128. Steroids and Sexhormones

Part 265[1])

Limonin, Part VI[2]). Synthesis of a Model Compound Incorporating Rings D and E of 14,15-Deepoxylimonin[3])

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Dedicated to Professor *George H. Büchi* on the occasion of his 60th birthday

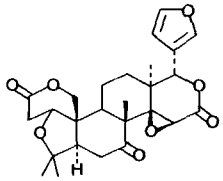
(11. V. 81)

Summary

Starting from the known formyl ketene thioacetal **6**, model compound **11** was synthesized. The key intermediates, the epimeric furylmethanols **7a** and **7b**, were converted into the same dithioortholactone **8b** *(Scheme 1)* and further elaborated into the model compound **11** *(Scheme 2)*, a versatile compound in the synthesis of limonin (**1**). The acid catalyzed conversion of the epimers **7a** and **7b** into **8b** may probably involve a hydride-transfer reaction with inversion of configuration at C(17) of alcohol **7a** *(Scheme 4*, row b).

1. Introduction. – In connection with our studies directed toward a partial synthesis of limonin (**1**) [2] we report in this paper a general method for the conversion of 17-keto steroids with 13α- and 13β-configuration into (3'-furyl)-substituted ring-D-δ-lactones, a structural moiety found in many naturally occurring compounds [3].

In the 13α series we chose the suitable A-ring-functionalized 17-keto steroid **2** as the starting material, from which the rings A and A' of limonin (**1**) can be built up by a previously developed method [4]. Our studies were also extended to the 13β series, with compound **18** (s. below) as a representative and easily accessible starting material.



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[1]) Part 264 : see [1a].
[2]) Limonin, Part V : see [1b].
[3]) Some exploratory experiments were performed by *W. Lottenbach* [1c].
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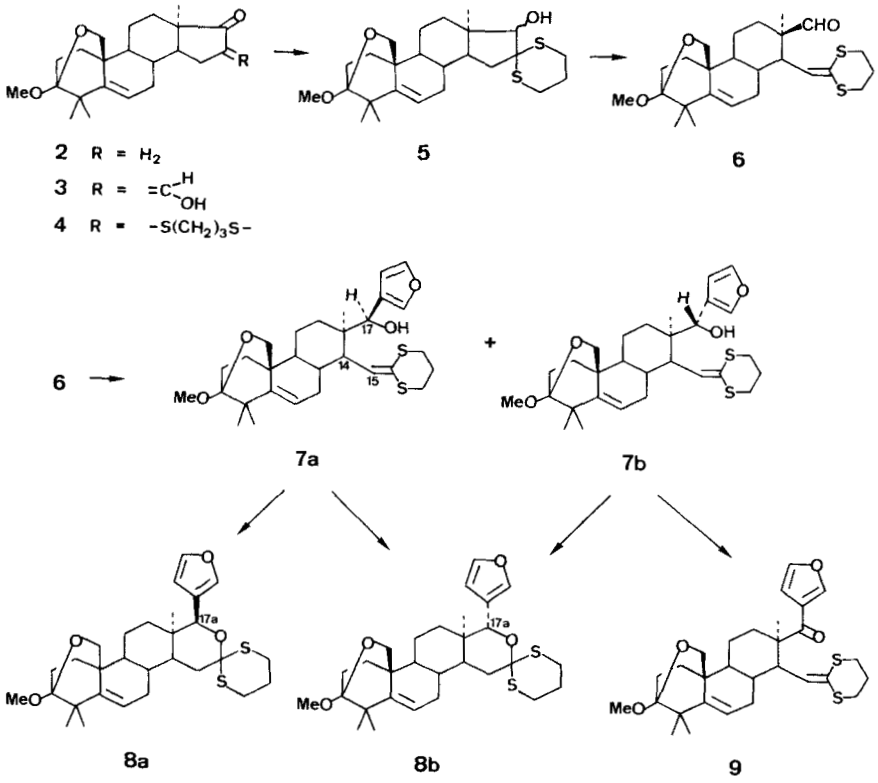
2. Results. – As indicated in *Scheme 1*, the hydroxy dithioacetal **5** was prepared from **2** (→ **3** → **4** → **5**), and cleaved with lead (IV) acetate to the ketene dithioacetal **6** as described before [5].

Scheme 1

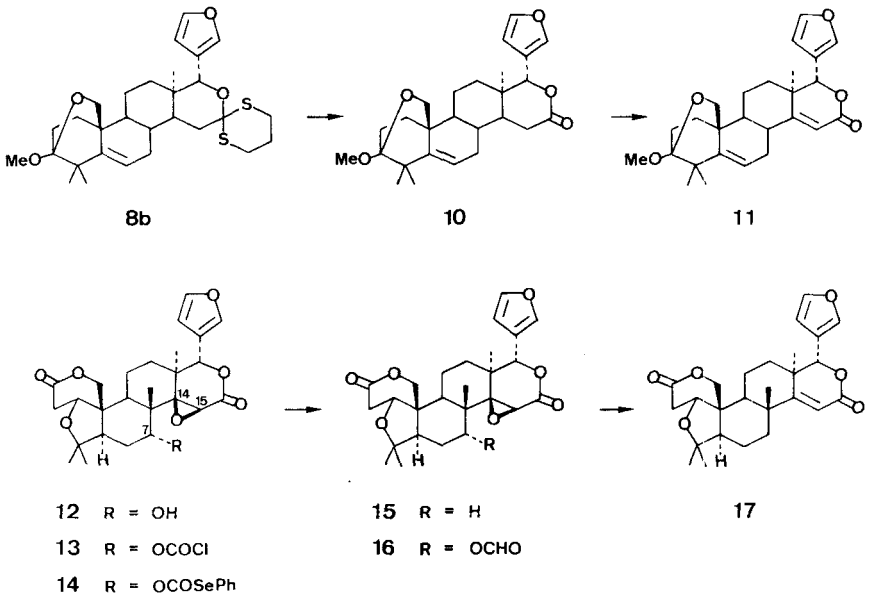


Reaction of **6** with 3-furyllithium [6] gave a mixture of the 17-epimeric alcohols **7a** and **7b** in a ratio of 3 : 7 separable by column chromatography. Alcohol **7b** could be converted into **7a** by oxidation with DMSO/trifluoroacetic anhydride [7] to ketone **9** followed by reduction with diisobutylaluminiumhydride; for the configurational assignment of the two epimers see discussion. Treatment of isomer **7b** with one equivalent of trifluoroacetic acid in anhydrous dichloromethane led to the dithioortholactone **8b**. Surprisingly, the epimer **7a**, on prolonged[5]) exposure to this acid under the same conditions, afforded the same dithioortholactone **8b**, with no detectable trace of the isomeric compound **8a**. Therefore, **8b** is the *thermodynamically* more stable epimer, with the furyl group in the energetically more favoured *quasi-equatorial* position (see discussion). On the other hand we succeeded to get the isomeric dithioortholactone **8a** from **7a** by reducing the amount of trifluoroacetic

[5]) The minimum reaction time to convert all starting material was 40 minutes at 0° instead of 10 minutes at the same temperature for the epimer **7b**.

acid to 0.25–0.35 mol-equiv. Compounds **8a** and **8b** can be distinguished clearly by their ^{1}H–NMR. spectra, **8a** shows for H–C(17a) a singulet at 4.62 ppm, and **8b** at 5.10 ppm.

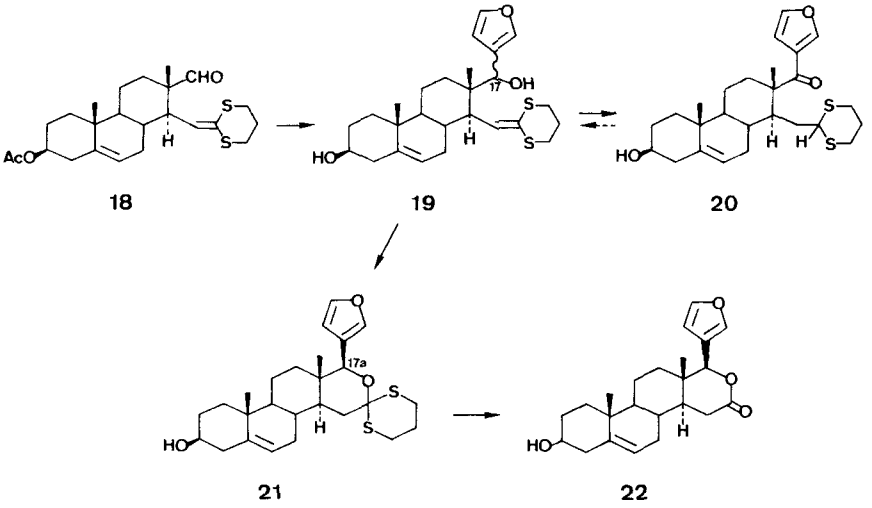
Scheme 2



As indicated in *Scheme 2*, the dithioacetal group of **8b** was removed by treatment with thallium(III) nitrate in wet methanol/tetrahydrofuran [8]. Overall yield for the transformation **7a** or **7b** → **8b** → **10** amount to 75–90%. The saturated lactone **10** was finally transformed into the α,β-unsaturated compound **11** by the standard selenylation selenoxide elimination method [9].

In order to determine the configuration at C(17a) of the model compounds **10** and **11** by spectroscopic correlation, we modified limonin (**1**) by removing the 7-oxo and the 14,15-epoxy functions to minimize steric and electronic interactions. Standard deoxygenation methods for removing oxo-functions failed. However, a method recently developed in our laboratory for the transformation of alcohols into hydrocarbons *via* the selenocarbonates [10] was successfully applied. Limonol (**12**) [11] was first treated with an excess of phosgene and triethylamine in boiling anhydrous tetrahydrofuran to generate the chloroformate **13**. This derivative was directly transformed to the selenocarbonate **14** by reacting with selenophenol, and **14** was finally heated under reflux with tributyltinhydride in mesitylene with a small amount of azo-bis(isobutyronitrile) (AIBN). The deoxo product **15**, obtained in 70% yield, was accompanied by some formate **16**, which could be converted *in situ* into alcohol **12** on prolonged heating and frequent addition of AIBN. Finally, the unsaturated lactone **17** was obtained by reducing the glycidolactone group with chromium(II) chloride in acetic acid [12].

Scheme 3



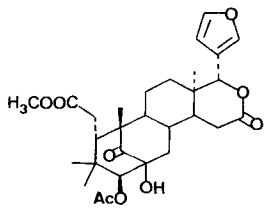
The reaction sequence with the model compound **18** [5] having β-configuration of CH_3(18) proceeded in a similar way (see *Scheme 3*), with the exception that the reaction of the formyl ketene thioacetal **18** with 3-furyllithium yielded only one alcohol **19** with unknown configuration at C(17). Acidic treatment of **19** gave the expected dithioortholactone **21**, and, as a by-product in about 5% yield, ketone **20**. Removal of the protecting dithioacetal group from **21** leading to the lactone **22** was performed with CH_3I in wet acetone [13].

3. Discussion. – As indicated in the *Table*, unsaturated lactone **11** shows characteristic signals for H–C(15) and H–C(17a), which are in good agreement with the corresponding signals of the limonin derivative **17**. This gives strong evidence for the *α-position* of the furyl substituent in **11**. A second proof for the configuration of this substituent at C(17a) can be drawn from the ^{13}C-NMR. spectra correlation of saturated model compound **10** and of methyl 3β-acetoxy-2-hydroxy-1-oxomeliacate (**23**) [14] [15] (see *Table*). These spectroscopic correlations are further supported by the mechanistic implications of the acid catalyzed isomerization **7a** → **8a** and **8b**.

Table. *Some ^{1}H-NMR. and ^{13}C-NMR. data of* **10**, **11**, **17**, *and* **23**[a])

^{1}H-NMR. data			H–C(15)	H–C(17a)
11			5.95	5.03
17			5.88	4.98
^{13}C-NMR. data	C(13)	C(14)	C(15)	C(17a)
10	35.2	46.0	34.8	76.5
23	35.2	45.4[b])	33.1[b])	76.7

[a]) Chemical shifts in ppm relative to tetramethylsilane (= 0 ppm) as internal standard.
[b]) Positions of these signals are strongly influenced by the nature of the acyloxy substituent in ring A.



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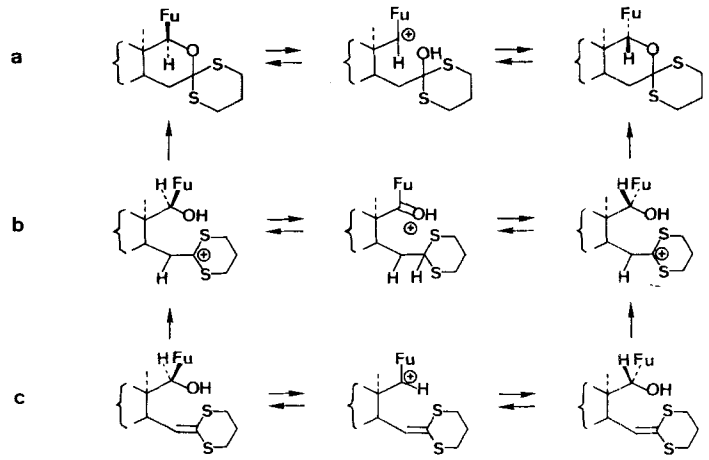
As has been shown, both furyl alcohols **7a** and **7b** surprisingly gave only one dithioortholactone **8b** on treatment with 1 mol-equiv. of trifluoroacetic acid in CH_2Cl_2. However, the C(17a) epimer **8a** was obtained by treating **7a** with only 0.25–0.35 mol-equiv. of acid (kinetic control of reaction). Furthermore, in the presence of 1 mol-equiv. of trifluoroacetic acid, **19** gave a small amount of ketone **20** in addition to the dithioortholactone **21**. Under forcing conditions **8b** was isolated as the thermodynamically most stable product, with the furyl substituent in a pseudo-equatorial α-position. This fact leads to the conclusion, that isomer **7b**, which affords dithioortholactone **8b** under kinetic and thermodynamic conditions, has the (17*R*)-configuration; therefore, **7a** has the (17*S*)-configuration. Similarly in the 13β series, compound **19** provided under thermodynamic control the dithioortholactone **21** with the furyl substituent at C(17a) in equatorial β-position. However, configuration at C(17) in alcohol **19** remaines undetermined. Appearance of ketone **20** *(vide supra)* points to an inversion mechanism at C(17) involving proton induced hydride shifts and sulfur stabilized cations [16] (*cf. Scheme 4*, row b). But inversion mechanisms involving cationic intermediates cannot be excluded at this moment (*cf. Scheme 4*, row a and c).

Scheme 4



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Experimental Part

General remarks. S. [4].

A. Partial Synthesis of Steroidal Compounds 11 and 22. – Grignard *reaction of* **6** *with 3-furyllithium.* A solution of 1 mmol of 3-furyllithium was prepared by mixing equivalent amounts of 3-bromofuran [17] and butyllithium at –78° in 5 ml of dry THF, followed by stirring for 30 min at –78°. A solution of 217 mg (0,48 mmol) crude aldehyde **6** (freshly prepared by fragmentation of 225 mg (0.5 mmol) **5** [5]) in 5 ml THF was added, and stirring was continued for 30 min at –78°. The mixture was then kept at 0° for 18 h. The resulting yellow solution was poured into ice cold 0. N HCl, the aqueous solution extracted with ethyl acetate, and the extracts washed with sat. $NaHCO_3$ – and sat. NaCl-solution, dried and evaporated. The resulting crude product (263 mg) was chromatographed on silica gel (250 g, ether/hexane 1 : 2) giving first 58 mg of **7a** and 11 mg of **7a/7b**, and then 136 mg of pure **7b**. Total yield: 205 mg (82%) **7a/7b** in a ratio of 3 : 7.

Data of (17S)-3β,19-epoxy-17-(3'-furyl)-3α-methoxy-,4,4-dimethyl-16,16-trimethylendithio-16,17-seco-13α-5,15-androstadien-17-ol (**7a**). M.p. 172–173°, $[\alpha]_D = -23°$ (c=3.14). – UV.: 212 (13500), 258 (10000). – IR.: 3600, 2870, 2830, 1725, 1585, 1500, 1460, 875. – ^{1}H-NMR.: 0.73 (*s*, 3 H–C(18)); 1.06–1.09 (2 *s*, 2 H_3C–C(4)); 1.80 (br. *s*, HO–C(17), exchangeable with D_2O); 0.6–2.5 (*m*, 15 H); 2.7–2.9 (*m*, 2 CH_2S); 3.26 (*s*, CH_3O); 3.74 (*d* × *d*, J=8, $J' \approx 2$) and 3.91 (*d*, J=8) (2 H–C(19)); 4.66 (*s*, H–C(17)); 5.54 (*d* × *d*, J=7, $J' \approx 2$ H–C(6)); 6.05 (*d*, J=11, H–C(15)); 6.35 (*m*, H–C(4')); 7.34 (*m*, H–C(2') and H–C(5')). – MS.: 516 (33, M^+), 313 (23), 287 (57), 185 (35), *145* (100), 119 (67).

Data of (17R)-3β,19-epoxy-17-(3'-furyl)-3α-methoxy-4,4-dimethyl-16,16-trimethylendithio-16,17-seco-13α-5,15-androstadien-17-ol (**7b**). M.p. 208–210°, $[\alpha]_D = -5°$ (c=3.69). – UV.: 212 (14000), 256 (8500). – IR. 3610, 2870, 2825, 1585, 1500, 875. – ^{1}H-NMR.: 0.95 (*s*, 3 H–C(18)); 1.06 and 1.09 (2 *s*, 2 H_3C–C(4)); 1.60 (br. *s*, HO–C(17), exchangeable with D_2O); 0.9–2.6 (*m*, 15 H); 2.7–2.95 (*m*, 2 CH_2S); 3.26 (*s*, CH_3O); 3.76 (*d* × *d*, J=8, $J' \approx 3$) and 3.94 (*d*, J=8) (2 H–C(19)); 5.04 (*m*, $w_{1/2} \approx 5$, H–C(17)); 5.54 (*d*, J=7, H–C(6)); 6.30 (*d*, J=11, H–C(15)); 6.34 (*m*, H–C(4')); 7.32 (*m*, H–C(2') and H–C(5')). – MS.: 516 (92, M^+), 287 (48), 185 (25), 145 (67), *106* (100).

$C_{29}H_{40}O_4S_2$ (516.77) Calc. C 67.42 H 7.80 S 12.41% Found C 67.42 H 7.93 S 12.49%

Synthesis of 3β,19-epoxy-17-(3'-furyl)-3α-methoxy-4,4-dimethyl-16,16-trimethylendithio-16,17-seco-13α-5,15-androstadien-17-one (**9**). To a solution of 75 µl (1 mmol) of DMSO in 1 ml of CH_2Cl_2 at –50° 21 µl (0.2 mmol) of trifluoroacetic anhydride were added. After stirring for 10 min at –50° 23 mg (0.045 mmol) of **7a/7b** in 1 ml of CH_2Cl_2 were added. After stirring for 30 min, 53 µl of triethylamine were added and the mixture was warmed to room temp., diluted with CH_2Cl_2, and washed twice with 10 ml of water. The crude product (26 mg), obtained by drying the organic phase with $MgSO_4 \cdot 2H_2O$ and evaporation of the solvent, was purified by chromatography (silica gel, hexane/ethyl acetate 2 : 1): 11 mg (48%) of **9**, m.p. 107–108°. – ^{1}H-NMR.: 1.04 and 1.06 (2 *s*, 2 H_3C–C(4)); 1.34 (*s*, 3 H–C(18)); 0.7–2.5 (*m*, 15 H); 2.65–2.9 (*m*, 2 CH_2S); 3.24 (*s*, CH_3O); 3.68 (*m*, 2 H–C(19)); 5.52 (*d* × *d*, J=7, $J' \approx 2$, H–C(6)); 6.40 (*d*, J=11, H–C(15)); 6.72 (*m*, H–C(4')); 7.36 (*m*, H–C(5')); 7.93 (*m*, H–C(2')). – MS.: *514* (100, M^+), 419 (6), 407 (13), 363 (8), 287 (12), 219 (15), 145 (69), 95 (60).

Synthesis of 17ξ-(3'-furyl)-16,16-trimethylendithio-16,17-seco-5,15-androstadiene-3β,17-diol (**19**). Aldehyde **18** (484 mg; 1,12 mmol) was treated as described for **6** with 4 mol-equiv. of 3-furyllithium. Chromatography of the crude product (622 mg) on silica gel (60 g, ether/cyclohexane 3 : 1) gave 333 mg (65%) of **19**, m.p. 223–225°, $[\alpha]_D \approx -1°$ (c =2.38). – UV.: 209 (14000), 259 (10000). – IR.: 3605, 2860, 2835, 1725, 1645, 1590, 1500, 910, 875. – ^{1}H-NMR.: 0.74 and 0.96 (2 *s*, 3 H–C(18) and 3H–C(19)); 1.54 (br. *s*, HO–C(3), exchangeable with D_2O); 0.8–3.0 (*m*, 17 H); 2.7–3.0 (*m*, 2 CH_2S); 3.17 (*d*, J=4, HO–C(17), exchangeable with D_2O); 3.25–3.7 (*m*, H–C(3)); 4.46 (*d*, J=4, on addition of $D_2O \rightarrow$ *s*, H–C(17)); 5.2–5.4 (*m*, H–C(6)); 5.82 (*d*, J=11, H–C(15)); 6.35 (*m*, H–C(4')); 7.32 (*m*, H–C(2') and H–C(5')). – MS.: 460 (12, M^+), 443 (4), 425 (1.5), *352* (100), 257 (14), 145 (31), 85 (1.5).

$C_{26}H_{36}O_3S_2$ (460.71) Calc. C 67.80 H 7.88 S 13.92% Found C 67.76 H 7.96 S 13.85%

General method for the acid catalyzed cyclization. (**7a** → **8b**, **7b** → **8b**, **19** → **21**). To a solution of 0,05–0.1 mmol of **7a**, **7b** or **19** in 5–10 ml of anh. dichloromethane cooled to 0°, a mol-equiv. of trifluoroacetic acid (dissolved in anh. dichloromethane to give a 10% solution) was added with stirring. After 10–20 min (40 min for **7b**), the reaction was quenched with sat. $NaHCO_3$-solution. The crude product obtained after normal work-up could be used without further purification. Analytical samples were obtained by chromatography on silica gel (**8b**: ether/hexane 1 : 2; **21** : cyclohexane/ethyl acetate 2 : 1).

Data of 3β,19-Epoxy-17aα-(3'-furyl)-3α-methoxy-4,4-dimethyl-16,16-trimethylendithio-17-oxa-13α-D-

homo-5-androstene (**8b**): amorphous solid, colorless. – IR.: 2970, 2920, 2860, 1500, 870. – ^{1}H-NMR.: 0.98 (*s*, 3 H–C(18)); 1.07 and 1.11 (2 *s*, 2 H_3C–C(4)); 0.8–3.8 (*m*, 21 H)); 3.28 (*s*, CH_3O); 3.78 (*d*× *d*, *J*=8 *J'*≈3) and 3.9 (*d*, *J*=8) (2 H–C(19)); 5.10 (*s*, H–C(17a)); 5.45–5.6 (*m*, H–C(6)); 6.38 (*m*, H–C(4')); 7.38 (*m*, H–C(2') and H–C(5')). – MS.: 516 (16, *M*$^+$), 410 (6), 367 (7), 287 (7), 277 (15), *106* (100).

Data of 17aβ-(3'-Furyl)-16,16-trimethylendithio-17-oxa-D-homo-5-androsten-3β-ol (**21**): slightly yellow amorphous solid. – IR.: 3600, 2960, 2850, 1500, 870. – ^{1}H-NMR.: 0.84 and 0.95 (2 *s*, 3 H–C(18) and 3 H–C(19)); 1.70 (br. *s*, HO–C(3), exchangeable with D_2O); 0.7–3.2 (*m*, 23 H); 3.3–3.7 (*m*, H–C(3)); 4.57 (*s*, H–C(17a)); 5.32 (*m*, H–C(6)); 6.36 (*m*, H–C(4')); 7.25–7.45 (*m*, H–C2') and H–C(5')).

Acid catalyzed cyclization with prevention of inversion at C(17) (**7a**→**8a**). A solution of 36 mg (0.07 mmol) of **7a** in 1 ml of anh. dichloromethane was cooled to 0° and treated for 1 h with 10 µl (0.2 mol-equiv.) of 10% trifluoroacetic acid. After quenching with aq. sat. $NaHCO_3$-solution and usual work-up, the crude product (30 mg) was chromatographed on silica gel (cyclohexane/ethylacetate 9 : 1) to give 11 mg of pure and 9 mg of less pure **8a** (*ca.* 50% yield). *3β,19-Epoxy-17aβ-(3'-furyl)-3α-methoxy-4,4-dimethyl-16,16-trimethylendithio-17-oxa-13α-D-homo-5-androstene* (**8a**): colorless amorphous solid. – IR.: 2970. 2920, 2860, 1500, 870. – ^{1}H-NMR.: 1.00 (*s*, 3 H–C(18)); 1.04 and 1.06 (2 *s*, 2 H_3C–C(4)); 0.7–4.0 (*m*, 21 H); 3.27 (*s*, CH_3O); 3.74 (br. *s*, $w_{½}$≈5, 2 H–C(19)); 4.62 (*s*, H–C(17a)); 5.53 (*d*× *d*, *J*=6, *J'*≈2, H–C(6)); 6.38 (*m*, H–C(4')); 7,34 (*m*, H–C(2') and H–C(5')).

Synthesis of 3β,19-epoxy-17aα-(3'-furyl)-3α-methoxy-4,4-dimethyl-17-oxa-13α-D-homo-5-androsten-16-one (**10**). A solution of 51 mg of $Tl(NO_3)_3$ in 1 ml of methanol was added dropwise with stirring to a solution of crude **8b**, obtained by cyclization of 31 mg (0.06 mmol) of **7b**, in 4 ml of wet methanol/THF 2 : 1 at 0°. A crystalline precipitate of $TlNO_3$ was immediately observed. After 30 min at 0° the precipitate was filtered off, and the solution concentrated *in vacuo*. Water and dichloromethane were added, and the organic layer was washed 3 times with water and dried. Evaporation *in vacuo* gave a crystalline product (31 mg), which was purified by column chromatography (silica gel, cyclohexane/ethyl acetate 2 : 1) 23 mg (90%) of **10**, m.p. 284–285°, $[\alpha]_D$ = –48° (*c*=1.37). – UV.: 207 (10000). – I ℞.: 2970, 2930, 2875, 2835, 1725, 1500, 905, 872. – ^{1}H-NMR.: 0.94 (*s*, 3 H–C(18)); 1.06 and 1.09 (2 *s*, 2 H_3C–C(4)); 0.8–2.6 (*m*, 13 H); 2.6–2.8 (*m*, 2 H–C(15)); 3.28 (*s*, CH_3O)); 3.74 (*d*× *d*, *J*=8 *J'*≈3) and 3.94 (*d*, *J*=8) (2 H–C(19)); 5.54 (*s*, H–C(17a)); 5.56 (*d*, *J*≈7, H–C(6)); 6.33 (*m*, H–C(4')); 7.38 (*m*, H–C(2') and H–C(5')). – ^{13}C-NMR.: 19.9 (C(11)); 22.3 *(qa);* 23.9 *(qa* and *t);* 25.9 *(qa);* 29.2 *(t);* 30.8 (2 *t*); 34.0 (C(8)); 34.8 (C(15)); 35.2 (C(13)); 36.3 *(s);* 43.7 *(s);* 44.6 and 46.0 (C(9) and C(14)); 49.4 (CH_3O); 70.7 (C(19)); *76.5* (C(17a)); 101.3 (C(3)); 109.7 (C(4')); 116.7 (C(6)); 121.1 (C(3')); 140.5 (C(5')); 143.0 (C(2')); 149.6 (C(5)); 170.7 (C(16)). – MS.: *426* (100, *M*$^+$), 383 (34), 365 (22), 288 (34), 245 (17), 105 (34), 95 (34).

$C_{26}H_{34}O_5$ (426.56) Calc. C 73.21 H 8.04% Found C 73.13 H 8.00%

Synthesis of 17aβ-(3'-furyl)-3β-hydroxy-17-oxa-D-homo-5-androsten-16-one (**22**). Crude **21**, obtained by cyclization of 68 mg (0.15 mmol) of **19**, was dissolved in 17 ml of CH_3I/acetone/water 1 : 15 : 1 and heated under reflux for 17 h. After evaporation of the solvent, water and dichloromethane were added, the organic layer was dried and the solvent evaporated *in vacuo*. Chromatography on silica gel (cyclohexane/ethyl acetate 1 : 1) gave 28 mg (51%) of **22**, m.p. 208–209°, $[\alpha]_D$ = –104° (*c*=1.31). – UV.: 208 (10000). – IR.: 3605, 2855, 2835, 1725, 1500, 870. – ^{1}H-NMR.: 0.84 and 0.96 (2 *s*, 3 H–C(18) and 3 H–C(19)); 1.74 (br.*s*, HO–C(3), exchangeable with D_2O); 0.8–2.5 (*m*, 16 H); 2.80 (*d*× *d*, *J*=18, *J'*≈5, H–C(15)); 3.3–3.8 (*m*, H–C(3)); 4,93 (*s*, H–C(17a)); 5.32 (*m*, H–C(6)); 6.35 (*m*, H–C(4')); 7.38 (*m*, H–C(2') and H–C(5')). – ^{13}C-NMR.: 11.2 *(qa);* 19.3 *(t* and *qa);* 30.6 *(t);* 31.3 *(t);* 31.9 *(t);* 32.6 (C(8)); 34.4 *(s);* 35.7 *(t);* 36.5 *(t);* 36.8 *(s);* 41.9 *(t);* 46.4 and 48.8 (C(9) and C(14)); 71.4 (C(3)); *85.5* (C(17a)); 109.8 (C(4')); 120.4 (C(6)); 120.9 (C(3')); 140.6 (C(5')); 140.7 (C(5)); 142.8 (C(2')); 170.8 (C(16)). – MS.: 370 (35, *M*$^+$), 352 (6), 337 (4), *232* (100), 214 (70), 138 (1).

$C_{23}H_{30}O_4$ (370.49) Calc. 74.56 H 8.16% Found C 74.46 H 8.25%

Synthesis of 3β,19-epoxy-17aα-(3'-furyl)-3α-methoxy-4,4-dimethyl-17-oxa-13α-D-homo-5,14-androstadien-16-one (**11**). A solution of 70 mg (0.16 mmol) of **10** in 1 ml of anh. THF containing 54 µl of dry hexamethylphosphoric triamide (HMPA) was slowly added within 10 min to 91 mg of lithium diisopropylamide in 0.5 ml of dry THF at –78°. After 10 min a solution of 163 mg of phenyselenyl chloride in 1 ml of dry THF was added. After complete addition the mixture was warmed to –20° and kept at –20° for 1 h. After the usual work-up, the crude mixture (120 mg) was chromatographed on silica gel (ether/hexane 1 : 1) yielding 70 mg (52%) of a 3 : 1[6]) mixture of both isomeric phenylselenylated lactones and 24 mg (34%) of **10**.

[6]) Ratio determined by NMR. spectroscopy.

Oxidation of this mixture was carried out by stirring a solution of 15 mg (0.03 mmol) in 0.2 ml of THF containing 6.6 µl of 30% H_2O_2-solution for 1 h at 20°. Usual work-up and chromatography on silica gel (hexane/ether 1 : 2) gave 5 mg (46%) of pure **11**, m.p. 228–229°. – UV.: 213 (14000). – IR.: 2980, 2935, 2875, 1712, 1620, 1500, 908, 875. – ^{1}H-NMR.: 1.07 (*s*, 3 H-C(18)); 1.10 (*s*, 2 H_3C–C(4)); 0.8–2.7 (*m*, 12 H); 3.28 (*s*, CH_3O); 3,74 (*d*× *d*, *J*=8, *J'* ≈ 3) and 3.90 (*d*, *J*=8) (2 H-C(19)); 5.03 (*s*, H-C(17a)); 5.80 (*d*× *d*, *J*=8, *J'* ≈ 2, H-C(6)); 5.95 (*m*, H-C(15)); 6.42 (*m*, H-C(4')); 7.40 *(m)* and 7.46 *(m)* (H-C(2') and H-C(5')). – MS.: 424 (81, *M*+), *381* (100), 328 (63), 300 (38), 285 (33), 258 (35), 199 (35), 95 (35), 91 (40).

B. Transformations of Limonin (1). – *Preparation of selenocarbonate* **14**. To a solution of 604 mg (1.28 mmol) of limonol (**12**) in the minimum amount of dry THF (about 60 ml), 10 ml of a 20% solution of phosgene in toluene and 0.2 ml of triethylamine were added, and the solution was heated under reflux for 24 h under N_2 at atmospheric pressure. After cooling to room temp., the excess of $COCl_2$ was removed by concentrating the solution to half of its volume *in vacuo*. Then 0.25 ml of pyridine and 5 ml of a 0.23**M** solution of selenophenol in benzene were added, and the mixture was stirred for 1 h. Usual work-up and chromatography on silica gel (chloroform/acetone 4 : 1) gave 408 mg (61%) of **14** and 224 mg (37%) of **12**. *Limonol phenyl selenocarbonate* (**14**), m.p. 261–262°, $[\alpha]_D$ = +24° (*c*=1.35). – UV.: 214 (17500). – IR.: 3020, 2970, 2880, 1755, 1600, 1500, 1440, 1110, 1020, 878. – ^{1}H-NMR.: 0.87 (*s*, 3 H), 1.10 (*s*, 3 H) and 1.23 (*s*, 6 H) (2 H_3 C–C(4), H_3 C–C(8) and 3 H–C(18)); 0.8–2.5 (*m*, 8 H); 2.53 (*d*× *d*, *J*=16, *J'* ≈ 2) and 2.89 (*d*× *d*, *J*=16, *J'*=4) (2 H–C(2)); 3.80 (*s*, H–C(15)); 3.94 (*m*, H–C(1)); 4.34 (*d*, *J*=13) and 4.50 (*d*, *J*=13) (2 H–C(19)); 5.07 (*d*× *d*, *J*=9, *J'*=5, H–C(7)); 5.51 (*s*, H–C(17a)); 6.30 (*m*, H–C(4')); 7.25–7.5 (*m*, H–C(2'), H–C(5'), H–C(3''), H–C(4'') and H–C(5'')); 7.5–7.8 (*m*, H–C(2'') and H–C(6'')). – MS.: 656 (0.2, *M*+), 641 (0.6), 612 (0.6), 591 (0.2), 579 (0.2), 455 (76), *383* (100), 95 (62).

$C_{33}H_{36}O_9Se$ (655.61) Calc. C 60.46 H 5.54% Found C 60.40 H 5.61%

Reduction of selenocarbonate **14**. A solution of 563 mg of **14** in 40 ml of mesitylene was heated to the boiling point; 0.5 ml of Bu_3SnH and a small amount of AIBN were added and the solution was heated under reflux for 30 min. Evaporation of the solvent and chromatography on silica gel (chloroform/acetone 4 : 1) gave 270 mg (68%) of **15**, 59 mg (14%) of **16** and 8 mg (2%) of **12**.

Data of 7-Deoxolimonin (**15**): m.p. 273–276°. – UV.: 206 (7000). – IR.: 3000, 2960, 2940, 2880, 1760, 1745, 1500, 878. – ^{1}H-NMR.: 0.95 *(s)*, 1.13 *(s)*, 1.23 *(s)* and 1.28 *(s)* (2 H_3C–C(4), H_3 C–C(8), and 3 H–C(18)); 0.8–2.6 (*m*, 10 H); 2.54 (*d*× *d*, *J*=16, J' ≈ 2) and 2.92 (*d*× *d*, *J*=16, *J'*=4) (2 H–C(2)); 3.83 (*s*, H–C(15)); 3.98 (*m*, H–C(1)); 4.47 (*m*, *w*½ ≈ 4, 2 H–C(19)); 5.60 (*s*, H–C(17a)); 6.32 (*m*, H–C(4')); 7.40 (*m*, H–C(2') and H–C(5')). – MS.: 456 (0.25, *M*+), 441 (2.5), 333 (14), *269* (100), 213 (25), 177 (20), 155 (17), 129 (14).

$C_{26}H_{32}O_7$ (456.54) Calc. C 68.40 H 7.07% Found. C 67.92 H 7.56%

Data of Limonol formate (**16**): ^{1}H-NMR.: 1.06 *(s)*, 1.10 *(s)*, 1.24 *(s)* and 1.26 *(s)* (2 H_3 C–C(4), H_3 C–C(8) and 3 H–C(18)); 0.8–2.5 (*m*, 8 H); 2.55 (*d*× *d*, *J*=16, *J'* ≈ 2) and 2.90 (*d*× *d*, *J*=16, *J'* ≈ 4) (2 H–C(2)); 3.72 (*s*, H–C(15)); 3.97 (*m*, H–C(1)); 4.35–4.6 (*m*, 2 H–C(19)); 5.08 (*d*× *d*, *J*=10, *J'*=5, H–C(7)); 5.44 (*s*, H–C(17a)); 6.30 (*m*, H–C(4')); 7.40 (*m*, H–C(2') and H–C(5')); 8.05 (*m*, HCOO–C(7)).

Synthesis of 14,15-deepoxy-7-deoxolimonin (**17**). Under exclusion of air 255 mg (0.56 mmol) of **15** were suspended in 20 ml of acetic acid. Then 3 ml of a filtered solution of Cr(II)Cl_2 (prepared from 6 g of amalgamated Zn powder and 3 g of Cr(III)$Cl_3 \cdot 6\ H_2O$ in 12 ml of water and 1.2 ml of conc. HCl-solution) were added and the mixture was heated under reflux for 4 h under N_2. Most of the acetic acid was evaporated *in vacuo* and the residue poured into hot water. Extraction with dichloromethane, washing the organic layer with $NaHCO_3$- and sat. NaCl-solution, followed by drying and evaporation of the solvent gave 233 mg (95%) of crude **17** (white solid), which could be purified by recrystallization (ether/methanol) or chromatography (chloroform/acetone 9 : 1), m.p. 360–363°. – UV.: 218 (13000). – IR.: 2980, 2940, 2880, 1745, 1720, 1500, 878. – ^{1}H-NMR.: 1.14 (*s*, 6 H), 1.19 (*s*, 3 H) and 1.26 (*s*, 3 H) (2 H_3C–C(4), H_3 C–C(8) and 3 H–C(18)); 1.0–2.5 (*m*, 10 H); 2.54 (*d*× *d*, *J*=16, *J'* ≈ 2) and 2.92 (*d*× *d*, *J*=16, *J'*=4) (2 H–C(2)); 3.98 (*m*, H–C(1)); 4.48 (*m*, *w*½ ≈ 4, 2 H–C(19)); 4.98 (*s*, H–C(17a)); 5.88 (*s*, H–C(15)); 6.38 (*m*, H–C(4')); 7.40 *(m)* and 7.46 *(m)* (H–C(2') and H–C(5')). – MS.: 368 (20), *344* (100), 262 (23), 188 (87).

$C_{26}H_{32}O_6$ (440.54) Calc. C 70.89 H 7.32% Found C 70.77 H 7.37%

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