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# Enantioselective Total Synthesis of the Oral Contraceptive Desogestrel by a Double Heck Reaction

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*Dedicated to Professor Miguel Yus on the occasion of his 60th birthday*

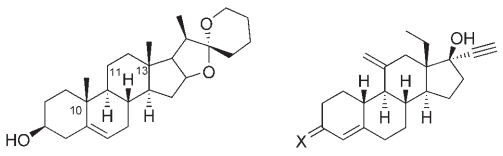
**Abstract:** A novel enantioselective total synthesis of the oral contraceptive desogestrel (**2**) is described, in which the tetracyclic steroid core is formed by a sequence of two consecutive Heck reactions. Conversion of the known enantiopure diketone **7** led to the chiral bicycle **6** which was used for a diastereoselective intermolecular Heck reaction with vinyliodide **5** to give **15**. In the following intramolecular Heck reaction, the tetracyclic ring system was formed to give **4**, from which the synthesis of desogestrel (**2**) was furnished.

**Keywords:** Birch reduction · contraceptives · Heck reaction · palladium · steroids

## Introduction

Progestagen desogestrel (13β-ethyl-11-methylene-18,19-dinor-17α-pregn-4-en-20-yn-17-ol) (**2**) is a highly potent third generation oral contraceptive. Moreover, its active metabolite, 3-ketodesogestrel (**3**), has been established as another progestagen of increasing importance in the last years.[1,2]

The industrial synthesis of desogestrel (**2**) consists of 24 steps using the natural occurring diosgenin (**1**) as starting material (Figure 1).[3] The procedure has several critical steps including the elongation of the angular methyl group at C-13 to an ethyl group and the removal of the methyl group at C-10 as well as the introduction of the methylene group at C-11. In addition, the availability of diosgenin (**1**) is not always guaranteed. Therefore a more efficient total synthesis of desogestrel (**2**) starting from simple substrates is highly wanted.




diosgenin (**1**)

X = H, H: desogestrel (**2**)
X = O: 3-ketodesogestrel (**3**)

Figure 1. Natural occurring diosgenin (**1**) and the synthetic oral contraceptive desogestrel (**2**) with its main metabolite 3-ketodesogestrel (**3**).

Here, we report a new efficient enantioselective total synthesis of desogestrel (**2**) using two consecutive Heck reactions[4,5] as key steps. This strategy which has been developed by us within the total synthesis of estradiol[6] and homosteroids[7,8] as well as of spinosyn[9] and cephalostatine analogues[10] has now proved to be successful also in the construction of steroid-cores with an angular ethyl group at C-13. Furthermore, also 3-ketodesogestrel (**3**) can be synthesized employing this approach. It should be noted that a few other approaches for the synthesis of desogestrel (**2**) have already been published.[11,12]

## Results and Discussion

Our retrosynthetic analysis of **2** leads to the B/C *cis*-fused compound **4** which can be further disassembled to the aromatic AB building block **5** and the chiral CD building block **6** (Scheme 1). For the formation of **4** from **5** and **6** a twofold Heck reaction was envisaged, whereas the *trans*-annulated hydrindene **6** could be obtained from the known ketone **7**, which in turn can be prepared in enantiopure form by the L-proline-catalyzed Hajos–Parrisch–Eder–Sauer–Wiechert procedure.[13,14]

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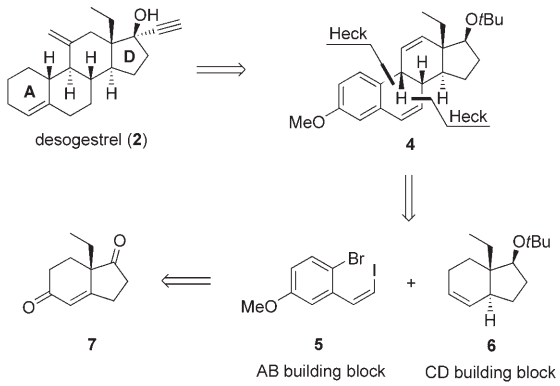
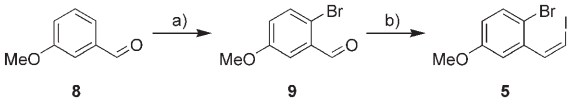



Scheme 1. Retrosynthetic analysis of desogestrel (**2**).

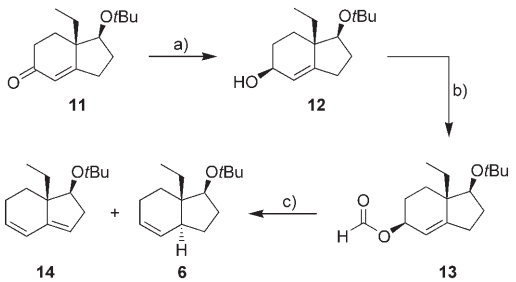
The synthesis of the aromatic compound **5** containing the required functionalities for the two Heck reactions was accomplished in two steps starting from the commercially available 3-methoxybenzaldehyde (**8**) (Scheme 2).




Scheme 2. Synthesis of the AB building block **5**. a) 1.14 equiv bromine, acetic acid, RT, 48 h, 80%; b) 1.25 equiv $[Ph_3PCH_2I]^+I^-$ (**10**), 1.25 equiv KHMDS in toluene, THF, RT, 10 min, addition of **9** at −78°C, 30 min.

Bromination of **8** with equimolar amounts of bromine in acetic acid at room temperature gave aldehyde **9** regioselectively. Wittig transformation with triphenylphosphonium salt **10** yielded **5** with the *Z* configuration of the iodo vinyl side chain in 79% with high stereoselectivity. The minor *E* isomer was removed by column chromatography.

Starting from compound **11**, a literature known derivative of **7**,[13] the novel CD building block **6** was available in three high yielding steps (Scheme 3). Reduction of the carbonyl group in **11** was carried out with DIBAL-H in dichloromethane at −78°C with attack of the hydride ion taking place

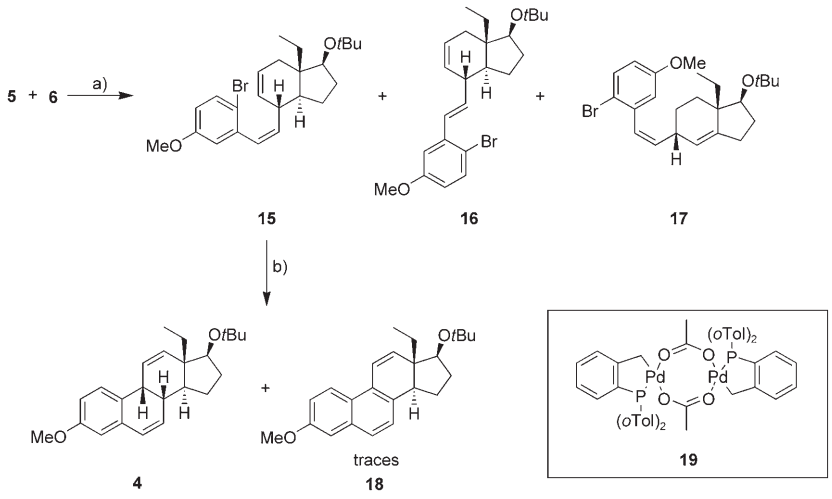



Scheme 3. Synthesis of the CD building block **6**. a) 1.20 equiv DIBALH in *n*-hexane, $CH_2Cl_2$, −78°C, 1 h, 95%; b) 2.06 equiv *N*-formylimidazole, THF, RT, 2 h, 97%; c) 1.27 mol% $Pd(OAc)_2$, 5.00 mol% P*n*$Bu_3$, dioxane, 90°C, 35 min, 97%, **6**/**14** 94:6.

from the less hindered α-face to give the alcohol **12** selectively. Treatment of **12** with *N*-formylimidazole afforded allyl formate **13** in excellent yield, which was further transformed into the desired **6** by an enantioselective Pd-catalyzed rearrangement. This type of reaction, first described by Tsuji et al.,[15] represents a convenient method to achieve the desired *trans*-annulation of the CD building block **6**. In this procedure the conjugated 3,5-diene **14** is formed in small amounts as byproduct. Separation of **6** and **14** by column chromatography was not possible, however, hydrindene **6**, containing up to 6% of **14**, could be used without any problems for the subsequent intermolecular Heck reaction.

For the first Heck reaction, coupling **5** and **6**, the use of $Pd(OAc)_2$ in the presence of $PPh_3$ and $Ag_2CO_3$ in DMF[16] was most appropriate (Scheme 4). Under these conditions the oxidative addition of the palladium catalyst took place exclusively at the more reactive vinyl iodide moiety in **5**. Moreover, the insertion into the double bond of **6** took place exclusively from the α-face *anti* to the angular ethyl group establishing the stereochemistry as needed for the synthesis of **2**. On the other hand, the regioselectivity is less pronounced leading to a 7:1-mixture of **15** and **17**. In addition, the *E* isomer **16** was obtained in a small amount probably by readdition of the Pd-H species onto **15** and β-hydride elimination of the formed Pd species. Due to similar polarities of compounds **15**, **16** and **17** separation of these isomers turned out to be difficult on simple silica gel and although compounds **16** and **17** can not react in an intramolecular Heck reaction pure **15** should be used for the next transformation. Fortunately, the purification could be achieved by column chromatography using silica gel loaded with 10% of $AgNO_3$ to give **15** in 56% yield. Construction of the tetracyclic steroid core from **15** was then successfully performed using the palladacene **19**[17] at 135°C to afford **4** in 94% yield. The reaction is highly diastereoselective leading only to the unnatural *cis* junction of the rings B and C. Compound **4** proved to be sensitive to oxygen which led to the formation of the aromatic product **18** being obtained, however, only in very small amounts if the reaction is performed under an inert atmosphere. Due to the sensitivity of **4** the crude material was used for the following transformation without purification; only the catalyst was removed by quick filtration through silica gel. The less sterically hindered benzylic $\Delta^{6,7}$-double bond in **4** was selectively hydrogenated in the presence of $PtO_2 \cdot H_2O$ to afford **20** (Scheme 5). Although **20** was more stable than the precursor **4** it was still found to be quite sensitive to air. This is presumably a consequence of the unnatural and therefore less stable *cis* fusion of the rings B and C. However, the $\Delta^{10,11}$-double bond in **20** was isomerized in the next step under basic conditions with KO*t*Bu in DMSO to obtain the enantiopure literature known compound **21** in 69% yield.[18] Cleavage of the *tert*-butyl group with $BF_3 \cdot Et_2O$ at RT afforded alcohol **22** in excellent yield. This compound has already been used as an intermediate in a synthesis of desogestrel (**2**);[11c] thus, synthesis of **22** can also be regarded as formal synthesis of **2**. How-

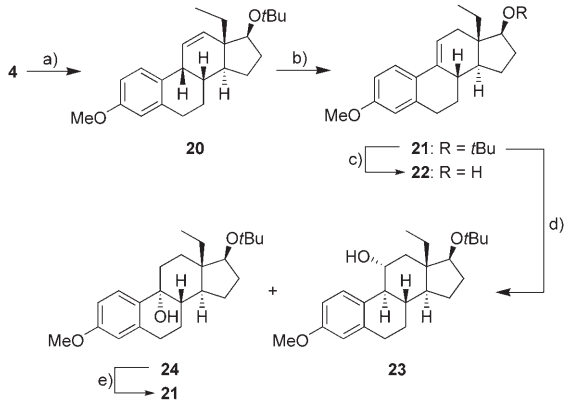
  



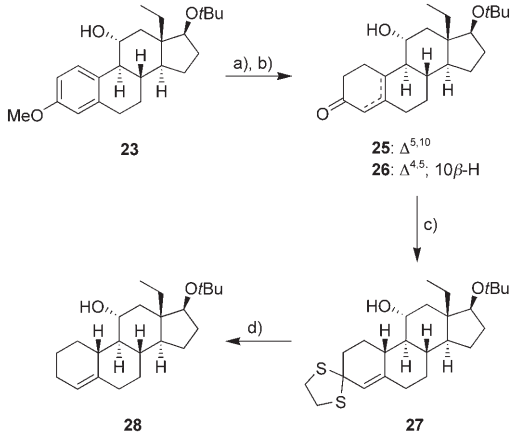

Scheme 4. Inter- and intramolecular Heck reaction of the AB building block **5** and the CD building block **6**. a) 1.81 mol% $Pd(OAc)_2$, 5.32 mol% $PPh_3$, 1.77 equiv $Ag_2CO_3$, DMF, 95°C, 4.5 h, 77%, **15**/**16**/**17** 7:1.7:1 (56% pure **15**); b) 2.03 mol% **19**, 2.57 equiv $nBu_4NOAc$, $CH_3CN$/DMF/$H_2O$ 5:5:1, 135°C, 5 h, 94%.

in liquid ammonia to afford **28** in 55% yield over four steps. Noteworthy, in this four-step sequence the compounds **26** and **27** were used as crude material since purification by column chromatography resulted in a dramatic loss of material.

The following oxidation of the 11-hydroxy group proceeded smoothly using Dess–Martin periodinane to obtain **29** in excellent yield and the formation of the required 11-*exo*-methylene group was then accomplished by a two step sequence (Scheme 7). Addition of $LiCH_2TMS$ in THF at −78°C afforded at first the tertiary al-




Scheme 5. Synthesis of **23**. a) 1.85 mol% $PtO_2 \cdot H_2O$, $H_2$, ethyl acetate, 39 h, RT, 91%; b) 2.61 equiv KO*t*Bu, DMSO, RT, 2.5 h, 89% (69% after recrystallization); c) 39.1 equiv $BF_3 \cdot Et_2O$, $CH_2Cl_2$, RT, 15 min, 96%; d) 4.88 equiv $BH_3$·THF, THF, RT, 3.5 h, then 30% aqueous $H_2O_2$, 30% aqueous NaOH, RT, 70 min and reflux, 2 h, 90% **23** and 7% **24**; e) conc. $H_2SO_4$, $CH_2Cl_2$, RT, 30 min, 50%.




Scheme 6. Synthesis of **28**. a) 9.33 equiv Li, $NH_3$, *i*PrOH, THF, −40°C, 1.5 h; b) 1 N HCl, acetone, MeOH, $H_2O$, RT, 19 h; c) 1.48 equiv 1,2-ethanedithiol, 0.594 equiv $BF_3 \cdot Et_2O$, RT, 3 h, d) 3.73 equiv Li, $NH_3$, THF, −40°C, 30 min, 55% over 4 steps.

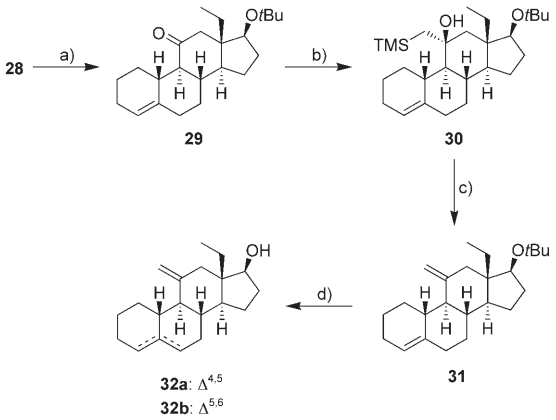
ever, we developed a new pathway for the formation of **2** from **21**, which is more efficient.

By hydroboration, **21** was converted into the alcohol **23** in 90% yield with the 11-hydroxy group being the basis for the construction of the 11-*exo*-methylene group. As byproduct, the regioisomer **24** was formed in 7% yield. Treatment of **24** with concentrated sulfuric acid in dichloromethane allowed a transformation back to the starting material **21**.

Birch reduction of **23** provided the corresponding 1,4-dihydro derivative which was subsequently treated with aqueous hydrochloric acid to give the unconjugated ketone **25** at first but with prolongation of the reaction time the thermodynamically more stable ketone **26** is formed (Scheme 6). Without purification **26** was converted into the dithioacetal **27** using 1,2-ethanedithiol in the presence of $BF_3 \cdot Et_2O$, which was followed by a reductive replacement with lithium cohol **31** which was converted by an acid-catalyzed Peterson olefination to give **32**. Both reactions proceeded in high yields and could also be performed as an one-pot reaction. Unfortunately, direct olefination methods of the ketone according to the Lombardo or Wittig procedure were not successful and led to a decomposition or no conversion of the starting material.

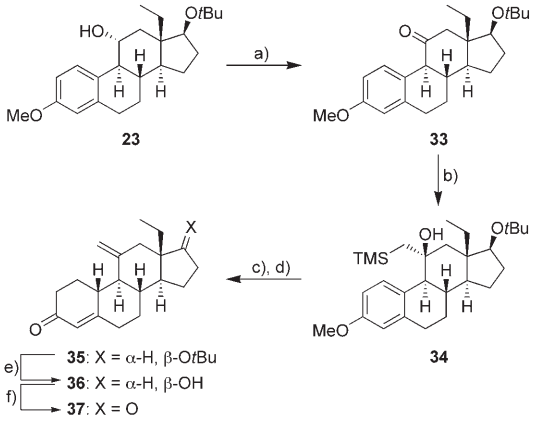
For the cleavage of the *tert*-butyl group in **31** we used as a standard procedure the treatment with $BF_3 \cdot Et_2O$ in dichloromethane for 10 min at 25°C. However, under these conditions a migration of the $\Delta^{4,5}$ double bond to the $\Delta^{5,6}$ position took place to give the desired **32a** and the undesired **32b** in a ratio of 1:2.5. Since the deprotection is much faster than the double bond isomerization, the problem could be solved by reducing the reaction time to only 15 s to afford the desired alcohol **32a** almost pure in a ratio of **32a**/**32b**




Scheme 7. Construction of the 11-*exo*-methylene group. a) 1.57 equiv Dess–Martin periodinane, $CH_2Cl_2$, RT, 1 h, 94%; b) 2.98 equiv $LiCH_2TMS$ in *n*-pentane, THF, −78°C, 20 min then RT, 30 min, 94%; c) conc. HCl, acetone, RT, 1 h, 95%; d) 27.3 equiv $BF_3{\cdot}Et_2O$, $CH_2Cl_2$, RT, 15 s, quant., **32a**/**32b** 96:4.

96:4, but it was not possible to separate the double bond isomers at this stage by chromatography or recrystallization. Employment of other reagents for the removal of the *tert*-butyl group like TMSI or $CF_3COOH$ effected only decomposition of the starting material. Therefore an alternative route starting from alcohol **23** was investigated to avoid a double bond migration in the deprotection step. For this purpose we oxidized **23** with the Dess–Martin periodinane to give ketone **33** which proved to be only moderately stable and was therefore used directly for the introduction of the 11-*exo*-methylene group (Scheme 8). The method of choice was once more the Peterson olefination as the Wittig and Lombardo olefination were not successful. Reaction of **33** with $LiCH_2TMS$ afforded **34** in good yield which was then subjected to a Birch reduction with lithium in liquid ammonia. The crude 1,4-dihydro derivative was subsequently treated with conc. HCl in acetone to cleave the enol ether

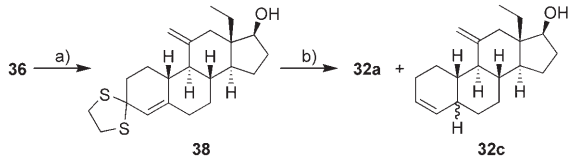



Scheme 8. Synthesis of **36** and **37**. a) 1.52 equiv Dess–Martin periodinane, $CH_2Cl_2$, RT, 1 h, 97%; b) 2.51 equiv $LiCH_2TMS$ in *n*-pentane, THF, −78°C, 30 min then RT, 10 min, 79%; c) 10.0 equiv Li, $NH_3$, *i*PrOH, THF, −40°C, 1.5 h; d) conc. HCl, acetone, RT, 15 h, 74% over two steps; e) 43.9 equiv $BF_3{\cdot}Et_2O$, $CH_2Cl_2$, RT, 10 min, quant.; f) 1.55 equiv Dess–Martin periodinane, $CH_2Cl_2$, RT, 80 min, 94%.

and achieve a double bond migration from the $\Delta^{5,10}$ to the thermodynamically more stable $\Delta^{4,5}$ position. Simultaneously, the 11-*exo*-methylene group was also formed by acid catalyzed elimination.

The following deprotection of the *tert*-butyl group with $BF_3{\cdot}Et_2O$ proceeded quantitatively and due to the 3-keto group no double bond isomerisation was observed. Oxidation of alcohol **36** with Dess–Martin periodinane afforded **37**, a compound that has been successfully converted to 3-ketodesogestrel (**3**) by Gao et al.[19] Besides, alcohol **36** is an intermediate in the enantioselective total synthesis of desogestrel (**2**) described by Corey et al.[11e]

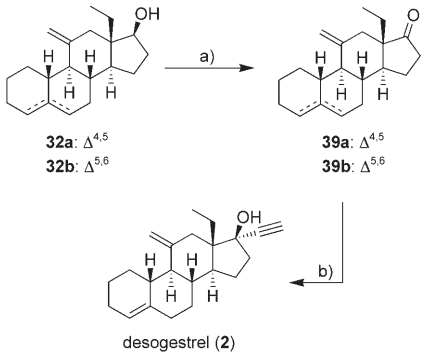
For the transformation of **36** into **2**, **36** was converted into the dithioacetal **38** employing 1,2-ethanedithiol in the presence of $BF_3{\cdot}Et_2O$ (Scheme 9). Subsequent reductive removal




Scheme 9. Synthesis of **32a** by reductive removal of the dithioacetal. a) 1.49 equiv 1,2-ethanedithiol, 0.567 equiv $BF_3{\cdot}Et_2O$, MeOH, RT, 2.5 h, 84%; b) 12.7 equiv Li, $NH_3$, THF, −40°C, 30 min, 96%, ratio **32a**/**32c** 92:8.

of the dithioacetal moiety with lithium in liquid ammonia at −40°C afforded the desired alcohol **32a**, but again a double bond isomer **32c** was formed as byproduct. In contrast to the synthesis of **32a** by Lewis-acid catalyzed deprotection of the *tert*-butyl group, the migration of the double bond took place from the $\Delta^{4,5}$ to the $\Delta^{3,4}$ position and also in this case separation by chromatography or recrystallization was not successful.

Thus, the synthesis had to be continued with a mixture of isomers and due to the better ratio the mixture of **32a** and **32b** from the first approach was chosen for the further transformation. Oxidation of the 17-hydroxy group with Dess–Martin periodinane afforded the isomers **39a** and **39b** in a ratio of 96:4 (Scheme 10). Attempts to purify **39a** by re-




Scheme 10. Synthesis of desogestrel (**2**). a) 1.50 equiv Dess–Martin periodinane, $CH_2Cl_2$, RT, 30 min, 96%, **39a**/**39b** 96:4; b) 42.0 equiv lithium, acetylene, ethylenediamine, RT, 2 h, then **39a**/**39b** 96:4, RT, 2 h, recrystallization afforded pure **2** in 83% yield.

crystallization were not successful and thus the mixture of **39a** and **39b** was used for the final step. The introduction of the 17β-acetylene group was carried out with lithium and acetylene in ethylendiamine according to a method described by Schwarz et al.[11c] The product obtained was purified by column chromatography and then subjected to recrystallization to afford pure desogestrel (**2**) in 83% yield.

## Conclusion

In conclusion, a new efficient enantioselective total synthesis of the oral contraceptive desogestrel (**2**) has been developed. Starting from compound **11**, the total synthesis of desogestrel (**2**) requires 18 steps with an overall yield of 9.8%. Key step for the construction of the steroid backbone was a two-fold Heck reaction of **5** and **6** that led to the intermediate **4**, which then could be converted into desogestrel (**2**) by common methods.

## Experimental Section

**General**: All moisture sensitive reactions were performed under argon in flame-dried flasks. All solvents were dried and distilled prior to use by means of usual laboratory methods. All reagents obtained from commercial sources were used without further purification. Thin-layer chromatography (TLC) was performed on precoated silica gel SIL G/$UV_{254}$ plates (Macherey-Nagel GmbH & Co. KG), and silica gel 60 (0.032–0.063 mm, Merck) was used for column chromatography. Phosphomolybdic acid dissolved in methanol (PMA) or vanillin dissolved in methanolic sulfuric acid were used as staining reagents for TLC analysis. UV spectra were recorded, using $CH_3CN$ or MeOH as solvents, on a Perkin–Elmer Lambda 2 spectrometer. IR spectra were recorded as KBr pellets or as films on a Bruker IFS 25 spectrometer. $^1H$ and $^{13}C$ NMR spectra were recorded with Mercury-200, VXR-200, Unity-300, Inova-500, Unity-600 (Varian), or AMX 300 (Bruker) spectrometers. Chemical shifts are reported in ppm using residual solvent as internal standard. Multiplicities of $^{13}C$ NMR peaks were determined with the attached proton test (APT) pulse sequence. Mass spectra were measured on a Finnigan MAT 95, TSQ 7000 or LCQ instrument. Elemental analysis was carried out by members of the Mikroanalytisches Labor, Institut für Organische und Biomolekulare Chemie, Georg-August-Universität Göttingen.

**2-Bromo-5-methoxybenzaldehyde (9)**: Bromine (5.72 mL, 111 mmol) was added at room temperature to a solution of 3-methoxybenzaldehyde (11.8 mL, 97.0 mmol). After stirring for 48 h, the mixture was poured into water (650 mL) and the precipitated product was filtered of and extensively washed with water. After drying in vacuo aldehyde **9** (16.7 g, 80%) was obtained as white solid. $^1H$ NMR (200 MHz, $CDCl_3$): $\delta=3.85$ (s, 3H, 5-$OCH_3$), 7.04 (dd, $J=8.8$, 3.2 Hz, 1H, 4-H), 7.42 (d, $J=3.2$ Hz, 1H, 6-H), 7.53 (d, $J=8.8$ Hz, 1H, 3-H), 10.32 ppm (s, 1H, 1-CHO); MS (70 eV, EI): $m/z$ (%): 214.1/216.1 (100/87) [$M^+$].

**(*Z*)-2-(2-Iodethenyl)-4-methoxybrombenzol (5)**: KHMDS (0.500 M in toluene, 70 mL, 35.0 mmol) was added at room temperature to a suspension of iodmethyltriphenylphosphonium iodide (**10**) (18.5 g, 34.9 mmol) in dry THF (200 mL). The mixture was stirred for 10 min at room temperature and then cooled to −78 °C. A solution of aldehyde **9** (6.00 g, 27.9 mmol) in dry THF (20 mL) was added slowly and stirring was continued for 30 min at −78 °C. The solution was then warmed to room temperature and poured into saturated aqueous $NH_4Cl$ (200 mL). The mixture was extracted with diethyl ether (3×150 mL), the combined organic layers were washed with saturated aqueous NaCl (100 mL) and dried over $Na_2SO_4$. The solvent was removed in vacuo and the residue was subjected to column chromatography (*n*-pentane). Vinyliodide **5** (7.51 g, 79%) was obtained as yellow oil. $R_f=0.17$ (*n*-pentane); $^1H$ NMR (300 MHz, $CDCl_3$): $\delta=3.84$ (s, 3H, 4-$OCH_3$), 6.74 (d, $J=8.5$ Hz, 1H, 2′-H), 6.78 (dd, $J=8.8$, 3.0 Hz, 1H, 5-H), 7.24 (d, $J=3.0$ Hz, 1H, 3-H), 7.31 (d, $J=8.5$ Hz, 1H, 1′-H), 7.47 ppm (d, $J=8.8$ Hz, 1H, 6-H); $^{13}C$ NMR (50.3 MHz, $CDCl_3$): $\delta=55.54$ (4-$OCH_3$), 83.46 (C-2′), 113.9 (C-1), 115.3, 116.1 (C-3, C-5), 133.4 (C-6), 138.1 (C-2), 139.0 (C-1′), 158.5 ppm (C-4); IR (film): $\tilde{\nu}=2933$, 1589, 1566, 1462, 1294, 1238, 1176, 1114, 1055, 1018, 860, 806, 722, 667 $cm^{-1}$; UV ($CH_3CN$): $\lambda_{max}$ (lg $\varepsilon$) = 200.5 nm (4.3589); MS (70 eV, EI): $m/z$ (%): 338.0/340.0 (56/56) [$M^+$], 132.1 (100) [$M^+$−Br−I].

**(+)-(1*S*,5*S*,7a*S*)-1-*tert*-Butoxy-7a-ethyl-7,7a-dihydroindan-5(6*H*)-ol (12)**: Compound **11** (9.00 g, 38.1 mmol) was dissolved in dry dichloromethane (135 mL) and cooled to −78 °C. DIBAL-H (1.00 M in *n*-hexane, 45.6 mL, 45.6 mmol) was slowly added and the resulting mixture was stirred for 40 min at −78 °C and 1 h at room temperature. The reaction mixture was carefully quenched with a saturated solution of $Na_2SO_4$ and then filtered through Celite. The filtrate was dried over $Na_2SO_4$ and the solvent was removed in vacuo. After purification of the residue by column chromatography on silica gel (*n*-pentane/EtOAc 4:1) **12** (8.62 g, 95%) was obtained as colorless oil, which solidified upon cooling. $R_f=0.15$ (*n*-pentane/EtOAc 9:1); m.p. 52 °C; $[\alpha]_D^{20}=+14.0$ ($c=1.0$ in $CHCl_3$); $^1H$ NMR (600 MHz, $CDCl_3$): $\delta=0.95$ (t, $J=7.6$ Hz, 3H, 7a-$CH_2CH_3$), 1.13 (s, 9H, 1-$OC(CH_3)_3$), 1.24 (dt, $J=13.4$, 3.2 Hz, 1H, 7-$H_a$), 1.38 (br s, 1H, 5-OH), 1.46 (dq, $J=14.5$, 7.6 Hz, 1H, 7a-$CH_aH_bCH_3$), 1.54 (m, 1H, 6-$H_a$), 1.65 (dq, $J=14.5$, 7.6 Hz, 1H, 7a-$CH_aH_bCH_3$), 1.65–1.73 (m, 1H, 2-$H_a$), 1.85–1.96 (m, 2H, 2-$H_b$, 6-$H_b$), 1.97–2.08 (m, 2H, 3-$H_a$, 7-$H_b$), 2.42 (m, 1H, 3-$H_b$), 3.43 (t, $J=8.7$ Hz, 1H, 1-H), 4.24 (m, 1H, 5-H), 5.39 ppm (s, 1H, 4-H); $^{13}C$ NMR (75.5 MHz, $CDCl_3$): $\delta=10.41$ (7a-$CH_2CH_3$), 24.82 (7a-$CH_2CH_3$), 26.56 (C-3), 28.60 (1-$OC(CH_3)_3$), 29.47 (C-6), 30.15 (C-2), 30.47 (C-7), 45.53 (C-7a), 67.94 (C-5), 72.46 (1-$OC(CH_3)_3$), 81.15 (C-1), 122.3 (C-4), 149.4 ppm (C-3a); IR (KBr): $\tilde{\nu}=3287$, 2970, 1462, 1389, 1362, 1200, 1091, 1046, 1005, 921, 893, 865, 754 $cm^{-1}$; UV ($CH_3CN$): $\lambda_{max}$ (lg $\varepsilon$) = 202 nm (3.9046); MS (DCI, $NH_3$): $m/z$ (%): 256.3 (2) [$M^+$+$NH_4$], 238.3 (64) [$M^+$−$H_2O$+$NH_4$], 221.3 (87) [$M^+$−$H_2O$+H], 182.2 (100) [$M^+$−$C_4H_9$+H]; elemental analysis calcd (%) for $C_{15}H_{26}O_2$ (238.4): C 75.58, H 10.99; found: C 75.60, H 10.71.

**(−)-(1*S*,5*S*,7a*S*)-1-*tert*-Butoxy-7a-ethyl-7,7a-dihydroindan-5-yl-formate (13)**: Formic acid (2.45 mL, 65.0 mmol) was slowly added at room temperature to a solution of *N*,*N*′-carbonyldiimidazole (10.5 g, 64.5 mmol) in THF (200 mL). The resulting mixture was stirred for 24 h at room temperature. The solvent was removed and the residue was dried for 30 min in vacuo and then resolved in THF (40 mL). A solution of alcohol **12** (7.46 g, 31.3 mmol) in THF (10 mL) was added at room temperature and the mixture was stirred for further 3 h. The solvent was removed in vacuo, the residue then resolved in *n*-pentane (200 mL) and decanted from insoluble components. The organic layer was washed with brine and dried over $Na_2SO_4$. Removal of the solvent afforded **13** (8.13 g, 97%) as colorless oil. $R_f=0.66$ (*n*-pentane/EtOAc 4:1); $[\alpha]_D^{20}=-60.0$ ($c=1.0$ in $CHCl_3$); $^1H$ NMR (500 MHz, $CDCl_3$): $\delta=0.94$ (t, $J=7.6$ Hz, 3H, 7a-$CH_2CH_3$), 1.13 (s, 9H, 1-$OC(CH_3)_3$), 1.32 (dt, $J=13.2$, 3.5 Hz, 1H, 7-$H_a$), 1.48 (dq, $J=14.8$, 7.6 Hz, 1H, 7a-$CH_aH_bCH_3$), 1.63 (dq, $J=14.8$, 7.6 Hz, 1H, 7a-$CH_aH_bCH_3$), 1.66–1.75 (m, 2H, 2-$H_a$, 6-$H_a$), 1.85–1.98 (m, 2H, 2-$H_b$, 6-$H_b$), 2.01 (ddd, $J=13.2$, 5.8, 3.5 Hz, 1H, 7-$H_b$), 2.08 (m, 1H, 3-$H_a$), 2.43 (m, 1H, 3-$H_b$), 3.46 (t, $J=8.7$ Hz, 1H, 1-H), 5.38–5.45 (m, 2H, 4-H, 5-H), 8.07 ppm (d, $J=0.9$ Hz, 1H, 5-OCHO); $^{13}C$ NMR (75.5 MHz, $CDCl_3$): $\delta=10.12$ (7a-$CH_2CH_3$), 24.63 (7a $CH_2CH_3$), 25.15 (C-6), 26.74 (C-3), 28.59 (1-$OC(CH_3)_3$), 29.52 (C-7), 30.03 (C-2), 45.54 (C-7a), 70.48 (C-5), 72.57 (1-$OC(CH_3)_3$), 80.44 (C-1), 117.6 (C-4), 152.3 (C-3a), 161.2 ppm (5-OCHO); IR (film): $\tilde{\nu}=2971$, 1724, 1462, 1363, 1181, 1083, 919, 871 $cm^{-1}$; UV ($CH_3CN$): $\lambda_{max}$ (lg $\varepsilon$) = 197.5 nm (4.0231); MS (DCI, $NH_3$): $m/z$ (%): 284.3 (2) [$M^+$+$NH_4$], 238.3 (100) [$M^+$−$CO_2$−$H_2$+$NH_4$]; elemental analysis calcd (%) for $C_{16}H_{26}O_3$ (266.4): C 72.14, H 9.84; found: C 72.06, H 9.66.

**(+)-(1*S*,3a*S*,7a*S*)-1-*tert*-Butoxy-7a-ethyl-3a,6,7,7a-tetrahydroindane (6)**: $Pd(OAc)_2$ (70.1 mg, 317 μmol) and P*n*$Bu_3$ (312 μL, 1.25 mmol) were added to a degassed solution of **13** (6.63 g, 24.9 mmol) in dry dioxane. The mixture was stirred for 15 min at room temperature and then heated to 90 °C. After gas evolution started (8 to 20 min) the mixture was stirred for further 30 min at 90 °C and then immediately cooled in an ice bath.

The solvent was removed in vacuo and the residue was purified by column chromatography on silica gel (*n*-pentane). The bicyclic **6** (5.36 g, 97%, **6**/**14** 94:6) was obtained as colorless liquid which contained a small amount of the diene **14**. $R_f$=0.19 (*n*-pentane); $[\alpha]_D^{20}$=+31.5 (*c*=1.0 in $CHCl_3$); $^1$H NMR (500 MHz, $CDCl_3$): $\delta$=1.01 (t, *J*=7.5 Hz, 3H, 7a-$CH_2CH_3$), 1.21 (s, 9H, 1-OC($CH_3$)$_3$), 1.13–1.21 (m, 1H, 7-H$_a$), 1.26–1.42 (m, 3H, 3-H$_a$, 7a-$CH_2CH_3$), 1.47–1.61 (m, 2H, 2-H$_a$, 3-H$_b$), 1.90–2.00 (m, 1H, 2-H$_b$), 2.00–2.14 (m, 4H, 3a-H, 6-H$_2$, 7-H$_b$), 3.49 (t, *J*=8.1 Hz, 1H, 1-H), 5.49–5.60 ppm (m, 2H, 4-H, 5-H); $^{13}$C NMR (75.5 MHz, $CDCl_3$): $\delta$=10.19 (7a-$CH_2CH_3$), 18.00 (7a-$CH_2CH_3$), 23.94 (C-3), 24.50 (C-6), 28.54 (1-OC($CH_3$)$_3$), 30.45 (C-7), 31.62 (C-2), 42.93 (C-7a), 44.76 (C-3a), 72.15 (1-O$C$($CH_3$)$_3$), 81.18 (C-1), 127.5, 127.9 ppm (C-4, C-5); IR (film): $\tilde{\nu}$=2972, 1637, 1463, 1389, 1362, 1252, 1195, 1122, 1071, 982, 936, 888, 678 cm$^{-1}$; UV ($CH_3CN$): $\lambda_{max}$ (lg $\varepsilon$)=237.5 nm (2.9597); MS (70 eV, EI): *m*/*z* (%): 222.2 (2) [$M^+$], 165.2 (40) [$M^+-C_4H_9$]; EI-HRMS: *m*/*z*: calcd for $C_{15}H_{26}O$: 222.1984; found: 222.1984.

**(−)-(1*S*,3a*S*,4*S*,7a*S*)-4-(*Z*)-(2-Bromo-5-methoxystyryl)-1-*tert*-butoxy-7a-ethyl-3a,4,7,7a-tetrahydroindane (15)**: $Pd(OAc)_2$ (24.7 mg, 110 μmol,), $PPh_3$ (85.7 mg, 327 μmol) and $Ag_2CO_3$ (2.99 g, 10.8 mmol) were added to a degassed solution of **6** (1.60 g, 7.20 mmol, **6**/**14** 94:6) in dry DMF (55 mL) with protection from light. The resulting suspension was treated with a solution of the vinyliodide **5** (1.22 g, 3.60 mmol) in dry and degassed DMF (5 mL). The mixture was warmed to 95 °C in a preheated oil bath for 70 min with stirring. Two other portions of the vinyliodide **5** (610 mg, 1.80 mmol) in DMF (2.5 mL) and (305 mg, 0.900 mmol) in DMF (1.5 mL) were added after 1 h and 2 h, respectively, and the mixture was stirred for further 60 min at 95 °C. Finally, another portion of vinyliodide **5** (305 mg, 900 μmol) in DMF (1.5 mL) was added together with $Pd(OAc)_2$ (4.5 mg, 20.0 μmol), $PPh_3$ (14.8 mg, 56.4 μmol) and $Ag_2CO_3$ (543 mg, 1.97 mmol) and stirring was continued for 70 min at 95 °C. Water (100 mL) was added to the hot reaction mixture and after cooling to room temperature the mixture was extracted with $Et_2O$ (4×40 mL). The organic layers were washed with brine (40 mL), dried over $Na_2SO_4$ and the solvent was evaporated in vacuo. The residue was then first purified by column chromatography on silica gel (EtOAc/*n*-pentane 1:100) and afterwards by a second column chromatography on silica gel that was loaded with 10% $AgNO_3$ (EtOAc/*n*-pentane 1:150). Compound **15** (1.76 g, 4.05 mmol, 56%) was obtained as colorless oil. In addition, analytical pure samples of the regioisomer **17** and the *E* isomer **16** were isolated. $R_f$=0.32 (*n*-pentane/$CH_2Cl_2$ 7:3); $[\alpha]_D^{20}$=−61.2 (*c*=1.0 in $CHCl_3$); $^1$H NMR (600 MHz, $CDCl_3$): $\delta$=0.90 (t, *J*=7.5 Hz, 7a-$CH_2CH_3$), 1.09–1.15 (m, 1H, 7a-C$H_a$H$_b$CH$_3$), 1.13 (s, 9H, 1-OC($CH_3$)$_3$), 1.16–1.24 (m, 1H, 3-H$_a$), 1.31–1.43 (m, 2H, 3a-H, 7a-CH$_a$$H_b$CH$_3$), 1.47–1.54 (m, 1H, 2-H$_a$), 1.60–1.72 (m, 2H, 3-H$_b$, 7-H$_a$), 1.83–1.91 (m, 1H, 2-H$_b$), 2.40 (dd, *J*=17.3, 5.7 Hz, 1H, 7-H$_b$), 3.02–3.08 (m, 1H, 4-H), 3.55 (t, *J*=8.5 Hz, 1H, 1-H), 3.78 (s, 3H, 5″-OCH$_3$), 5.41–5.46 (m, 2H, 1′-H, 5-H), 5.69–5.73 (m, 1H, 6-H), 6.44 (d, *J*=11.3 Hz, 1H, 2′-H), 6.69 (dd, *J*=8.8, 3.1 Hz, 1H, 4″-H), 6.81 (d, *J*=3.1 Hz, 1H, 6″-H), 7.44 ppm (d, *J*=8.8 Hz, 1H, 3″-H); $^{13}$C NMR (126 MHz, $CDCl_3$): $\delta$=10.55 (7a-$CH_2CH_3$), 18.25 (7a-$CH_2CH_3$), 24.43 (C-3), 28.60 (1-OC($CH_3$)$_3$), 30.73 (C-2), 34.47 (C-7), 38.84 (C-4), 42.64 (C-7a), 47.54 (C-3a), 55.44 (5″-OCH$_3$), 72.23 (1-O$C$-($CH_3$)$_3$), 82.68 (C-1), 114.3 (C-4″), 114.4 (C-2″), 115.9 (C-6″), 127.4 (C-6), 129.1 (C-5), 129.3 (C-2′), 133.0 (C-3″), 136.5 (C-1′), 138.6 (C-1″), 158.4 ppm (C-5″); IR (KBr): $\tilde{\nu}$=2967, 1591, 1567, 1463, 1413, 1362, 1297, 1236, 1196, 1162, 1126, 1059, 1018, 878, 687 cm$^{-1}$; UV ($CH_3CN$): $\lambda_{max}$ (lg $\varepsilon$)=202.5 (4.3905), 214.0 (4.3863), 291.0 nm (3.3289); MS (70 eV, EI): *m*/*z* (%): 432.3/343.3 (4/4) [$M^+$], 279.3 (32) [$M^+-$Br$-C_4H_{10}O$]; EI-HRMS: *m*/*z*: calcd for $C_{24}H_{33}BrO_2$: 432.1664, found: 432.1663.

**(−)-17β-*tert*-Butoxy-13β-ethyl-3-methoxy-9β-gona-1,3,5(10),6,11-pentaene (4)**: A solution of **15** (1.59 g, 3.67 mmol) and *n*$Bu_4NOAc$ (2.84 g, 9.43 mmol) in $CH_3CN$/DMF/$H_2O$ 5:5:1 (60 mL) was carefully degassed. Herrmann–Beller catalyst[19] **19** (69.7 mg, 74.3 μmol) was added, the resulting mixture was warmed to 135 °C with a preheated oil bath and stirred for 5 h. The hot solution was then treated with water (200 mL), cooled to room temperature and extracted with $Et_2O$ (3×50 mL). The combined organic layers were washed with brine (50 mL), dried over $Na_2SO_4$ and the solvent was evaporated in vacuo. The residue was then quickly filtered through silica gel (EtOAc/*n*-pentane 5:95) to give **4** (1.22 g, 94%) as a slightly yellow oil which contained some minor impurities and was used directly in the next step due to its moderate stability. $R_f$=0.27 ($Et_2O$/*n*-pentane 1:99); $^1$H NMR (500 MHz, $CDCl_3$): $\delta$=1.05 (t, *J*=7.5 Hz, 3H, 13-$CH_2CH_3$), 1.11 (s, 9H, 17-OC($CH_3$)$_3$), 1.22–1.33 (m, 1H, 13-C$H_a$H$_b$CH$_3$), 1.34–1.58 (m, 2H, 15-H$_2$, 16-H$_a$), 1.61–1.77 (m, 2H, 14-H, 13-CH$_a$$H_b$CH$_3$), 1.82–1.91 (m, 1H, 16-H$_b$), 2.71 (m, 1H, 8-H), 3.51 (dd, *J*=8.8, 7.0 Hz, 1H, 17-H), 3.66 (m, 1H, 9-H), 3.78 (s, 3H, 3-OCH$_3$), 5.88 (dd, *J*=9.8, 6.0 Hz, 1H, 7-H), 6.13 (dd, *J*=10.1, 1.1 Hz, 1H, 12-H), 6.24 (dd, *J*=10.1, 4.5 Hz, 1H, 11-H), 6.33 (d, *J*=9.8 Hz, 1H, 6-H), 6.55 (d, *J*=2.8 Hz, 1H, 4-H), 6.70 (dd, *J*=8.4, 2.8 Hz, 1H, 2-H), 7.21 ppm (d, *J*=8.4 Hz, 1H, 1-H); $^{13}$C NMR (50.3 MHz, $CDCl_3$): $\delta$=10.67 (13-$CH_2CH_3$), 22.19 (C-15), 22.89 (13-$CH_2CH_3$), 28.60 (17-OC($CH_3$)$_3$), 32.12 (C-16), 33.57 (C-8), 36.94 (C-9), 42.48 (C-14), 45.64 (C-13), 55.18 (3-OCH$_3$), 72.34 (17-O$C$($CH_3$)$_3$), 78.18 (C-17), 112.0 (C-2, C-4), 126.6 (C-6), 126.8 (C-11), 127.7 (C-1), 129.3 (C-10), 131.1 (C-7), 134.0 (C-5, C-12), 157.9 ppm (C-3); MS (70 eV, EI): *m*/*z* (%): 352.4 (37) [$M^+$], 295.3 (46) [$M^+-C_4H_9$]; EI-HRMS: *m*/*z*: calcd for $C_{24}H_{32}O_2$: 352.2402, found: 352.2402.

**(−)-17β-*tert*-Butoxy-13β-ethyl-3-methoxy-9β-gona-1,3,5(10),11-tetraene (20)**: A mixture of $PtO_2$·$H_2O$ (22.6 mg, 63.7 μmol) and **4** (1.22 g, 3.45 mmol) in ethyl acetate (115 mL) was stirred for 39 h under a hydrogen atmosphere at room temperature. The solvent was removed in vacuo and the residue purified by column chromatography on silica gel (*n*-pentane/$CH_2Cl_2$ 4:1) to afford steroid **20** (1.12 g, 91%) as colorless oil. $R_f$=0.24 (*n*-pentane/EtOAc 98:2); $[\alpha]_D^{20}$=−151.4 (*c*=0.50 in $CHCl_3$); $^1$H NMR (600 MHz, $CDCl_3$): $\delta$=1.04 (t, *J*=7.5 Hz, 3H, 13-$CH_2CH_3$), 1.11 (s, 9H, 17-OC($CH_3$)$_3$), 1.31 (dq, *J*=13.5, 7.5 Hz, 1H, 13-C$H_a$H$_b$CH$_3$), 1.36–1.44 (m, 1H, 15-H$_a$), 1.45–1.52 (m, 1H, 14-H), 1.52–1.71 (m, 4H, 7-H$_a$, 15-H$_b$, 16-H$_a$, 13-CH$_a$$H_b$CH$_3$), 1.76–1.84 (m, 1H, 7-H$_b$), 1.90–1.98 (m, 1H, 16-H$_b$), 2.38 (m, 1H, 8-H), 2.52 (dt, *J*=15.9, 4.4 Hz, 1H, 6-H$_a$), 2.73 (m, 1H, 6-H$_b$), 3.44 (d, *J*=7.0 Hz, 1H, 9-H), 3.52 (dd, *J*=8.5, 7.5 Hz, 1H, 17-H), 3.77 (s, 3H, 3-OCH$_3$), 6.05 (s, 2H, 11-H, 12-H), 6.62 (d, *J*=2.8 Hz, 1H, 4-H), 6.75 (dd, *J*=8.5, 2.8 Hz, 1H, 2-H), 7.25 ppm (d, *J*=8.5 Hz, 1H, 1-H); $^{13}$C NMR (151 MHz, $CDCl_3$): $\delta$=10.80 (13-$CH_2CH_3$), 22.40 (C-15), 22.79 (13-$CH_2CH_3$), 25.45 (C-7), 26.21 (C-6), 28.63 (17-OC($CH_3$)$_3$), 31.00 (C-8), 32.18 (C-16), 38.37 (C-9), 43.40 (C-14), 45.69 (C-13), 55.14 (3-OCH$_3$), 72.30 (17-O$C$($CH_3$)$_3$), 78.66 (C-17), 112.1 (C-2), 113.2 (C-4), 129.1 (C-1), 129.8 (C-11), 131.5 (C-10), 133.6 (C-12), 138.7 (C-5), 157.0 ppm (C-3); IR (KBr): $\tilde{\nu}$=2932, 1610, 1500, 1466, 1361, 1257, 1197, 1089, 1043, 911, 793 cm$^{-1}$; UV ($CH_3CN$): $\lambda_{max}$ (lg $\varepsilon$)=200.0 (4.5815), 260.5 nm (3.7309); MS (70 eV, EI): *m*/*z* (%): 354.3 (56) [$M^+$], 297.2 (100) [$M^+-C_4H_9$]; EI-HRMS: *m*/*z*: calcd for $C_{24}H_{34}O_2$: 354.2559, found: 354.2559.

**(+)-17β-*tert*-Butoxy-13β-ethyl-3-methoxygona-1,3,5(10),9(11)-tetraene (21)**: A solution of steroid **20** (1.19 g, 3.35 mmol) in dry DMSO (90 mL) was treated with KO*t*Bu (981 mg, 8.76 mmol) with stirring for 2.5 h at room temperature. Water (100 mL) and brine (50 mL) were added and the mixture was extracted with MTBE (3×50 mL). The combined organic layers were washed with brine (50 mL) and dried over $Na_2SO_4$. Evaporation of the solvent and filtration through silica gel (*n*-pentane/EtOAc/$NEt_3$ 95:5:1) afforded a colorless oil, which solidified after standing. The enantiopure steroid **21** (821 mg, 2.31 mmol, 69%) was obtained after recrystallization from ethanol as colorless needles. $R_f$=0.29 (*n*-pentane/EtOAc 98:2); $[\alpha]_D^{20}$=+98.5 (*c*=1.0 in $CHCl_3$), lit.:[18] +97.13 (*c*=1.0 in $CHCl_3$); $^1$H NMR (600 MHz, $C_6D_6$): $\delta$=1.23 (s, 9H, 17-OC($CH_3$)$_3$), 1.24 (t, *J*=7.5 Hz, 3H, 13-$CH_2CH_3$), 1.26–1.37 (m, 3H, 7-H$_a$, 14-H, 15-H$_a$), 1.40–1.47 (m, 1H, 13-C$H_a$H$_b$CH$_3$), 1.57–1.65 (m, 2H, 15-H$_b$, 13-CH$_a$$H_b$CH$_3$), 1.69–1.76 (m, 1H, 16-H$_a$), 1.82–1.91 (m, 3H, 7-H$_b$, 12-H$_a$, 16-H$_b$), 2.09–2.15 (m, 1H, 8-H), 2.63 (ddd, *J*=17.6, 5.9, 1.5 Hz, 12-H$_b$), 2.68 (ddd, *J*=16.7, 5.0, 1.6 Hz, 1H, 6-H$_a$), 2.77 (ddd, *J*=16.7, 13.0, 5.3 Hz, 1H, 6-H$_b$), 3.38 (s, 3H, 3-OCH$_3$), 3.42 (t, *J*=8.6 Hz, 1H, 17-H), 6.14–6.17 (m, 1H, 11-H), 6.64 (d, *J*=2.7 Hz, 1H, 4-H), 6.77 (dd, *J*=8.8, 2.7 Hz, 1H, 2-H), 7.56 ppm (d, *J*=8.8 Hz, 1H, 1-H); $^{13}$C NMR (126 MHz, $C_6D_6$): $\delta$=11.15 (13-$CH_2CH_3$), 19.07 (13-$CH_2CH_3$), 24.29 (C-15), 28.79 (17-OC-($CH_3$)$_3$), 28.96 (C-7), 30.48 (C-6), 31.89 (C-16), 35.93 (C-12), 39.37 (C-8), 42.93 (C-13), 48.76 (C-14), 54.73 (3-OCH$_3$), 72.13 (17-O$C$($CH_3$)$_3$), 83.18 (C-17), 113.0 (C-2), 113.6 (C-4), 118.0 (C-11), 125.8 (C-1), 128.3 (C-10), 136.4, 137.5 (C-5, C-9), 159.1 ppm (C-3); IR (KBr): $\tilde{\nu}$=2969, 1606, 1497, 1468, 1388, 1362, 1317, 1279, 1233, 1197, 1133, 1110, 1081, 1049, 908, 869, 841, 812 cm$^{-1}$; UV ($CH_3CN$): $\lambda_{max}$ (lg $\varepsilon$)=213.5 (4.2925), 263.0 (4.2821),

298.5 nm (3.4977); MS (70 eV, EI): *m/z* (%): 354.5 (100) [$M^+$], 297.3 (65) [$M^+-C_4H_9$]; EI-HRMS: *m/z*: calcd for $C_{24}H_{34}O_2$: 354.2559, found: 354.2559.

**(+)-13β-Ethyl-3-methoxygona-1,3,5(10),9(11)-tetraene-17β-ol (22)**: A stirred solution of steroid **21** (48.8 mg, 138 μmol) in dichloromethane (6.8 mL) was treated with $BF_3{\cdot}EtO_2$ (48% in $Et_2O$, 680 μL, 5.39 mmol) and stirring was continued for 15 min at room temperature. The reaction was quenched with saturated aqueous $NaHCO_3$ (20 mL) and the layers were separated. The aqueous layer was extracted with dichloromethane (3×10 mL), the combined organic layers were dried over $Na_2SO_4$ and the solvent was removed in vacuo. Column chromatography on silica gel (*n*-pentane/EtOAc/$NEt_3$ 80:20:1) of the residue afforded alcohol **22** (39.4 mg, 96%) as colorless oil, which was crystallized from methanol. $R_f$=0.10 (*n*-pentane/EtOAc 9:1); $[\alpha]_D^{20}=+123.5$ ($c$=1.0 in $CHCl_3$) lit.:[20] +124, ($c$=1.0 in $CHCl_3$); $^1$H NMR (600 MHz, $C_6D_6$): $\delta$=1.29 (t, $J$=7.5 Hz, 3H, 13-$CH_2CH_3$), 1.21–1.31 (m, 3H, 7-$H_a$, 14-H, 15-$H_a$), 1.37 (dq, $J$=14.7, 7.5 Hz, 1H, 13-$CH_aH_bCH_3$), 1.45 (dq, $J$=14.7, 7.5 Hz, 1H, 13-$CH_aH_bCH_3$), 1.52–1.61 (m, 2H, 15-$H_b$, 16-$H_a$), 1.79–1.85 (m, 2H, 7-$H_b$, 12-$H_a$), 1.89–1.96 (m, 1H, 16-$H_b$), 2.03–2.10 (m, 1H, 8-H), 2.59 (ddd, $J$=17.8, 5.7, 1.8 Hz, 1H, 12-$H_b$), 2.64 (ddd, $J$=16.7, 5.3, 1.8 Hz, 1H, 6-$H_a$), 2.73 (ddd, $J$=16.7, 13.1, 5.3 Hz, 1H, 6-$H_b$), 3.38 (s, 3H, 3-$OCH_3$), 3.62 (t, $J$=8.8 Hz, 1H, 17-H), 6.10 (m, 1H, 11-H), 6.62 (d, $J$=2.7 Hz, 1H, 4-H), 6.76 (dd, $J$=8.8, 2.7 Hz, 1H, 2-H), 7.53 ppm (d, $J$=8.8 Hz, 1H, 1-H); $^{13}$C NMR (126 MHz, $C_6D_6$): $\delta$=11.00 (13-$CH_2CH_3$), 18.48 (13-$CH_2CH_3$), 23.86 (C-15), 28.87 (C-7), 30.40 (C-6), 31.27 (C-16), 35.50 (C-12), 39.24 (C-8), 43.36 (C-13), 48.99 (C-14), 54.74 (3-$OCH_3$), 83.96 (C-17), 113.0 (C-2), 113.6 (C-4), 117.8 (C-11), 125.8 (C-1), 128.3 (C-10), 136.3, 137.5 (C-5, C-9), 159.1 ppm (C-3); IR (KBr): $\tilde{\nu}$=3405, 2934, 1607, 1497, 1463, 1279, 1233, 1167, 1111, 1047, 909, 879, 810 cm$^{-1}$; UV ($CH_3CN$): $\lambda_{max}$ (lg $\varepsilon$)=263.0 (4.2707), 298.0 nm (3.4612); MS (DCI, $NH_3$): *m/z* (%): 299.2 (100) [$M^+$+H]; EI-HRMS: *m/z*: calcd for $C_{20}H_{26}O_2$: 298.1933, found: 298.1933.

**(−)-17β-*tert*-Butoxy-13β-ethyl-11α-hydroxy-3-methoxygona-1,3,5(10)-triene (23)**: $BH_3{\cdot}THF$ (1.00 M in THF, 8.00 mL, 8.00 mmol) was added at room temperature to a solution of **21** (581 mg, 1.64 mmol) in dry THF and the resulting mixture was stirred for 3.5 h. Then water (0.55 mL) was carefully added, followed by the addition of ice-cold 30% aqueous NaOH (3.0 mL) and ice-cold 30% aqueous $H_2O_2$ (3.0 mL). Stirring was then continued for 70 min at room temperature and 2 h at 60 °C. Water (50 mL) was added and the mixture was extracted with $Et_2O$ (3×15 mL). The combined organic layers were washed with saturated aqueous $Na_2SO_3$, dried over $Na_2SO_4$ and the solvent was removed in vacuo. Column chromatography on silica gel (*n*-pentane/EtOAc 9:1) of the residue afforded alcohol **23** (552 mg, 90%) as white foam. In addition, small amounts of the regioisomer **24** (42.8 mg, 7%) were obtained. $R_f$=0.23 (*n*-pentane/EtOAc 9:1); $[\alpha]_D^{20}=-75.5$ ($c$=1.0 in $CHCl_3$); $^1$H NMR (600 MHz, $CDCl_3$): $\delta$=1.03–1.09 (m, 4H, 12-$H_a$, 13-$CH_2CH_3$), 1.09–1.19 (m, 1H, 13-$CH_aH_bCH_3$), 1.16 (s, 9H, 17-$OC(CH_3)_3$), 1.20–1.30 (m, 2H, 14-H, 15-$H_a$), 1.37–1.46 (m, 3H, 7-$H_a$, 8-H, 13-$CH_aH_bCH_3$), 1.54–1.63 (m, 3H, 15-$H_b$, 16-$H_a$, 11-OH), 1.84–1.90 (m, 1H, 7-$H_b$), 1.93–2.01 (m, 1H, 16-$H_b$), 2.11 (t, $J$=9.9 Hz, 1H, 9-H), 2.53 (dd, $J$=12.2, 4.7 Hz, 1H, 12-$H_b$), 2.77–2.87 (m, 2H, 6-$H_2$), 3.55 (t, $J$=8.3 Hz, 1H, 17-H), 3.79 (s, 3H, 3-$OCH_3$), 4.08 (ddd, $J$=10.8, 9.9, 4.7 Hz, 1H, 11-H), 6.66 (d, $J$=2.8 Hz, 1H, 4-H), 6.73 (dd, $J$=8.7 ?z, 2.8 Hz, 1H, 2-H), 7.85 ppm (d, $J$=8.7 Hz, 1H, 1-H); $^{13}$C NMR (126 MHz, $CDCl_3$): $\delta$=9.49 (13-$CH_2CH_3$), 18.94 (13-$CH_2CH_3$), 22.80 (C-15), 26.98 (C-7), 28.58 (17-$OC(CH_3)_3$), 28.63 (C-6), 31.44 (C-16), 37.04 (C-8), 44.06 (C-12), 44.67 (C-13), 50.37 (C-9), 50.88 (C-14), 55.15 (3-$OCH_3$), 70.63 (C-11), 72.31 (17-$OC(CH_3)_3$), 82.05 (C-17), 110.9 (C-2), 113.7 (C-4), 127.1 (C-1), 132.7 (C-10), 139.1 (C-5), 157.6 ppm (C-3); IR (KBr): $\tilde{\nu}$=3406, 2936, 1609, 1498, 1464, 1389, 1362, 1255, 1196, 1132, 1092, 1059, 868 cm$^{-1}$; UV ($CH_3CN$): $\lambda_{max}$ (lg $\varepsilon$)=200.0 (4.6396), 218.0 (3.9241), 277.0 nm (3.2455); MS (70 eV, EI): *m/z* (%): 372.4 (100) [$M^+$]; EI-HRMS: *m/z*: calcd for $C_{24}H_{36}O_3$: 372.2664, found: 372.2664.

**(−)-17β-*tert*-Butoxy-13β-ethyl-11α-hydroxy-gona-4-en-3-one (26)**: A solution of steroid **23** (434 mg, 1.17 mmol) in dry THF (20 mL) was slowly added at −40 °C to a mixture of condensed ammonia (50 mL) and *i*PrOH (2.5 mL). Small pieces of lithium (75.8 mg, 10.9 mmol) were added portionwise over a period of 90 min, so that the deep blue color of the mixture maintained over this time. Then solid $NH_4Cl$ was slowly added until the color disappeared and the ammonia was distilled off at room temperature. The residue was dissolved in water (30 mL) and MTBE (20 mL), the layers were separated and the aqueous layer was extracted with MTBE (2×30 mL). The combined organic extracts were dried over $Na_2SO_4$ and the solvent was removed in vacuo to give a white foam, which was resolved in acetone/methanol/water 2:5:1 (36 mL). The solution was treated with 1 N HCl (6.75 mL) and stirred for 19 h at room temperature. The mixture was then neutralized with saturated aqueous $NaHCO_3$ (5 mL) and the solvent removed in vacuo. Water (20 mL) and MTBE (30 mL) were added to the residue, the layers separated and the aqueous layer was extracted with MTBE (2×30 mL). The combined organic extracts were dried over $Na_2SO_4$ and the solvent evaporated. Crude steroid **26** (418 mg 1.16 mmol) was obtained as colorless foam and was used in the next step without further purification. An analytical pure sample was obtained after column chromatography on silica gel (*n*-pentane/EtOAc 65:35). $R_f$=0.17 (*n*-pentane/EtOAc 7:3); $[\alpha]_D^{20}=-28.7$ ($c$=1.0 in $CHCl_3$); $^1$H NMR (600 MHz, $CDCl_3$): $\delta$=0.91 (t, $J$=11.5 Hz, 1H, 12-$H_a$), 1.04 (t, $J$=7.4 Hz, 3H, 13-$CH_2CH_3$), 1.11 (s, 9H, 17-$OC(CH_3)_3$), 1.00–1.25 (m, 5H, 7-$H_a$, 9-H, 14-H, 15-$H_a$, 13-$CH_aH_bCH_3$), 1.40–1.58 (m, 5H, 8-H, 15-$H_b$, 16$_a$-H, 13-$CH_aH_bCH_3$, 11-OH), 1.83–1.95 (m, 2H, 7-$H_b$, 16-$H_b$), 2.15–2.32 (m, 4H, 1-$H_a$, 2-$H_a$, 6-$H_a$, 10-H), 2.38 (dd, $J$=12.2, 4.5 Hz, 1H, 12-$H_b$), 2.38–2.49 (m, 3H, 1-$H_b$, 2-$H_b$, 6-$H_b$), 3.45 (t, $J$=8.5 Hz, 1H, 17-H), 3.71 (ddd, $J$=10.7, 9.5, 4.5 Hz, 1H, 11-H), 5.80 ppm (t, $J$=1.5 Hz, 1H, 4-H); $^{13}$C NMR (126 MHz, $CDCl_3$): $\delta$=9.61 (13-$CH_2CH_3$), 19.18 (13-$CH_2CH_3$), 22.87 (C-15), 27.50 (C-1), 28.51 (17-$OC(CH_3)_3$), 31.31 (C-16), 31.54 (C-7), 35.97 (C-6), 36.26 (C-2), 39.64 (C-8), 43.93 (C-13), 44.16 (C-10), 44.92 (C-12), 49.99 (C-14), 54.56 (C-9), 71.94 (C-11), 72.30 (17-$OC(CH_3)_3$), 81.94 (C-17), 124.4 (C-4), 167.8 (C-5), 200.8 ppm (C-3); IR (KBr): $\tilde{\nu}$=3432, 2969, 1659, 1446, 1389, 1361, 1257, 1197, 1133, 1088, 901, 758 cm$^{-1}$; UV ($CH_3CN$): $\lambda_{max}$ (lg $\varepsilon$)=237.5 (4.1616), 283.0 (2.3193), 314.0 nm (2.3067); MS (70 eV, EI): *m/z* (%): 360.3 (22) [$M^+$]; ESI-HRMS: *m/z*: calcd for [$C_{23}H_{36}O_3$+$H^+$]: 361.27372, found: 361.27398.

**(+)-17β-*tert*-Butoxy-13β-ethyl-3,3-ethylenedithio-11α-hydroxy-gona-4-ene (27)**: 1,2-Ethanedithiol (144 μL, 162 mg, 1.72 mmol) and $BF_3{\cdot}Et_2O$ (48% in $Et_2O$, 87.0 μL, 670 μmol) were added at room temperature to a solution of crude **26** (418 mg, 1.16 mmol) in methanol (40 mL) and the mixture was stirred for 3 h. Saturated aqueous $NaHCO_3$ (5 mL) and water (20 mL) were added and methanol was evaporated in vacuo. The aqueous layer was extracted with MTBE (2×30 mL) and the combined organic layers were dried over $Na_2SO_4$. Evaporation of the solvent afforded crude **27** (507 mg, 1.16 mmol) as white foam, which was used in the next step without further purification. An analytical pure sample was obtained by column chromatography on silica gel (*n*-pentane/EtOAc 4:1). $R_f$=0.33 (*n*-pentane/EtOAc 9:1); $[\alpha]_D^{20}=+42.3$ ($c$=1.0 in $CHCl_3$); $^1$H NMR (600 MHz, $CDCl_3$): $\delta$=0.80 (q, $J$=9.9 Hz, 1H, 9-H), 0.86 (t, $J$=11.6 Hz, 1H, 12-$H_a$), 0.90–0.98 (m, 1H, 7-$H_a$), 1.00–1.06 (m, 1H, 14-H), 1.03 (t, $J$=7.3 Hz, 3H, 13-$CH_2CH_3$), 1.11 (s, 9H, 17-$OC(CH_3)_3$), 1.08–1.32 (m, 4H, 8-H, 15-$H_a$, 13-$CH_aH_bCH_3$, 11-OH), 1.38–1.56 (m, 3H, 15-$H_b$, 16-$H_a$, 13-$CH_aH_bCH_3$), 1.65–1.70 (m, 1H, 7-$H_b$), 1.86–2.05 (m, 5H, 1-$H_a$, 2-$H_a$, 6-$H_a$, 10-H, 16-$H_b$), 2.20–2.26 (m, 2H, 2-$H_b$, 6-$H_b$), 2.32–2.38 (m, 1H, 1-$H_b$), 2.36 (dd, $J$=12.4, 4.6 Hz, 1H, 12-$H_b$), 3.21–3.27 (m, 1H, S-$CH_aH_bCH_2$-S), 3.29–3.38 (m, 3H, S-$CH_aH_bCH_2$-S), 3.44 (t, $J$=8.3 Hz, 1H, 17-H), 3.64 (ddd, $J$=11.2, 9.9, 4.6 Hz, 1H, 11-H), 5.60 ppm (d, $J$=1.0 Hz, 1H, 4-H); $^{13}$C NMR (126 MHz, $CDCl_3$): $\delta$=9.61 (13-$CH_2CH_3$), 19.14 (13-$CH_2CH_3$), 22.90 (C-15), 28.54 (17-$OC(CH_3)_3$), 29.28 (C-1), 31.17 (C-7), 31.37 (C-16), 35.47 (C-6), 39.64, 39.66, 39.74 (C-8, S-$CH_2CH_2$-S), 40.29 (C-2), 42.31 (C-10), 44.07 (C-13), 45.11 (C-12), 50.13 (C-14), 55.23 (C-9), 65.64 (C-3), 72.23 (17-$OC(CH_3)_3$), 72.61 (C-11), 82.10 (C-17), 125.7 (C-4), 142.0 ppm (C-5); IR (KBr): $\tilde{\nu}$=3444, 2929, 2873, 1440, 1389, 1361, 1197, 1132, 1073, 912, 861, 757 cm$^{-1}$; UV ($CH_3CN$): no absorption; MS (70 eV, EI): *m/z* (%): 436.3 (100) [$M^+$]; ESI-HRMS: *m/z*: calcd for [$C_{25}H_{40}O_2S_2$ + $H^+$]: 437.25425, found: 437.25412.

**(+)-17β-*tert*-Butoxy-13β-ethyl-11α-hydroxygona-4-ene (28)**: A solution of crude steroid **27** (507 mg, 1.16 mmol) in dry THF (20 mL) was slowly added at −40 °C to condensed ammonia (40 mL). Small pieces of lithium (30.0 mg, 4.32 mmol) were added portionwise over a period of 30 min, so that the deep blue color of the mixture maintained over this time. Then solid $NH_4Cl$ was slowly added until the color disappeared and the ammo-

nia was distilled off at room temperature. The residue was dissolved in water (30 mL) and MTBE (20 mL), the layers were separated and the aqueous layer was extracted with MTBE (2×30 mL). The combined organic extracts were dried over $Na_2SO_4$, the solvent was removed in vacuo and the residue was subjected to column chromatography on silica gel (*n*-pentane/EtOAc 97:3). Steroid **28** (221 mg, 637 μmol, 55% over four steps) was obtained as colorless oil. $R_f$=0.21 (*n*-pentane/EtOAc 97:3); $[\alpha]_D^{20}$=+20.5 (*c*=1.0 in $CHCl_3$); $^1$H NMR (600 MHz, $CDCl_3$): $\delta$=0.80 (q, *J*=9.9 Hz, 1H, 9-H), 0.85–0.94 (m, 2H, 7-$H_a$, 12-$H_a$), 1.01–1.07 (m, 1H, 14-H), 1.04 (t, *J*=7.4 Hz, 3H, 13-$CH_2CH_3$), 1.12 (s, 9H, 17-OC$(CH_3)_3$), 1.14–1.23 (m, 2H, 15-$H_a$, 13-C$H_aH_bCH_3$), 1.27–1.33 (m, 2H, 2-$H_a$, 8-H), 1.33–1.46 (m, 2H, 15-$H_b$, 13-C$H_aH_bCH_3$), 1.46–1.57 (m, 2H, 16-$H_a$, 11-OH), 1.61–1.72 (m, 3H, 1-$H_a$, 2-$H_b$, 7-$H_b$), 1.86–1.98 (m, 3H, 3-$H_2$, 16-$H_b$), 1.98–2.06 (m, 2H, 6-$H_a$, 10-H), 2.17–2.24 (m, 2H, 1-$H_b$, 6-$H_b$), 2.37 (dd, *J*=12.2, 4.7 Hz, 1H, 12-$H_b$), 3.45 (t, *J*=8.2 Hz, 1H, 17-H), 3.67 (ddd, *J*=11.2, 9.4, 4.7 Hz, 1H, 11-H), 5.43 ppm (d, *J*=1.9 Hz, 1H, 4-H); $^{13}$C NMR (126 MHz, $CDCl_3$): $\delta$=9.60 (13-$CH_2CH_3$), 19.13 (13-$CH_2CH_3$), 21.93 (C-2), 22.96 (C-15), 25.37 (C-3), 28.53 (17-OC$(CH_3)_3$), 30.00 (C-1), 31.39 (C-16), 31.70 (C-7), 36.03 (C-6), 39.97 (C-8), 43.42 (C-10), 44.00 (C-13), 44.85 (C-12), 50.20 (C-14), 55.73 (C-9), 72.19 (C-11), 72.64 (17-O$C(CH_3)_3$), 82.19 (C-17), 120.9 (C-4), 140.3 ppm (C-5); IR (KBr): $\tilde{\nu}$=3423, 2927, 1445, 1389, 1362, 1198, 1132, 1074, 910, 808 cm$^{-1}$; UV ($CH_3CN$): no absorption; MS (70 eV, EI): *m*/*z* (%): 346.3 (23) [$M^+$]; ESI-HRMS: *m*/*z*: calcd for [$C_{23}H_{38}O_2$ + $Na^+$]: 369.27640, found: 369.27633.

**(+)-17β-*tert*-Butoxy-13β-ethylgona-4-en-11-one (29)**: A solution of steroid **28** (243 mg, 702 μmol) in dichloromethane (20 mL) was treated with Dess–Martin periodinane (467 mg, 1.10 mmol) and stirred for 60 min at room temperature. Saturated aqueous $NaHCO_3$ (3.0 mL) and 10% aqueous $Na_2S_2O_3$ (3.0 mL) were added and the mixture was stirred for further 45 min. The layers were separated and the aqueous layer was extracted with dichloromethane (3×20 mL). The combined organic extracts were dried over $Na_2SO_4$, the solvent was removed in vacuo and the residue was filtered through a short column of silica gel (*n*-pentane/EtOAc 95:5) to give ketone **29** (227 mg 94%) as colorless oil. $R_f$=0.51 (*n*-pentane/EtOAc 95:5); $[\alpha]_D^{20}$=+142.0 (*c*=1.0 in $CHCl_3$); $^1$H NMR (600 MHz, $CDCl_3$): $\delta$=0.83–0.90 (m, 1H, 1-$H_a$), 0.97–1.08 (m, 5H, 7-$H_a$, 13-$CH_2CH_3$, 13-C$H_aH_bCH_3$), 1.10 (s, 9H, 17-OC$(CH_3)_3$), 1.30 (dq, *J*=12.1, 6.5 Hz, 1H, 15-$H_a$), 1.36–1.46 (m, 1H, 2-$H_a$), 1.46–1.54 (m, 1H, 13-C$H_aH_bCH_3$), 1.54–1.66 (m, 5H, 2-$H_b$, 8-H, 14-H, 15-$H_b$, 16-$H_a$), 1.70–1.77 (m, 2H, 7-$H_b$, 9-H), 1.88–1.96 (m, 3H, 3-$H_2$, 6-$H_a$), 1.96–2.04 (m, 1H, 16-$H_b$), 2.01 (d, *J*=11.3 Hz, 1H, 12-$H_a$), 2.16–2.21 (m, 1H, 6-$H_b$), 2.23–2.31 (m, 2H, 1-$H_a$, 10-H), 2.77 (d, *J*=11.3 Hz, 1H, 12-$H_b$), 3.66 (t, *J*=8.2 Hz, 1H, 17-H), 5.45 ppm (s, 1H, 4-H); $^{13}$C NMR (126 MHz, $CDCl_3$): $\delta$=9.18 (13-$CH_2CH_3$), 20.12 (13-$CH_2CH_3$), 21.76 (C-2), 22.07 (C-15), 25.47 (C-3), 28.43 (17-OC$(CH_3)_3$), 28.93 (C-1), 31.73 (C-16), 31.91 (C-7), 34.91 (C-6), 35.34 (C-10), 41.90 (C-8), 49.32 (C-13), 50.82 (C-12), 51.18 (C-14), 60.96 (C-9), 72.47 (17-O$C(CH_3)_3$), 81.40 (C-17), 122.1 (C-4), 138.6 (C-5), 212.1 ppm (C-11); IR (film): $\tilde{\nu}$=2927, 1708, 1435, 1389, 1362, 1253, 1195, 1128, 1076, 917, 808, 757 cm$^{-1}$; UV ($CH_3CN$): $\lambda_{max}$ (lg $\varepsilon$)=194.0 nm (3.8334); MS (70 eV, EI): *m*/*z* (%): 344.4 (64) [$M^+$]; ESI-HRMS: *m*/*z*: calcd for [$C_{23}H_{36}O_2$ + $H^+$]: 345.27881, found: 345.27886.

**(+)-17β-*tert*-Butoxy-13β-ethyl-11β-hydroxy-11α-trimethylsilylmethylgona-4-ene (30)**: $LiCH_2TMS$ (1.00 M in *n*-pentane, 880 μL) was added in one portion at −78 °C to a solution of ketone **29** (102 mg, 295 μmol) in dry THF (12 mL). Stirring was continued at −78 °C for 20 min, then the mixture was warmed to room temperature and stirred for further 30 min. Water (30 mL) was added and the aqueous phase was extracted with $Et_2O$ (3×15 mL). The combined organic layers were washed with saturated aqueous NaCl (15 mL) and dried over $Na_2SO_4$. The solvent was removed in vacuo and the residue was subjected to column chromatography on silica gel (*n*-pentane/EtOAc 95:5) to afford steroid **30** (120 mg, 94%) as colorless foam. $R_f$=0.69 (*n*-pentane/EtOAc 95:5); $[\alpha]_D^{20}$=+22.3 (*c*=1.0 in $CHCl_3$); $^1$H NMR (600 MHz, $CDCl_3$): $\delta$=0.10 (s, 9H, 11-$CH_2Si(CH_3)_3$), 0.87 (dq, *J*=12.6, 4.0 Hz, 1H, 7-$H_a$), 0.95 (dt, *J*=12.1, 6.8 Hz, 1H, 14-H), 1.02 (d, *J*=14.3 Hz, 1H, 12-$H_a$), 1.04 (t, *J*=10.1 Hz, 1H, 9-H), 1.06 (d, *J*=15.0 Hz, 1H, 11-C$H_aH_bSi(CH_3)_3$), 1.13 (s, 9H, 17-OC$(CH_3)_3$), 1.15 (t, *J*=7.4 Hz, 3H, 13-$CH_2CH_3$), 1.22–1.30 (dq, *J*=12.1, 6.4 Hz, 1H, 15-$H_a$), 1.31 (s, 1H, 11-OH), 1.38–1.45 (m, 2H, 2-$H_a$, 13-C$H_aH_bCH_3$), 1.45–1.56 (m, 4H, 8-H, 15-$H_b$, 16-$H_a$, 13-C$H_aH_bCH_3$), 1.54 (d, *J*=15.0 Hz, 1H, 11-C$H_aH_bSi(CH_3)_3$), 1.63–1.70 (m, 1H, 2-$H_b$), 1.72 (dquint., *J*=12.6, 2.5 Hz, 1H, 7-$H_b$), 1.83–1.91 (m, 2H, 1-$H_a$, 16-$H_b$), 1.93–1.99 (m, 3H, 1-$H_b$, 3-$H_2$), 1.99–2.07 (m, 1H, 6-$H_a$), 2.17–2.24 (m, 2H, 6-$H_b$, 10-H), 2.47 (d, *J*=14.3 Hz, 1H, 12-$H_b$), 3.35 (t, *J*=8.3 Hz, 1H, 17-H), 5.41 ppm (br s, 1H, 4-H); $^{13}$C NMR (126 MHz, $CDCl_3$): $\delta$=1.06 (11-$CH_2Si(CH_3)_3$), 10.93 (13-$CH_2CH_3$), 19.94 (13-$CH_2CH_3$), 21.37 (C-2), 23.40 (C-15), 25.62 (C-3), 28.66 (17-OC$(CH_3)_3$), 29.69 (C-1), 31.19 (C-16), 32.63 (C-7), 36.00 (11-$CH_2Si(CH_3)_3$), 36.49 (C-6), 39.29 (C-8), 40.59 (C-10), 43.13 (C-13), 50.62 (C-12), 50.70 (C-14), 56.81 (C-9), 72.17 (17-O$C(CH_3)_3$), 77.18 (C-11), 84.12 (C-17), 120.0 (C-4), 142.0 ppm (C-5); IR (film): $\tilde{\nu}$=3627, 2928, 1658, 1436, 1389, 1362, 1248, 1197, 1133, 1080, 1028, 911, 838, 760, 688 cm$^{-1}$; UV ($CH_3CN$): $\lambda_{max}$ (lg $\varepsilon$)=198.5 nm (3.7757); MS (70 eV, EI): *m*/*z* (%): 432.4 (7) [$M^+$]; ESI-HRMS: *m*/*z*: calcd for [$C_{27}H_{48}O_2Si$ + $Na^+$]: 455.33158, found: 455.33193.

**(+)-17β-*tert*-Butoxy-13β-ethyl-11-methylenegona-4-ene (31)**: A solution of **30** (201 mg, 464 μmol) in acetone (20 mL) was treated with conc. HCl (0.37 mL) and stirred for 60 min at room temperature. The mixture was then neutralized with saturated aqueous $NaHCO_3$ (10 mL) and the acetone was removed in vacuo. The aqueous residue was diluted with water (20 mL) and extracted with $Et_2O$ (4×10 mL). The combined extracts were washed with saturated aqueous NaCl (10 mL) and dried over $Na_2SO_4$. Evaporation of the solvent and column chromatography on silica gel (*n*-pentane/EtOAc 99:1) of the obtained residue afforded steroid **31** (152 mg, 95%) as colorless oil, which solidified on standing. $R_f$=0.53 (*n*-pentane/EtOAc 100:1); $[\alpha]_D^{20}$=+112.3 (*c*=1.0 in $CHCl_3$); $^1$H NMR (600 MHz, $C_6D_6$): $\delta$=0.88–1.00 (m, 2H, 7-$H_a$, 14-H), 1.10 (s, 9H, 17-OC$(CH_3)_3$), 1.20 (dq, *J*=12.3, 6.5 Hz, 1H, 15-$H_a$), 1.24–1.40 (m, 8H, 1-$H_a$, 8-H, 9-H, 15-$H_b$, 13-$CH_2CH_3$, 13-C$H_aH_bCH_3$), 1.44–1.52 (m, 2H, 2-$H_a$, 13-C$H_aH_bCH_3$), 1.47 (d, *J*=12.2 Hz, 1H, 12-$H_a$), 1.59–1.68 (m, 3H, 2-$H_b$, 7-$H_b$, 16-$H_a$), 1.76–1.84 (m, 1H, 16-$H_b$), 1.94–2.06 (m, 3H, 3-$H_2$, 6-$H_a$), 2.24–2.38 (m, 3H, 1-$H_b$, 6-$H_b$, 10-H), 2.85 (d, *J*=12.2 Hz, 1H, 12-$H_b$), 3.31 (t, *J*=8.3 Hz, 1H, 17-H), 4.79 (s, 1H, 11-C$H_aH_b$), 5.06 (d, *J*=1.1 Hz, 1H, 11-C$H_aH_b$), 5.57 ppm (d, *J*=2.1 Hz, 1H, 4-H); $^{13}$C NMR (151 MHz, $C_6D_6$): $\delta$=9.44 (13-$CH_2CH_3$), 19.70 (13-$CH_2CH_3$), 22.44 (C-2), 22.74 (C-15), 26.16 (C-3), 28.71 (17-OC$(CH_3)_3$), 29.69 (C-1), 32.02 (C-16), 32.16 (C-7), 36.11 (C-6), 37.06 (C-10), 42.43 (C-8), 45.54 (C-12), 46.29 (C-13), 52.52 (C-14), 55.63 (C-9), 72.18 (17-O$C(CH_3)_3$, 82.38 (C-17), 108.3 (11-$CH_2$), 121.5 (C-4), 140.2 (C-5), 147.8 ppm (C-11); IR (film): $\tilde{\nu}$=2927, 1642, 1437, 1388, 1362, 1197, 1118, 1079, 892, 759 cm$^{-1}$; UV ($CH_3CN$): $\lambda_{max}$ (lg $\varepsilon$)=197.0 (4.1979), 248.0 (2.1226), 254.0 (2.1315), 260.0 nm (2.0541); MS (70 eV, EI): *m*/*z* (%): 342.4 (26) [$M^+$]; EI-HRMS: *m*/*z*: calcd for $C_{24}H_{38}O$: 342.2923, found: 342.2923.

**(+)-17β-*tert*-Butoxy-13β-ethyl-3-methoxygona-1,3,5(10)-trien-11-one (33)**: A solution of steroid **23** (309 mg, 828 μmol) in dichloromethane (15 mL) was treated with Dess–Martin periodinane (533 mg, 1.26 mmol) and stirred for 60 min at room temperature. Saturated aqueous $NaHCO_3$ (7.2 mL) and 10% aqueous $Na_2S_2O_3$ (7.2 mL) were added and the mixture was stirred for further 45 min. The layers were separated and the aqueous layer was extracted with dichloromethane (3×20 mL). The combined organic extracts were dried over $Na_2SO_4$, the solvent was removed in vacuo and the residue was filtered through a short column of silica gel (*n*-pentane/EtOAc 9:1) to give the ketone **33** (298 mg, 805 μmol, 97%) as colorless foam, which was used directly in the next step because of its low stability. $R_f$=0.38 (*n*-pentane/EtOAc 9:1); $[\alpha]_D^{20}$=+211.3 (*c*=1.0 in $CHCl_3$); $^1$H NMR (600 MHz, $CDCl_3$): $\delta$=1.04 (t, *J*=7.3 Hz, 3H, 13-$CH_2CH_3$), 1.08–1.15 (m, 1H, 13-C$H_aH_bCH_3$), 1.15 (s, 9H, 17-OC$(CH_3)_3$), 1.39–1.59 (m, 3H, 7-$H_a$, 15-$H_a$, 13-C$H_aH_bCH_3$), 1.65–1.74 (m, 2H, 15-$H_b$, 16-$H_a$), 1.86–1.97 (m, 3H, 7-$H_b$, 8-H, 14-H), 2.04–2.12 (m, 1H, 16-$H_b$), 2.19 (d, *J*=11.5 Hz, 1H, 12-$H_a$), 2.75–2.89 (m, 2H, 6-$H_2$), 2.94 (d, *J*=11.5 Hz, 1H, 12-$H_b$), 3.42 (d, *J*=10.2 Hz, 1H, 9-H), 3.75–3.78 (m, 1H, 17-H), 3.77 (s, 1H, 3-$OCH_3$), 6.61 (d, *J*=2.7 Hz, 1H, 4-H), 6.75 (dd, *J*=8.8, 2.7 Hz, 1H, 2-H), 7.29 ppm (d, *J*=8.8 Hz, 1H, 1-H); $^{13}$C NMR (126 MHz, $CDCl_3$): $\delta$=9.29 (13-$CH_2CH_3$), 20.21 (13-$CH_2CH_3$), 22.03 (C-15), 27.57 (C-7), 28.47 (17-OC$(CH_3)_3$), 30.03 (C-6), 31.84 (C-16), 40.35 (C-8), 49.68 (C-13), 50.87, 50.91 (C-12, C-14), 55.16 (3-$OCH_3$), 55.46 (C-9), 72.57 (17-O$C(CH_3)_3$), 81.41 (C-17), 111.4 (C-2), 113.7 (C-4), 123.9 (C-10), 131.0 (C-1), 138.3 (C-5), 157.9 (C-3), 210.0 ppm (C-11); IR (KBr): $\tilde{\nu}$=2971, 1712, 1610, 1502, 1464, 1362, 1246, 1195, 1120, 1089, 1039 cm$^{-1}$; UV ($CH_3CN$): $\lambda_{max}$ (lg $\varepsilon$)=200.5 (4.6748), 277.0 (3.2073), 284.0 nm (3.1842); MS (ESI,

MeOH/$NH_4OAc$): *m/z* (%): 371.3 (26) [$M^+$+H], 758.5 (100) [$2M^+$ +$NH_4$]; ESI-HRMS: *m/z*: calcd for [$C_{24}H_{34}O_3$+$H^+$]: 371.25807, found: 371.25791.

**(−)-17β-*tert*-Butoxy-13β-ethyl-11β-hydroxy-3-methoxy-11α-trimethylsilylmethylgona-1,3,5(10)-triene (34)**: $LiCH_2TMS$ (1.00 M in *n*-pentane, 2.02 mL, 2.02 mmol) was added in one portion at −78 °C to a stirred solution of ketone **33** (298 mg, 805 μmol) in dry THF (60 mL). Stirring was continued at −78 °C for 30 min, then the mixture was warmed to room temperature and stirred for further 10 min. Water (100 mL) was added and the aqueous phase was extracted with $Et_2O$ (3×30 mL). The combined organic layers were washed with saturated aqueous NaCl (30 mL) and dried over $Na_2SO_4$. The solvent was removed in vacuo and the residue was subjected to column chromatography on silica gel (*n*-pentane/EtOAc/$NEt_3$ 97:3:1) to afford steroid **34** (291 mg, 79%) as colorless foam. $R_f$=0.61 (*n*-pentane/EtOAc 9:1); $[\alpha]_D^{20}$=−53.3 (*c*=1.0 in $CHCl_3$); $^1$H NMR (600 MHz, $CDCl_3$): $\delta$=0.13 (s, 9H, 11-$CH_2Si(CH_3)_3$), 1.10 (d, *J*=14.2 Hz, 1H, 12-$H_a$), 1.14 (d, *J*=15.1 Hz, 1H, 11-$CH_aH_bSi(CH_3)_3$), 1.17 (s, 9H, 17-$OC(CH_3)_3$), 1.18 (t, *J*=7.4 Hz, 3H, 13-$CH_2CH_3$), 1.23–1.29 (m, 1H, 14-H), 1.32–1.45 (m, 2H, 13-$CH_aH_bCH_3$, 11-OH), 1.45–1.60 (m, 3H, 7-$H_a$, 16-$H_a$, 13-$CH_aH_bCH_3$), 1.60–1.76 (m, 4H, 7-$H_b$, 8-H, 15-$H_2$), 1.90 (d, *J*=15.1 Hz, 1H, 11-$CH_aH_bSi(CH_3)_3$), 1.91–1.98 (m, 1H, 16-$H_b$), 2.21 (d, *J*=11.0 Hz, 1H, 9-H), 2.63–2.69 (m, 2H, 6-$H_2$), 2.65 (d, *J*=14.2 Hz, 1H, 12-$H_b$), 3.45 (t, *J*=8.0 Hz, 1H, 17-H), 3.79 (s, 3H, 3-$OCH_3$), 6.71 (d, *J*=2.9 Hz, 1H, 4-H), 6.72 (dd, *J*=8.6, 2.9 Hz, 1H, 2-H), 7.85 ppm (d, *J*=8.6 Hz, 1H, 1-H); $^{13}$C NMR (126 MHz, $CDCl_3$): $\delta$=0.73 (11-$CH_2Si(CH_3)_3$), 11.08 (13-$CH_2CH_3$), 20.19 (13-$CH_2CH_3$), 23.31 (C-15), 26.06 (C-7), 28.62 (17-$OC(CH_3)_3$), 28.69 (C-6), 31.07 (C-16), 33.77, 33.94 (C-8, 11-$CH_2Si(CH_3)_3$), 43.75 (C-13), 49.14 (C-12), 52.29 (C-14), 53.20 (C-9), 55.12 (3-$OCH_3$), 72.25 (17-$OC(CH_3)_3$), 76.17 (C-11), 83.83 (C-17), 109.9 (C-2), 113.6 (C-4), 128.3 (C-1), 130.8 (C-10), 142.4 (C-5), 157.1 ppm (C-3); IR (KBr): $\tilde{\nu}$=3629, 2950, 1610, 1578, 1497, 1466, 1389, 1362, 1254, 1133, 1196, 1088, 1049, 928, 841, 689 $cm^{-1}$; UV ($CH_3CN$): $\lambda_{max}$ (lg $\varepsilon$)= 199.5 (4.5721), 225.5 (3.8272), 276.5 (3.1354), 281.5 nm (3.1066); MS (70 eV, EI): *m/z* (%): 458.4 (7) [$M^+$], 73.1 (100) [$C_3H_9Si^+$]; ESI-HRMS: *m/z*: calcd for [$C_{28}H_{46}O_3Si$+$Na^+$]: 481.31084, found: 481.31084.

**(+)-17β-*tert*-Butoxy-13β-ethyl-11-methylenegona-4-en-3-one (35)**: A solution of steroid **34** (172 mg, 375 μmol) in dry THF (14 mL) was slowly added at −40 °C to a mixture of condensed ammonia (35 mL) and *i*PrOH (1.8 mL). Small pieces of lithium (26.0 mg, 3.75 mol) were added portionwise over a period of 90 min, so that the deep blue color of the mixture maintained. Then solid $NH_4Cl$ was slowly added until the color disappeared and the ammonia was distilled off at room temperature. The residue was dissolved in water (30 mL) and MTBE (20 mL), the layers were separated and the aqueous layer was extracted with MTBE (2×30 mL). The combined organic extracts were dried over $Na_2SO_4$ and the solvent was removed in vacuo to give a white foam, which was resolved in acetone (20 mL). The solution was treated with conc. HCl (0.50 mL) and stirred for 15 h at room temperature. The mixture was then neutralized with saturated aqueous $NaHCO_3$ (5 mL) and the acetone was removed in vacuo. Water (20 mL) and MTBE (20 mL) were added to the residue, the layers separated and the aqueous layer was extracted with MTBE (2× 20 mL). The combined organic extracts were dried over $Na_2SO_4$, the solvent evaporated and the residue subjected to column chromatography on silica gel (*n*-pentane/EtOAc 1:1). Compound **35** (99.4 mg, 74%) was obtained as colorless crystals. $R_f$=0.23 (*n*-pentane/EtOAc 1:1); $[\alpha]_D^{20}$= +156.0 (*c*=1.0 in $CHCl_3$); $^1$H NMR (600 MHz, $CDCl_3$): $\delta$=0.99–1.07 (m, 1H, 7-$H_a$), 1.02 (t, *J*=7.4 Hz, 3H, 13-$CH_2CH_3$), 1.12 (s, 9H, 17-$OC(CH_3)_3$), 1.17–1.25 (m, 2H, 14-H, 11-$CH_aH_bCH_3$), 1.25–1.34 (m, 1H, 15-$H_a$), 1.35–1.53 (m, 5H, 1-$H_a$, 8-H, 9-H, 15-$H_b$, 13-$CH_aH_bCH_3$), 1.53–1.61 (m, 2H, 12-$H_a$, 16-$H_a$), 1.77–1.82 (m, 1H, 7-$H_b$), 1.89–1.97 (m, 1H, 16-$H_b$), 2.17–2.24 (m, 1H, 6-$H_a$), 2.29 (ddd, 16.6, 13.9, 4.7 Hz, 1H, 2-$H_a$), 2.38 (dt, *J*=16.6, 4.3 Hz, 1H, 2-$H_b$), 2.46 (dt, *J*=14.6, 3.0 Hz, 1H, 6-$H_b$), 2.51 (dq, *J*=13.8, 4.3 Hz, 1H, 1-$H_b$), 2.54–2.60 (m, 1H, 10-H), 2.79 (d, *J*=12.2 Hz, 1H, 12-$H_b$), 3.51 (t, *J*=8.3 Hz, 1H, 17-H), 4.77 (s, 1H, 11-$CH_aH_b$), 5.00 (s, 1H, 11-$CH_aH_b$), 5.86 ppm (s, 1H, 4-H); $^{13}$C NMR (126 MHz, $CDCl_3$): $\delta$=8.70 (13-$CH_2CH_3$), 19.13 (13-$CH_2CH_3$), 22.34 (C-15), 28.26 (C-1), 28.49 (17-$OC(CH_3)_3$), 30.14 (C-7), 31.49 (C-16), 35.37 (C-6), 36.96 (C-2), 37.59 (C-10), 41.39 (C-8), 44.85 (C-12), 45.73 (C-13), 52.12 (C-14), 54.24 (C-9), 72.32 (17-$OC(CH_3)_3$), 81.83 (C-17), 106.1 (11-$CH_2$), 125.5 (C-4), 146.3 (C-11), 166.8 (C-5), 200.0 ppm (C-3); IR (KBr): $\tilde{\nu}$=3080, 2963, 1672, 1614, 1454, 1360, 1257, 1199, 1116, 1078, 897, 747 $cm^{-1}$; UV ($CH_3CN$): $\lambda_{max}$ (lg $\varepsilon$)=196.5 (4.0609), 236.5 (4.2588), 308.0 nm (2.2252); MS (70 eV, EI): *m/z* (%): 356.5 (7) [$M^+$], 300.4 (100) [$M^+$−$C_4H_8$]; ESI-HRMS: *m/z*: calcd for [$C_{24}H_{36}O_2$+$H^+$]: 357.27881, found: 357.27912.

**(+)-13β-Ethyl-17β-hydroxy-11-methylenegona-4-en-3-one (36)**: A solution of steroid **35** (107 mg, 300 μmol) in dichloromethane (17 mL) was treated with $BF_3{\cdot}EtO_2$ (48% in $Et_2O$, 1.66 mL, 13.2 mmol) and stirred for 10 min at room temperature. The mixture was quenched with saturated aqueous $NaHCO_3$ (20 mL) and the layers were separated. The aqueous layer was extracted with dichloromethane (3×10 mL), the combined organic layers were dried over $Na_2SO_4$ and the solvent was removed in vacuo. Column chromatography on silica gel (*n*-pentane/EtOAc 1:1) of the residue afforded alcohol **36** (90.0 mg, quant.) as white solid. $R_f$=0.36 (*n*-pentane/EtOAc 1:1); $[\alpha]_D^{20}$= +187.3 (*c*=1.0 in $CHCl_3$), +180.0 (*c*= 0.53 in $C_6H_6$), lit.:[11e] +180.6 (*c*=0.53 in $C_6H_6$); $^1$H NMR (600 MHz, $CDCl_3$): $\delta$=1.00–1.08 (m, 1H, 7-$H_a$), 1.04 (t, *J*=7.5 Hz, 3H, 13-$CH_2CH_3$), 1.21–1.36 (m, 3H, 14-H, 15-$H_a$, 13-$CH_aH_bCH_3$), 1.36–1.52 (m, 4H, 1-$H_a$, 8-H, 9-H, 13-$CH_aH_bCH_3$), 1.52–1.64 (m, 3H, 12-$H_a$, 15-$H_b$, 16-$H_a$), 1.77–1.82 (m, 2H, 7-$H_b$, 17-OH), 2.08–2.15 (m, 1H, 16-$H_b$), 2.17–2.24 (m, 1H, 6-$H_a$), 2.92 (ddd, *J*=16.7, 13.8, 4.7 Hz, 2-$H_a$), 2.38 (dt, *J*=16.7, 4.1 Hz, 1H, 2-$H_b$), 2.46 (dt, *J*=14.6, 3.1 Hz, 1H, 6-$H_b$), 2.50 (dq, *J*=13.6, 4.4 Hz, 1H, 1-$H_b$), 2.54–2.59 (m, 1H, 10-H), 2.85 (d, *J*=12.4 Hz, 1H, 12-$H_b$), 3.82 (t, *J*=8.5 Hz, 1H, 17-H), 4.79 (s, 1H, 11-$CH_aH_b$), 5.01 (s, 1H, 11-$CH_aH_b$), 5.86 ppm (t, *J*=1.9 Hz, 1H, 4-H); $^{13}$C NMR (126 MHz, $CDCl_3$): $\delta$=8.87 (13-$CH_2CH_3$), 18.55 (13-$CH_2CH_3$), 22.07 (C-15), 28.23 (C-1), 30.08 (C-7), 30.90 (C-16), 35.30 (C-6), 36.91 (C-2), 37.56 (C-10), 41.49 (C-8), 44.33 (C-12), 46.53 (C-13), 52.14 (C-14), 54.05 (C-9), 82.89 (C-17), 108.5 (11-$CH_2$), 125.5 (C-4), 146.0 (C-11), 166.7 (C-5), 200.1 ppm (C-3); IR (KBr): $\tilde{\nu}$= 3487, 2946, 1664, 1613, 1417, 1354, 1261, 1207, 1110, 1067, 904, 880 $cm^{-1}$; UV ($CH_3CN$): $\lambda_{max}$ (lg $\varepsilon$)=200.0 (4.1316), 236.5 (4.1212), 314.5 nm (2.1443); MS (70 eV, EI): *m/z* (%): 300.3 (17) [$M^+$], 282.3 (100) [$M^+$ −$H_2O$]; ESI-HRMS: *m/z*: calcd for [$C_{20}H_{28}O_2$+$H^+$]: 301.21621, found: 301.21633.

**(+)-13β-Ethyl-3,3-ethylenedithio-11-methylenegona-4-en-17β-ol (38)**: 1,2-Ethanedithiol (28.0 μL, 31.5 mg, 334 μmol) were added at room temperature to a solution of **36** (67.4 mg, 224 μmol) in methanol (8.0 mL) and $BF_3{\cdot}Et_2O$ (48% in $Et_2O$, 16.5 μL, 127 μmol) and the mixture was stirred for 2.5 h. Saturated aqueous $NaHCO_3$ (5 mL) was added and methanol was evaporated in vacuo. The aqueous residue was diluted with water (20 mL) and extracted with MTBE (3×15 mL). The combined organic layers were dried over $Na_2SO_4$ and the solvent was evaporated in vacuo. Filtration through silica gel (*n*-pentane/EtOAc 7:3) afforded steroid **38** (70.7 mg, 84%) as white solid. $R_f$=0.54 (*n*-pentane/EtOAc 7:3); $[\alpha]_D^{20}$= +159.5 (*c*=1.0 in $CHCl_3$), +168.0 (*c*=0.98 in $C_6H_6$), lit.:[11d] +148.0 (*c*= 1.0 in $CHCl_3$), lit.:[11e] +142.3 (*c*=0.98 in $C_6H_6$); $^1$H NMR (600 MHz, $CDCl_3$): $\delta$=0.89–0.97 (m, 1H, 7-$H_a$), 1.03 (t, *J*=7.5 Hz, 3H, 13-$CH_2CH_3$), 1.19–1.43 (m, 7H, 1-$H_a$, 8H, 9-H, 14-H, 15-$H_a$, 13-$CH_2CH_3$), 1.48 (br s, 1H, 17-OH), 1.50–1.59 (m, 2H, 15-$H_b$, 16-$H_a$), 1.61 (d, *J*=12.3 Hz, 1H, 12-$H_a$), 1.67 (dq, *J*=12.6, 3.3 Hz, 1H, 7-$H_b$), 1.91 (m, 1H, 6-$H_a$), 2.02–2.15 (m, 2H, 2-$H_a$, 16-$H_b$), 2.16–2.26 (m, 3H, 2-$H_b$, 6-$H_b$, 10-H), 2.28–2.34 (m, 1H, 1-$H_b$), 2.80 (d, *J*=12.2 Hz, 1H, 12-$H_b$), 3.21–3.27 (m, 1H, S-$CH_aH_bCH_2$-S), 3.33–3.41 (m, 3H, S-$CH_aH_bCH_2$-S), 3.81 (t, *J*=8.5 Hz, 1H, 17-H), 4.74 (s, 1H, 11-$CH_aH_b$), 4.96 (s, 1H, 11-$CH_aH_b$), 5.64 ppm (d, *J*=1.3 Hz, 1H, 4-H); $^{13}$C NMR (151 MHz, $CDCl_3$): $\delta$=8.95 (13-$CH_2CH_3$), 18.50 (13-$CH_2CH_3$), 22.09 (C-15), 28.59 (C-1), 31.03 (C-16), 31.09 (C-7), 34.91 (C-6), 35.86 (C-10), 39.59, 39.97 (S-$CH_2CH_2$-S), 40.49 (C-2), 41.95 (C-8), 44.40 (C-12), 46.65 (C-13), 52.36, 54.56 (C-9, C-14), 65.76 (C-3), 83.15 (C-17), 108.3 (11-$CH_2$), 126.2 (C-4), 141.6 (C-5), 146.8 ppm (C-11); IR (KBr): $\tilde{\nu}$=3516, 3074, 2927, 1636, 1439, 1275, 1132, 1056, 894, 842, 769, 602 $cm^{-1}$; UV ($CH_3CN$): no absorption; MS (70 eV, EI): *m/z* (%): 379.3 (100) [$M^+$]; ESI-HRMS: *m/z*: calcd for [$C_{22}H_{32}OS_2$+$H^+$]: 377.19673, found: 377.19672.

**(+)-13β-Ethyl-11-methylenegona-4-en-17β-ol (32a)**: ***Method A***: $BF_3{\cdot}EtO_2$ (48% in $Et_2O$, 0.760 mL, 6.04 mmol) was added very fast at room temperature to a solution of steroid **31** (75.7 mg, 221 μmol) in dichloromethane (7.6 mL). After 15 s reaction time, the mixture was quenched under vigorous stirring with saturated aqueous $NaHCO_3$-Lsg (3.0 mL).

Water (10 mL) was added and the mixture was then extracted with dichloromethane (3×5 mL). The combined organic extracts were washed with saturated aqueous NaCl (5 mL), dried over $Na_2SO_4$ and the solvent was evaporated in vacuo. Column chromatography on silica gel (*n*-pentane/EtOAc 4:1) of the residue afforded alcohol **32a** which contained traces of the double bond isomer **32b** (63.4 mg, quant., **32a**/**32b** = 96:4) as white solid.

***Method B***: A solution of steroid **38** (90.9 mg, 241 μmol.) in dry THF (2.0 mL) was slowly added at −40 °C to condensed ammonia (6.0 mL). Small pieces of lithium (21.3 mg, 3.07 mmol) were added portionwise over a period of 30 min, so that the deep blue color of the mixture maintained. Then solid $NH_4Cl$ was slowly added until the color disappeared and the ammonia was distilled off at room temperature. The residue was dissolved in water (15 mL) and MTBE (5 mL), the layers were separated and the aqueous layer was extracted with MTBE (2×10 mL). The combined organic extracts were dried over $Na_2SO_4$, the solvent was removed in vacuo and the residue was subjected to column chromatography on silica gel (*n*-pentane/EtOAc 97:3). Steroid **32a**, which contained small amounts of the double bond isomer **32c** (66.2 mg, 96 %, **32a**/**32c** 92:8) was obtained as white solid. $R_f$ = 0.43 (*n*-pentane/EtOAc 4:1); $[\alpha]_D^{20}$ = +140.2 (*c* = 1.0 in $CHCl_3$) lit.:[11d] +138 (*c* = 1.0 in $CHCl_3$); $^1$H NMR (600 MHz, $CDCl_3$): $\delta$ = 0.83–0.92 (m, 1H, 7-$H_a$), 1.04 (t, *J* = 7.5 Hz, 3H, 13-$CH_2CH_3$), 1.07–1.15 (m, 1H, 1-$H_a$), 1.18–1.46 (m, 7H, 2-$H_a$, 8-H, 9-H, 14-H, 15-$H_a$, 13-$CH_2CH_3$), 1.47–1.68 (m, 6H, 2-$H_b$, 7-$H_b$, 12-$H_a$, 15-$H_b$, 16-$H_a$, 17-OH), 1.90–1.98 (m, 3H, 3-$H_2$, 6-$H_a$), 2.07–2.15 (m, 1H, 16-$H_b$), 2.16–2.28 (m, 3H, 1-$H_b$, 6-$H_b$, 10-H), 2.80 (d, *J* = 12.2 Hz, 1H, 12-$H_b$), 3.91 (t, *J* = 8.5 Hz, 1H, 17-H), 4.75 (s, 1H, 11-C$H_aH_b$), 4.94 (s, 1H, 11-C$H_aH_b$), 5.46 ppm (s, 1H, 4-H); $^{13}$C NMR (126 MHz, $CDCl_3$): $\delta$ = 8.99 (13-$CH_2CH_3$), 18.54 (13-$CH_2CH_3$), 21.93 (C-2), 22.14 (C-15), 25.65 (C-3), 29.12 (C-1), 31.08 (C-16), 31.67 (C-7), 35.51 (C-6), 36.60 (C-10), 42.21 (C-8), 44.55 (C-12), 46.70 (C-13), 52.57 (C-14), 55.06 (C-9), 83.28 (C-17), 108.2 (11-$CH_2$), 121.3 (C-4), 139.9 (C-5), 147.2 ppm (C-11); IR (KBr): $\tilde{\nu}$ = 3356, 2933, 1638, 1436, 1298, 1117, 1056, 910, 893, 805 $cm^{-1}$; UV ($CH_3CN$): $\lambda_{max}$ (lg $\varepsilon$) = 201.5 nm (4.0987); MS (70 eV, EI): *m*/*z* (%): 268.3 (69) [$M^+$], 268.3 (100) [$M^+ - H_2O$]; EI-HRMS: *m*/*z*: calcd for $C_{20}H_{30}O$: 286.2297; found: 286.2300.

**(+)-13β-Ethyl-11-methylenegona-4-en-17-one (39a)**: A solution of steroid **32a** (86.0 mg, 300 μmol, **32a**/**32b** = 96:4) in dichloromethane (8.5 mL) was treated with Dess–Martin periodinane (192 mg, 451 μmol) and stirred for 30 min at room temperature. Saturated aqueous $NaHCO_3$ (1.5 mL) and 10 % aqueous $Na_2S_2O_3$ (1.5 mL) were added and the mixture was stirred for further 45 min. The layers were separated and the aqueous layer was extracted with dichloromethane (3×5 mL). The combined organic extracts were dried over $Na_2SO_4$, the solvent was removed in vacuo and the residue was filtered through a short column of silica gel (*n*-pentane/EtOAc 4:1) to give the ketone **39a** which contained traces of the double bond isomer **39b** (81.8 mg, 96 %, **39a**/**39b** = 96:4) as colorless crystals. $R_f$ = 0.57 (*n*-pentane/EtOAc 9:1); $[\alpha]_D^{20}$ = +168.2 (*c* = 1.0 in $CHCl_3$), lit.:[11a] +166 (*c* = 1.0 in $CHCl_3$); $^1$H NMR (600 MHz, $CDCl_3$): $\delta$ = 0.73 (t, *J* = 7.5 Hz, 3H, 13-$CH_2CH_3$), 0.90–0.98 (m, 1H, 7-$H_a$), 1.06–1.13 (m, 1H, 1-$H_a$), 1.21–1.28 (m, 1H, 13-C$H_aH_bCH_3$), 1.33 (t, *J* = 10.6 Hz, 1H, 9-H), 1.35–1.45 (m, 2H, 2-$H_a$, 8-H), 1.51–1.66 (m, 4H, 2-$H_b$, 14-H, 15-$H_a$, 13-C$H_aH_bCH_3$), 1.75 (dq, *J* = 12.5, 3.4 Hz, 1H, 7-$H_b$), 1.80 (d, *J* = 12.7 Hz, 1H, 12-$H_a$), 1.84–1.98 (m, 4H, 3-$H_2$, 6-$H_a$, 15-$H_b$), 2.08 (dt, *J* = 19.2, 8.7 Hz, 1H, 16-$H_a$), 2.14–2.28 (m, 3H, 1-$H_b$, 6-$H_b$, 10-H), 2.35–2.41 (m, 1H, 16-$H_b$), 2.54 (d, *J* = 12.7 Hz, 1H, 12-$H_b$), 4.80 (s, 1H, 11-C$H_aH_b$), 4.89 (d, *J* = 0.9 Hz, 1H, 11-C$H_aH_b$), 5.46 ppm (s, 1H, 4-H); $^{13}$C NMR (126 MHz, $CDCl_3$): $\delta$ = 7.16 (13-$CH_2CH_3$), 18.04 (13-$CH_2CH_3$), 20.78 (C-15), 21.83 (C-2), 25.60 (C-3), 29.04 (C-1), 30.95 (C-7), 35.26 (C-6), 36.08 (C-16), 36.53 (C-10), 39.59 (C-12), 41.49 (C-8), 52.29 (C-14), 52.94 (C-13), 55.01 (C-9), 110.0 (11-$CH_2$), 121.7 (C-4), 139.4 (C-5), 146.0 (C-11), 218.9 ppm (C-17); IR (KBr): $\tilde{\nu}$ = 2922, 1727, 1635, 1441, 1224, 1082, 1004, 891, 807, 768, 638 $cm^{-1}$; UV ($CH_3CN$): $\lambda_{max}$ (lg $\varepsilon$) = 192.0 nm (4.2561); MS (70 eV, EI): *m*/*z* (%): 284.2 (100) [$M^+$]; EI-HRMS: *m*/*z*: calcd for $C_{20}H_{28}O$: 284.2140; found: 284.2136.

**(+)-13β-Ethyl-17α-ethinyl-11-methylenegona-4-en-17β-ol (desogestrel) (2)**: Acetylene was passed at room temperature into a solution of lithium (61.2 mg, 8.82 mmol) in dry ethylenediamine over a period of 2 h. Then a solution of ketone **39a** (59.6 mg, 210 μmol, **39a**/**39b** 96:4) in dry THF (3.2 mL) was slowly added. Stirring at room temperature was continued for 2 h with the acetylene flow being maintained. The reaction mixture was poured into 2 N HCl (50 mL) and extracted with diethyl ether (4× 20 mL). The combined organic extracts were washed with saturated aqueous NaCl (20 mL), dried over $Na_2SO_4$ and the solvent was removed in vacuo. Purification of the residue by column chromatography on silica gel (*n*-pentane/EtOAc 93:7 → *n*-pentane/EtOAc 9:1) afforded desogestrel (**2**) (54.1 mg, 83 %) as colorless oil, which was crystallized from *n*-pentane. $R_f$ = 0.33 (*n*-pentane/EtOAc 9:1); $[\alpha]_D^{20}$ = +54.5 (*c* = 1.0 in $CHCl_3$), lit.:[12a] +55 (*c* = 1.0 in $CHCl_3$); $^1$H NMR (600 MHz, $CDCl_3$): $\delta$ = 0.89–0.98 (m, 1H, 7-$H_a$), 1.04 (t, *J* = 7.4 Hz, 3H, 13-$CH_2CH_3$), 1.10–1.18 (m, 1H, 1-$H_a$), 1.29–1.39 (m, 3H, 2-$H_a$, 8-H, 9-H), 1.39–1.48 (m, 3H, 2-$H_b$, 13-$CH_2CH_3$), 1.58–1.69 (m, 3H, 7-$H_b$, 15-$H_2$), 1.78 (ddd, *J* = 7.6, 10.3, 12.8 Hz, 1H, 14-H), 1.87 (br s, 1H, 17-OH), 1.91–1.98 (m, 3H, 3-$H_2$, 6-$H_a$), 2.10 (ddd, *J* = 14.0, 12.0, 3.6 Hz, 1H, 16-$H_a$), 2.17–2.27 (m, 3H, 1-$H_b$, 6-$H_b$, 10-H), 2.27 (d, *J* = 12.3 Hz, 1H, 12-$H_a$), 2.34 (ddd, *J* = 14.0, 9.7, 6.0 Hz, 1H, 16-$H_b$), 2.60 (s, 1H, 17-C≡CH), 2.61 (d, *J* = 12.3 Hz, 1H, 12-$H_b$), 4.78 (s, 1H, 11-C$H_aH_b$), 4.98 (s, 1H, 11-C$H_aH_b$), 5.46 ppm (s, 1H, 4-H); $^{13}$C NMR (126 MHz, $CDCl_3$): $\delta$ = 9.13 (13-$CH_2CH_3$), 19.79 (13-$CH_2CH_3$), 21.88, 21.93 (C-2, C-15), 25.67 (C-3), 29.08 (C-1), 31.69 (C-7), 35.51 (C-6), 36.56 (C-10), 39.77 (C-16), 40.59 (C-12), 42.57 (C-8), 50.39 (C-13), 52.39 (C-14), 54.63 (C-9), 74.05 (C-17), 81.12 (17-C≡CH), 87.83 (17-C≡CH), 108.5 (11-$CH_2$), 121.3 (C-4), 139.9 (C-5), 147.5 ppm (C-11); IR (KBr): $\tilde{\nu}$ = 3542, 3286, 3090, 2928, 2872, 1640, 1465, 1337, 1259, 1121, 1033, 898, 808, 675, 631 $cm^{-1}$; UV ($CH_3CN$): no absorption; MS (70 eV, EI): *m*/*z* (%): 310.1 (53) [$M^+$]; EI-HRMS: *m*/*z*: calcd for $C_{22}H_{30}O$: 310.2297; found: 310.2293.

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