.16, H 8.83; found: C 77.12, H 8.78.

(3*a*,5*a*)-3-Hydroxy-C-homopregn-12-ene-11,20-dione (= (3*aS*,4*S*,6*aS*,6*bS*,8*aS*,10*R*,12*aS*,12*bS*)-4-Acetyl-4,5,6,6*a*,6*b*,7,8,8*a*,9,10,11,12,12*a*,12*b*-tetradecahydro-10-hydroxy-3*a*,12*a*-dimethylnaphth[2,1-*e*]azulen-1(3*aH*)-one; **14**). To a soln. of compound **13** (34.2 mg, 0.10 mmol) in dry THF (10 ml) was added 1*M* *K*-Selectride in THF (0.20 ml) at –78°, and the mixture was stirred at –78° for 1 h. Then, the reaction was quenched by adding H<sub>2</sub>O (1 ml). The mixture was extracted with AcOEt (2 × 10 ml), the combined org. phase washed with H<sub>2</sub>O and brine, dried (Na<sub>2</sub>SO<sub>4</sub>), and concentrated and the residue purified by CC (SiO<sub>2</sub>, AcOEt/hexanes 1:1.5): **14** (28 mg, 81%). White solid. M.p. 162–164° (AcOEt/hexanes).  $[\alpha]_D^{20}$  = +12.42 (*c* = 0.4350, CHCl<sub>3</sub>). IR: 3435, 2927, 1704, 1651, 1444, 1358, 1017, 730. <sup>1</sup>H-NMR: 6.26 (*d*, *J* = 12.3, 1 H); 5.79 (*d*, *J* = 12.3, 1 H); 4.04 (*s*, 1 H); 2.70 (*t*, *J* = 9.9, 1 H); 2.46 (*d*, *J* = 12.6, 1 H); 2.14 (*s*, 3 H); 0.91 (*s*, 3 H); 0.87 (*s*, 3 H). <sup>13</sup>C-NMR: 208.9; 208.2; 144.3; 129.9; 71.0; 66.2; 61.0; 52.7; 51.1;

39.1; 38.6; 35.4; 32.1; 31.5; 31.2; 30.6; 29.2; 29.1; 24.2; 22.9; 15.4; 12.6. Anal. calc. for  $C_{22}H_{32}O_3$  (344.49): C 76.70, H 9.36; found: C 76.62, H 9.58.

(3*a*,5*a*)-3-Hydroxy-C-homopregnane-11,20-dione (= (3*a*S,4*S*,6*a*S,6*b*S,8*a*S,10*R*,12*a*S,12*b*S)-4-Acetyl-hexadecahydro-10-hydroxy-3*a*,12*a*-dimethylnaphth[2,1-*e*]azulen-1(2H)-one; **3**). Compound **14** (17.2 mg, 0.05 mmol) in EtOH (5 ml) was hydrogenated by  $H_2$  (60 psi) in the presence of 10% Pd/C (5 mg) at r.t. for 12 h. Then the black precipitate was filtrated, and most of the EtOH of the filtrate was evaporated. The residue was diluted with AcOEt (15 ml), the mixture washed with  $H_2O$  and brine, dried ( $Na_2SO_4$ ), and concentrated, and the crude product purified by CC ( $SiO_2$ , AcOEt/hexanes 1:1.5): **3** (17 mg, 98%). White solid. M.p. 146–148° (AcOEt/hexanes).  $[\alpha]_D^{20} = +86.52$  ( $c = 1.1023$ ,  $CHCl_3$ ). IR: 3411 (br.), 2926, 1701, 1692, 1445, 1357, 1017, 731.  $^1H$ -NMR: 4.04 (s, 1 H); 2.58 (t,  $J = 9.3$ , 1 H); 2.40 (d,  $J = 12.6$ , 1 H); 2.30–2.27 (m, 2 H); 2.11 (s, 3 H); 0.95 (s, 3 H); 0.86 (s, 3 H).  $^{13}C$ -NMR: 216.5; 209.7; 71.1; 66.1; 64.1; 54.7; 46.5; 40.4; 39.5; 39.0; 37.5; 35.0; 32.5; 31.8; 31.6; 31.0; 29.0; 28.9; 25.5; 22.9; 14.2; 12.5. Anal. calc. for  $C_{22}H_{34}O_3$  (346.50): C 76.26, H 9.89; found: C 76.22, H 9.80.

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