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Synthesis of Triaromatic Steroid Hydrocarbons Methylated at Position 2, 3 or 6: Molecular Fossils of Yet Unknown Biological Origin.

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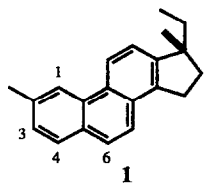
Abstract: C_{21-29} triaromatic steroid hydrocarbons bearing a methyl group at unusual positions 2, 3 or 6 have been synthesized from pregnenolone, cholesterol or stigmasterol *via* stera-3,5-dienes. Their occurrence in various sedimentary rocks and petroleums suggests the presence of yet unknown biological precursors.

INTRODUCTION

After deposition at the bottom of lakes and seas, sedimentary organic matter undergoes various chemical transformations such as dehydration, hydrogenation and aromatization, under the effect of temperature, time and mineral catalysis, leading to the formation of products which are usually less polar and thus easier to analyse than their functionalized biological precursors.[1] The discovery of structurally uncommon substances in sediments may therefore indicate the presence of yet unknown substances in living organisms. For example, the identification of C_{31}-C_{35} hopanes in geological samples has prompted the discovery of novel bacterial lipids such as hopanetetrol.[2] The recent identification of triaromatic steroid hydrocarbons bearing a methyl group at position 2, 3 or 6 (**1-3**) in sedimentary rocks and petroleums[3] is puzzling since possible steroidal precursors are rare in living organisms.[3,4] Moreover, the concomitant occurrence of 3β-alkylsteranes,[5] 3β-carboxysteranes[6] and 3-methyltriaromatic steroid hydrocarbons[3] in various sediments is of particular importance because nearly all biological sterols bear an alcohol group at position 3β which has essential biochemical functions. We wish to report here the synthesis of triaromatic steroid hydrocarbons methylated at unusual positions 2, 3 or 6.



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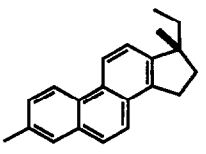
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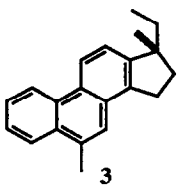
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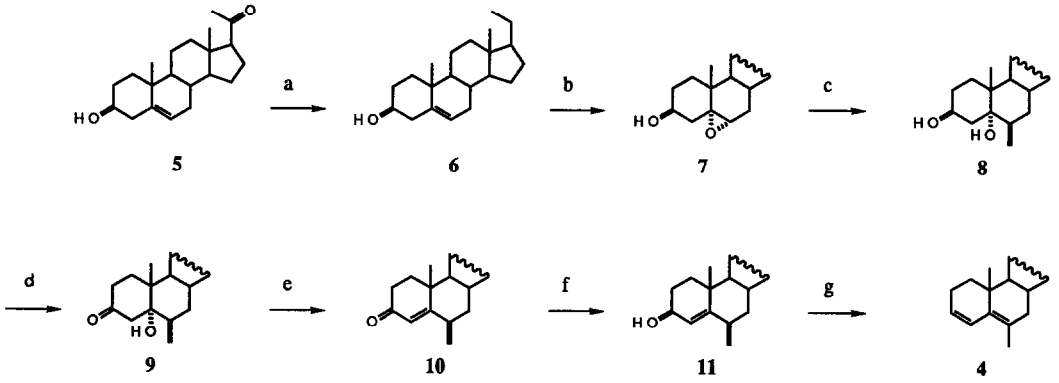
RESULTS AND DISCUSSION

Synthesis of 6-methylpregna-3,5-diene **4**

Wolff-Kishner reduction[7-9] of pregnenolone **5** gave quantitatively the unsaturated alcohol **6** (scheme 1). Epoxidation[10,11] of **6** with metachloroperbenzoic acid led to the epoxide **7**[12] in good yield (93%). The epoxide **7** was further methylated with methyl magnesium iodide[13] in refluxing toluene-diethyl ether. Noteworthy, no conversion was observed during attempts to open the epoxide ring of **7** with methyl magnesium iodide at 0°C or lithium dimethyl copper. The secondary alcohol function of the diol **8** was then selectively oxidized with Jones reagent[14] to give the keto-ol **9**. Ster-5β-ol-3-ones may be dehydrated either in acidic[15] or basic[14] media. Thus, treatment of **9** with *p*-toluenesulfonic acid monohydrate furnished rapidly the α,β-unsaturated ketone **10**. The reduction of cholest-4-en-3-one with lithium aluminium hydride in refluxing diethyl ether is known to give two alcoholic diastereoisomers.[16] Only the more stable 3β-OH epimer **11** was formed by treatment of **10** with lithium aluminium hydride at -78°C.[17] Stera-3,5-diol,[18] ster-4-en-3-ol[19] and ster-5-en-3-ol[20] may be dehydrated in acidic media. Accordingly, the allylic alcohol **11** was rapidly dehydrated with *p*-toluenesulfonic acid monohydrate at room temperature to afford the conjugated 3,5-diene **4**. The absence of other possible dienes, such as 2,4- or 4,6-diene, was confirmed by ^{1}H-NMR analysis.

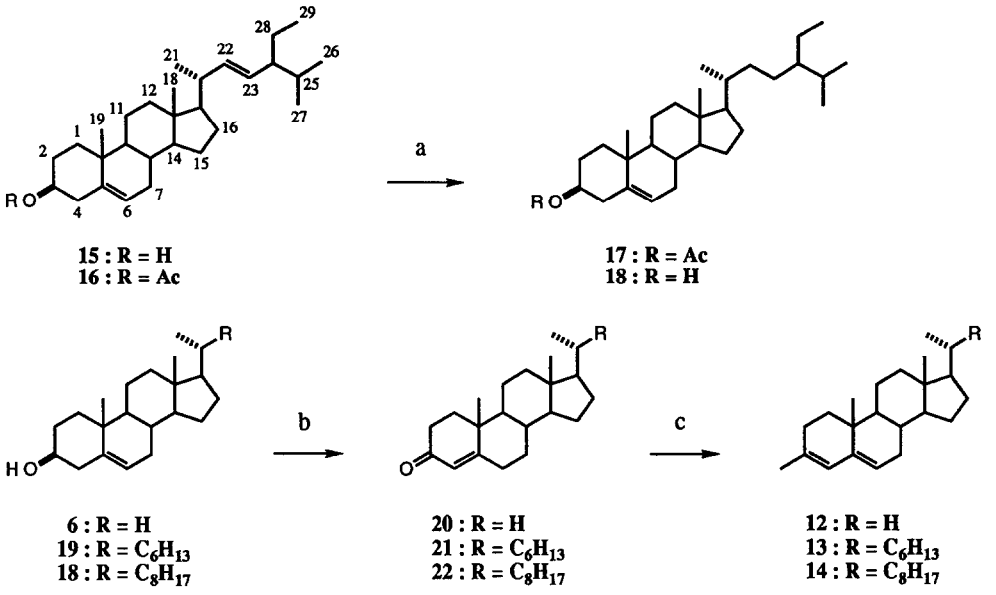


Scheme 1. a) i. N_2H_2, DEG, *n*-BuOH, 130°C, ii. KOH, 220°C; b) MCPBA, CH_2Cl_2; c) MeMgI, Et_2O, toluene, 65°C; d) CrO_3, H_2SO_4, acetone; e) pTsOH, CH_2Cl_2, toluene, 54°C; f) $LiAlH_4$, Et_2O, -78°C; g) pTsOH, toluene.

Synthesis of 3-methylstera-3,5-dienes **12-14**

Acetylation of stigmasterol **15**[21] was followed by selective 22-23 double bond hydrogenation of the acetate **16**[21] over platinum dioxide[22] to give the acetate **17** (scheme 2). This hydrogenation must be carefully followed by thin layer chromatography over silica gel impregnated with silver nitrate to avoid further hydrogenation of the less reactive 5-6 double bond. Subsequent hydrolysis of **17** with potassium hydroxide afforded the unsaturated alcohol **18**.[21] Oppenauer oxidation[23] of pregn-5-en-3β-ol **6**,[7] cholesterol **19**[23] and stigmast-5-en-3β-ol **18**[21] with aluminium *tert*-butoxide furnished the conjugated enones **20-22**. Methylation of cholest-4-en-3-one **21** has been previously performed with methyl magnesium iodide.[19] Treatment of the

enones **20-22** with methyl lithium at -23°C followed by dehydration of allylic alcohol epimers with *p*-toluenesulfonic acid monohydrate gave the 3-methyl-3,5-dienes **12-14** in good overall yields (81-99%).



15 : R = H
16 : R = Ac

17 : R = Ac
18 : R = H

6 : R = H
19 : R = C_6H_{13}
18 : R = C_8H_{17}

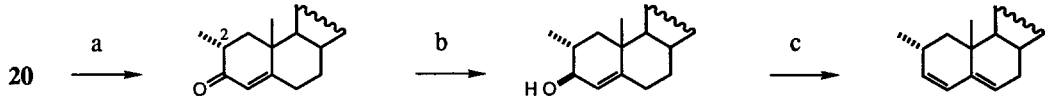
20 : R = H
21 : R = C_6H_{13}
22 : R = C_8H_{17}

12 : R = H
13 : R = C_6H_{13}
14 : R = C_8H_{17}

Scheme 2. a) i. pTsOH, Ac_2O, AcOH, ii. H_2, PtO_2, AcOEt, iii. KOH, MeOH; b) i. $(tBuO)_3Al$, acetone, toluene, 75°C, ii. H_2SO_4, 20°C; c) i. MeLi, Et_2O, -23°C, ii. pTsOH, toluene.

Synthesis of 2α-methyl-3,5-diene **23**

Ster-4-en-3-ones are selectively methylated in the α' position by treatment of the kinetic dienolate with methyl iodide.[24,25] Thus, the α'-methylated enone **24** was obtained from the enone **20** after basic equilibration[25] of the 2ξ-methyl epimers to the more stable 2α position (scheme 3). Noteworthy, these two epimers are separable by gas chromatography. Reduction of the enone **24** with lithium aluminium hydride at -78°C afforded only the unsaturated alcohol **25** which was then dehydrated in acid medium to give the 3,5-diene **23**. ^{1}H-NMR spectrum of **23** shows a doublet for the 2α-methyl group, thus excluding possible 1,3- or 2,4-dienes.



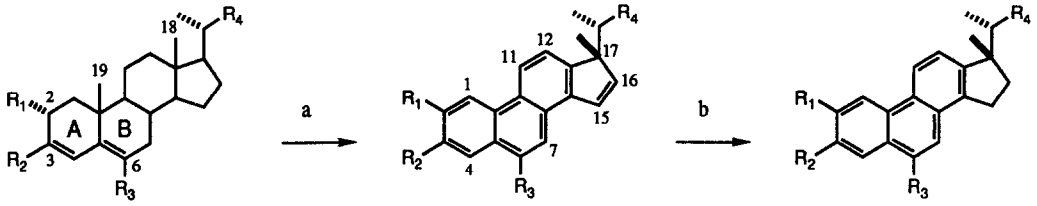
24 **25** **23**

Scheme 3. a) i. (iPr-, cyclohexyl-)NLi, MeI, THF, 0°C, ii. KOH, MeOH, reflux; b) $LiAlH_4$, Et_2O, -78°C; c) pTsOH, toluene.

Synthesis of triaromatic steroid hydrocarbons

The C-19 methyl group of stera-3,5-dienes may be removed by phenanthraquinone dehydrogenation[26] (scheme 4). However dehydrogenation of the methylstera-3,5-dienes **I** led to high proportions of non-demethylated products (33-91%). In order to evaluate the influence of additional methyl groups at position 2, 3 or 6 on the efficiency of C-19 demethylation, this reaction was tested with cholesta-3,5-diene **26**, prepared from cholesterol **19** by elimination of the *p*-toluenesulfonate **27**[27] in basic medium.[28] Dehydrogenation of cholesta-3,5-diene **26** gave only low proportions of non-demethylated products (0-7 %), thus suggesting that the presence of an additional methyl group on ring A or B hinders the removal of the C-19 methyl group.

After phenanthraquinone dehydrogenation[26] of **I**, the crude, a complex mixture of demethylated and non-demethylated polyenes, was treated with chloranil[26] affording octaenes **II** in low overall yields (1-6 %). Noteworthy, octaenes substituted with one chlorine atom were sometimes detected as by-products. The molecular structures of octaenes **II** were unambigously assessed by ^{1}H-NMR with ^{1}H-^{1}H decoupling and nOe experiments. The 15,16 double bond of **II** was then hydrogenated[29] on Pd/C to give triaromatic steroid hydrocarbons **III**. This hydrogenation must be carefully followed by thin layer chromatography over silica gel impregnated with silver nitrate to avoid further hydrogenation. A good correlation is observed between ^{1}H-NMR chemical shifts of methyl groups at position 2 (**1**, 2.62 ppm), 3 (**2**, 2.56 ppm) or 6 (**3**, 2.76 ppm) and those of structurally homologous methylphenanthrenes:[30] 3-methylphenanthrene (2.62 ppm), 2-methylphenanthrene (2.56 ppm) and 9-methylphenanthrene (2.72 ppm), respectively.



I **II** **III**

R_1:	CH_3	H	H	H	H
R_2:	H	CH_3	H	CH_3	CH_3
R_3:	H	H	CH_3	H	H
R_4:	H	H	H	C_6H_{13}	C_8H_{17}
I:	**23**	**12**	**4**	**13**	**14**
II:	**28**	**29**	**30**	**31**	**32**
III:	**1**	**2**	**3**	**33**	**34**

Scheme 4. a) i. Phenanthraquinone, anisole, 155°C, ii. Chloranil, xylene, 144°C; b) H_2, Pd/C, EtOH.

Acknowledgements: this research was supported by the *Institut Français du Pétrole*, the *Institut National de la Recherche Agronomique* and the *Centre National de la Recherche Scientifique*. We are grateful to Drs. J.-M. Trendel, H. Callot and R. Ocampo for helpful discussions and assistance.

EXPERIMENTAL

General

The reactions were followed by thin layer chromatography (**TLC**) on plates (10 cm) precoated with silicagel (0.25 mm) containing fluorescein. Silicagel-$AgNO_3$ plates were prepared by immersion of precoated plates in a solution of 10% silver nitrate in ethanol-water (3:1 v/v) for 45 s. After drying at room temperature (48 h), the plates were heated for 1 h at 120°C. The plates were developed by UV irradiation (254 nm, 365 nm), then immersion in sulfuric acid-ethanol (5%) and heating. Column chromatography (**CC**) was performed on silicagel (0.043-0.060 mm). Gas chromatography (**GC**): fused silica capillary column (30 m, 0.25 mm), phenyl(5%)-methylpolysiloxane phase (0.1 μm), flame ionization detector, H_2 carrier gas (2.5 ml/min.), 50-80°C at 25°/min then 80-300°C at 3°/min. The purity of products was checked by **GC** to be more than 98%, otherwise specified. Mass spectra were recorded on a gas chromatograph-mass spectrometer: **GC** conditions as above except He carrier gas (3.5 ml/min.), electronic impact (70 eV, otherwise specified), ion source 250°C. High performance liquid chromatography (**HPLC**): column (25 cm, 21.2 mm), octadecylsilane phase, methanol eluant (9 ml/min.), refractive index detector.

Elemental analyses (**EA**) were performed at the *service central de microanalyse du C.N.R.S.* (*division de Strasbourg*). Melting points (**mp**) were determined on a heating microscope and are uncorrected. Nuclear magnetic resonance spectra of hydrogen nuclei (**^{1}H-NMR**) were recorded in $CDCl_3$ solutions at 200 MHz. Chemical shifts refer to the signal of tetramethylsilane ($\delta = 0$ ppm) and were determined relative to the residual solvent peak ($CHCl_3$: $\delta = 7.27$ ppm). Coupling constants (J) are measured in Hz. Coupling patterns are described by abbreviations: *s* (singlet), *d* (doublet), *t* (triplet) and *m* (multiplet). Steroids are named according to IUPAC-IUB rules.[31]

Synthesis

1: 2,17-Dimethyl-18,19-dinor-17α-pregna-1,3,5,7,9,11,13-heptaene. Useful literature: ref. 29. CAUTION, reaction mixtures must be purged with argon before and after hydrogenation to avoid explosion (H_2 and O_2). The octaene **28** (7 mg) was dissolved in ethanol (20 ml). A catalytic amount of 10% palladium on charcoal was added and the mixture was hydrogenated under stirring for 0.5 h. The catalyst was removed by filtration (3x). Concentration of the filtrate under reduced pressure gave the heptaene **1** as a colorless oil which solidified upon standing (6.5 mg, 92%). **R_f**: 0.47 (silicagel, hexane), 0.91 (silicagel-$AgNO_3$, CH_2Cl_2). **^{1}H-NMR**: 0.86 (*t*, J 7.4, 3H, 21-CH_3), 1.34 (*s*, 3H, CH_3-17), 1.55-1.83 (*m*, 2H, 20-CH_2), 1.90-2.30 (*m*, 2H, 16-CH_2), 2.62 (*s*, 3H, CH_3-2), 3.26 (*t*, J 7.1-7.5, 2H, 15-CH_2), 7.39 (*dd*, $J_{3,4}$ 8.1, J 1.5, 1H, H-3), 7.41 (*d*, J 8.5, 1H, H-12), 7.68 (*d*, J 9.7, 1H, H-6 or H-7), 7.73 (*d*, J 9.5, 1H, H-7 or H-6), 7.77 (*d*, J 8.2, 1H, H-4), 8.46 (*s*, 1H, H-1), 8.56 (*d*, J 8.5, 1H, H-11). **MS**: m/z (%), 274 (M^+, 20), 259 (M^+-CH_3, 5), 245 (M^+-C_2H_5, 100), 230 (12), 229 (13), 228 (6), 215 (13), 123 (7), 115 (7), 101 (4).

2: 3,17-Dimethyl-18,19-dinor-17α-pregna-1,3,5,7,9,11,13-heptaene. Prepared from **29** as for **1**. Colorless solid (99%). **mp**: 93-95°C (CH_2Cl_2-MeOH). **R_f**: 0.45 (silicagel, hexane), 0.91 (silicagel-$AgNO_3$, CH_2Cl_2). **^{1}H-NMR**: 0.87 (*t*, J 7.4, 3H, 21-CH_3), 1.34 (*s*, 3H, CH_3-17), 1.60-1.80 (*m*, 2H, 20-CH_2), 1.90-2.40 (*m*, 2H, 16-CH_2), 2.56 (*s*, 3H, CH_3-3), 3.27 (*t*, J 7.3, 2H, 15-CH_2), 7.42 (*d*, J 8.4, 1H, H-12), 7.46 (*dd*, $J_{1,2}$ 8.2, J 1.6, 1H, H-2), 7.66 (*s*, 1H, H-4), 7.69 (*d*, J 9.0, 1H, H-6 or H-7), 7.75 (*d*, J 9.1, 1H, H-7 or

H-6), 8.54 (*d*, J 8.4, 1H, H-11), 8.57 (*d*, J 8.5, 1H, H-1). **MS**: m/z (%), 274 (M^+, 20), 259 (M^+-CH_3, 4), 245 (M^+-C_2H_5, 100), 230 (12), 229 (17), 228 (9), 215 (16), 115 (7), 101 (4).

3: 6,17-Dimethyl-18,19-dinor-17α-pregna-1,3,5,7,9,11,13-heptaene. Prepared from **30** as for **1**. Colorless oil which solidified upon standing (99%). **R_f**: 0.44 (silicagel, hexane), 0.89 (silicagel-$AgNO_3$, CH_2Cl_2). **^{1}H-NMR**: 0.86 (*t*, J 7.4, 3H, 21-CH_3), 1.44 (*s*, 3H, CH_3-17), 1.55-1.85 (*m*, 2H, 20-CH_2), 1.90-2.30 (*m*, 2H, 16-CH_2), 2.76 (*s*, 3H, CH_3-6), 3.25 (*t*, J 7.3, 2H, 15-CH_2), 7.37 (*d*, J 8.5, 1H, H-12), 7.60 (*s*, 1H, H-7), 7.55-7.69 (*m*, 2H, H-2, H-3), 8.00-8.08 (*m*, 1H, H-4), 8.54 (*d*, J 8.4, 1H, H-11), 8.68-8.74 (*m*, 1H, H-1). **MS**: m/z (%), 274 (M^+, 20), 259 (M^+-CH_3, 5), 245 (M^+-C_2H_5, 100), 230 (12), 229 (13), 228 (6), 215 (13), 123 (7), 115 (7), 101 (4).

4: 6-Methylpregna-3,5-diene. Prepared from **11** as for **23**. Colorless oil which solidified upon standing (89%). **R_f** (silicagel): 1.00 (CH_2Cl_2), 0.82 (hexane). **^{1}H-NMR**: 0.60 (*s*, 3H, 18-CH_3), 0.93 (*s*, 3H, 19-CH_3), 1.68 (*s*, 3H, CH_3-6), 5.55-5.70 (*m*, 1H, H-3), 6.33 (*d*, J 10.1, 1H, H-4). **MS** (50 eV): m/z (%), 298 (M^+, 100), 283 (M^+-CH_3, 83), 269 (8), 241 (6), 213 (6), 191 (8), 173 (15), 163 (35), 159 (58), 145 (22), 121 (23), 105 (18), 91 (18), 81 (13).

6: Pregn-5-en-3β-ol. Useful literature: refs. 7-9. A stirred solution of 3β-hydroxypregn-5-en-20-one **5** (pregnenolone, 25 g, 79 mmol) in diethylene glycol (500 ml), *n*-butanol (200 ml) and hydrazine hydrate (63 ml, 1264 mmol) was refluxed for 4 h under argon. *n*-Butanol, water and excess of hydrazine hydrate were removed by distillation. After cooling to 80°C, potassium hydroxide (62 g, 1106 mmol) was added slowly and the mixture was heated to 220°C for 4 h then cooled to 20°C. Following addition of water (100 ml) the mixture was extracted with diethyl ether (3x). The combined organic layers were washed with water (3x), dried over sodium sulfate, filtered and concentrated under reduced pressure to give the alcohol **6** as a colorless solid (23.61 g, 99%). **mp**: 132-133°C (MeOH-CH_2Cl_2, lit. 132[7,8],134[9]). **EA**: calc. for $C_{21}H_{34}O$: 83.38% C, 11.33% H; found: 83.47% C, 11.30% H. **R_f** (silicagel): 0.11 (CH_2Cl_2), 0.67 (Et_2O). **R_f** of the intermediary 3β-hydroxypregn-5-en-20-one hydrazone (silicagel): 0.00 (CH_2Cl_2), 0.56 (Et_2O). **^{1}H-NMR**: 0.58 (*s*, 3H, 18-CH_3), 1.02 (*s*, 3H, 19-CH_3), 3.40-3.65 (*m*, 1H, H-3), 5.35 (*d*, J 5, 1H, H-6). **MS**: m/z (%), 302 (M^+, 77), 287 (M^+-CH_3, 41), 284 (M^+-H_2O, 55), 269 (76), 217 (60), 191 (100), 163 (80), 145 (66), 121 (65), 107 (86), 91 (75), 81 (81), 67 (47), 55 (64).

7: 5α,6α-Epoxypregnan-3β-ol. Useful literature: refs. 10-12. To a stirred solution of the alcohol **6** (6 g, 19.83 mmol) in methylene chloride (200 ml) was added dropwise at 15°C a solution of purified[10] metachloroperbenzoic acid (3.77 g, 21.82 mmol) in methylene chloride (50 ml). After 1 h the solution was transfered, washed with a solution of sodium carbonate (5%, 2x) then brine (3x), dried over sodium sulfate, filtered and concentrated under reduced pressure to give **7** as a pale-green solid (5.90 g, 93%). **mp**: 145-149°C (acetone-water, lit. 160[12]). **EA**: calc. for $C_{21}H_{34}O_2$: 79.19% C, 10.76% H; found: 79.38% C, 10.80% H. **R_f**: 0.47 (silicagel, Et_2O). **^{1}H-NMR**: 0.51 (*s*, 3H, 18-CH_3), 1.06 (*s*, 3H, 19-CH_3), 2.90 (*d*, J 4.4, 1H, H-6), 3.80-4.10 (*m*, 1H, H-3). **MS**: m/z (%), 318 (M^+, 49), 300 (M^+-H_2O, 35), 285 (25), 247 (28), 153 (43), 149 (39), 135 (40), 123 (62), 109 (51), 93 (60), 81 (75), 67 (55), 55 (100), 41 (92).

8: 6β-Methylpregnane-3β,5α-diol. Useful literature: ref. 13. To the Grignard reagent prepared from methyl iodide (18 ml, 290.4 mmol), magnesium (7.06 g, 290.4 mmol) and anhydrous diethyl ether (200 ml) was added the epoxide **7** (18.5 g, 58.08 mmol) in dry toluene (300 ml) under stirring. The solution was refluxed for 3 h, cooled to 0°C and quenched slowly with a saturated solution of ammonium chloride (200 ml).

The organic layer was separated. The aqueous layer was extracted with diethyl ether (2x). The combined organic layers were washed with water (2x), dried over magnesium sulfate, filtered and concentrated under reduced pressure to give an impure (TLC) pale-yellow solid (20 g). Recrystallisation (2x) from acetone-hexane gave the diol **8** as a colorless solid (11.73 g, 60%). **mp** 184-185°C (needles). **EA**: calc. for $C_{22}H_{38}O_2$: 78.99% C, 11.45% H; found: 78.05% C, 11.57% H. **R_f**: 0.37 (silicagel, Et_2O). **^{1}H-NMR**: 0.58 (*s*, 3H, 18-CH_3), 1.04 (*d*, J 9, 3H, CH_3-6β), 1.06 (*s*, 3H, 19-CH_3), 4.00-4.40 (*m*, 1H, H-3). **MS**: m/z (%), 316 (M^+-H_2O, 57), 301 (85), 298 (85), 283 (100), 262 (74), 159 (60), 121 (68), 105 (92), 95 (58), 81 (85), 55 (90), 41 (79).

9: 5α-Hydroxy-6β-methylpregnan-3-one. Useful literature: ref. 14. To a stirred solution of 6β-methylpregnane-3β,5α-diol **8** (6.48 g) in acetone (500 ml) and methylene chloride (200 ml), was added dropwise at 0°C Jones reagent until the orange color did not disappear. Following addition of methanol (200 ml), diethyl ether (400 ml) and water (600 ml), the organic layer was separated. The aqueous layer was extracted with diethyl ether (2x). The combined organic layers were washed with water (2x), dried over sodium sulfate, filtered and concentrated under reduced pressure to give the keto-ol **9** as a colorless solid (6.43 g, 99%). **mp**: 232-233°C (CH_2Cl_2-MeOH, plates). **EA**: calc. for $C_{22}H_{36}O_2$: 79.46% C, 10.91% H; found: 79.55% C, 11.12% H. **R_f**: 0.83 (silicagel, Et_2O). **^{1}H-NMR**: 0.61 (*s*, 3H, 18-CH_3), 1.08 (*d*, J 7.7, 3H, CH_3-6β), 1.25 (*s*, 3H, 19-CH_3), 2.02 (*d*, J 14.8, 1H, H-4), 2.30-2.45 (*m*, 2H, H-2), 3.00 (*d*, J 14.8, 1H, H-4). **MS**: m/z (%), 332 (M^+, 8), 317 (M^+-CH_3, 17), 289 (9), 275 (13), 262 (100), 261 (37), 247 (16), 163 (17), 123 (18), 109 (19), 95 (22), 81 (29), 55 (36), 43 (78), 41 (30).

10: 6β-Methylpregn-4-en-3-one. Useful literature: ref. 15. A stirred solution of the keto-ol **9** (6.2 g, 18.64 mmol), *p*-toluenesulfonic acid monohydrate (3.55 g, 18.64 mmol) in toluene (200 ml) and methylene chloride (200 ml) was refluxed for 1 h under argon then cooled to 20°C. Following addition of a saturated solution of sodium hydrogencarbonate (70 ml), methylene chloride (200 ml) and water (300 ml), the organic layer was separated. The aqueous layer was extracted with methylene chloride (2x). The combined organic layers were washed with water (3x), dried over sodium sulfate, filtered and concentrated under reduced pressure to give the ketone **10** as a pale-yellow solid (4.6 g, 78%). **mp**: 113-114°C (acetone-methanol, needles). **EA**: calc. for $C_{22}H_{34}O$: 84.02% C, 10.90% H; found: 84.25% C, 10.89% H. **R_f** (silicagel): 0.36 (CH_2Cl_2). **^{1}H-NMR**: 0.61 (*s*, 3H, 18-CH_3), 1.06 (*d*, J 6.4, 3H, CH_3-6β), 1.18 (*s*, 3H, 19-CH_3), 2.3-2.5 (*m*, 3H, H-2 and H-6), 5.78 (*d*, J 1.6, 1H, H-4). **MS** (50 eV): m/z (%), 314 (M^+, 49), 299 (M^+-CH_3, 100), 281 (14), 243 (18), 241 (11), 191 (15), 175 (27), 161 (16), 133 (13), 123 (11), 81 (11), 55 (16).

11: 6β-Methylpregn-4-en-3β-ol. Prepared from **10** as for **25**. Colorless solid (99%). **mp**: 116-120°C (MeOH). **EA**: calc. for $C_{22}H_{36}O$: 83.48% C, 11.46% H; found: 83.41% C, 11.53% H. **R_f**: 0.17 (silicagel, CH_2Cl_2). **^{1}H-NMR**: 0.58 (*s*, 3H, 18-CH_3), 0.99 (*d*, J 6.5, 3H, CH_3-6β), 1.05 (*s*, 3H, 19-CH_3), 4.10-4.30 (*m*, 1H, H-3), 5.25 (*d*, J 1.7, 1H, H-4). **MS** (50 eV): m/z (%), 316 (M^+, 17), 298 (M^+-H_2O, 72), 283 (39), 269 (11), 246 (29), 245 (39), 231 (23), 217 (17), 190 (16), 175 (28), 159 (28), 135 (23), 121 (54), 105 (100), 91 (40), 81 (37), 67 (26), 55 (30).

12: 3-Methylpregna-3,5-diene. Useful literature: refs. 18,19. To a stirred solution of the enone **20** (5.6 g, 18.51 mmol) in anhydrous diethyl ether (250 ml) was added dropwise a solution of methyllithium (40.73 mmol) in hexane (25 ml) under argon at -23°C. The mixture was warmed to 0°C then quenched slowly with a saturated solution of ammonium chloride (30 ml), then water (100 ml). The organic layer was separated. The aqueous layer was extracted with diethyl ether (2x). The combined organic layers were washed with water (3x),

dried over magnesium sulfate, filtered and concentrated under reduced pressure to give a mixture of 3-ξ-methylpregn-4-en-3-ols as a colorless solid (5.85 g). **Rf**: 0.16, 0.32 (silicagel, CH_2Cl_2). A mixture of these epimers (5.84 g 18.45 mmol) and *p*-toluenesulfonic acid monohydrate (4.21 g, 22.14 mmol) in toluene (130 ml) was stirred under argon for 2 h then quenched with a saturated solution of sodium hydrogencarbonate. The organic layer was separated. The aqueous layer was extracted with toluene (2x). The combined organic layers were washed with water (3x), dried over sodium sulfate, filtered and concentrated under reduced pressure to give the diene **12** (5.51 g, 99%) as a colorless solid. **mp:** 85-89°C (CH_2Cl_2-MeOH). **EA**: calc. for $C_{22}H_{34}$: 88.52% C, 11.48% H; found: 88.58% C, 11.54% H. **Rf** (silicagel): 0.68 (hexane), 1.00 (CH_2Cl_2). **^{1}H-NMR**: 0.61 (*s*, 3H, 18-CH_3), 0.94 (*s*, 3H, 19-CH_3), 1.73 (s, 3H, CH_3-3), 5.25-5.35 (*m*, 1H, H-6), 5.71 (*s*, 1H. H-4). **MS**: m/z (%), 298 (M^+, 100), 283 (M^+-CH_3, 17), 163 (32), 135 (14), 122 (18), 119 (14), 105 (11), 91 (11), 81 (11).

13: 3-Methylcholesta-3,5-diene. Useful literature: refs. 18,19. Prepared from **21** as for **12**. Colorless solid (98%). **mp**: 78-78.5°C (CH_2Cl_2-MeOH, lit. 77[18], 79[19]). **EA**: calc. for $C_{28}H_{46}$: 87.88% C, 12.12% H; found: 87.90% C, 11.86% H. **Rf** (silicagel): 0.66 (hexane), 1.00 (CH_2Cl_2). **Rf** of intermediary 3ξ-methylcholest-4-en-3-ols: 0.80, 0.89 (silicagel, Et_2O). **^{1}H-NMR**: 0.70 (*s*, 3H, 18-CH_3), 0.862 (*d*, J 6.6, 3H, 26-CH_3 or 27-CH_3), 0.865 (*d*, J 6.5, 3H, 26-CH_3 or 27-CH_3), 0.916 (*d*, J 6.3, 3H, 21-CH_3), 0.924 (*s*, 3H, 19-CH_3), 1,72 (*s*, 3H, CH_3-3), 5,29 (*d*, J 3.3, 1H, H-6), 5.70 (*s*, 1H, H-4). **MS**: m/z (%), 382 (M^+, 100), 377 (M^+-CH_3, 14), 269 (4), 247 (8), 227 (4), 159 (13), 147 (21), 135 (16), 119 (15), 107 (13), 95 (21), 81 (23), 69 (9), 55 (16), 43 (21), 41 (14).

14: 3-Methylstigmasta-3,5-diene. Prepared from **22** as for **12**. Colorless solid (81%). **mp**: 102-103°C (CH_2Cl_2-MeOH). **Rf** (silicagel): 0.65 (hexane), 1.00 (CH_2Cl_2). **EA**: calc. for $C_{30}H_{50}$: 87.73% C, 12.27% H; found: 87.64% C, 12.25% H. **^{1}H-NMR**: 0.70 (*s*, 3H, 18-CH_3), 0.811 (*d*, J 6.8, 3H, 26-CH_3 or 27-CH_3), 0.834 (*d*, J 6.8, 3H, 26-CH_3 or 27-CH_3), 0.843 (*t*, J 7.3, 3H, 29-CH_3), 0.923 (*d*, J 6.4, 3H, 21-CH_3), 0.924 (*s*, 3H, 19-CH_3), 1.72 (*s*, 3H, CH_3-3), 5.29 (*d*, J 3.4, 1H, H-6), 5.70 (*s*, 1H, H-4). **MS**: m/z (%), 410 (M^+, 100), 395 (M^+-CH_3, 10), 275 (4), 269 (4), 227 (4), 159 (10), 147 (18), 135 (12), 119 (12), 107 (10), 95 (17), 81 (17), 69 (7), 57 (13), 55 (13), 43 (23), 41 (11).

16: (22E)-Stigmasta-5,22-dien-3β-ol acetate. Useful literature: refs. 21,32. Commercial (22E)-stigmasta-5,22-dien-3β-ol **15** (stigmasterol, 95%, Aldrich) was recrystallised from ethyl acetate[32] to give needles, **mp** 166-168°C (lit. 169[32,33]). **Rf**: 0.14 (silicagel, CH_2Cl_2). **^{1}H-NMR**: 0.70 (*s*, 3H, 18-CH_3), 0.77-0.86 (*m*, 9H, 26-CH_3, 27-CH_3, 29-CH_3), 1.01 (*s*, 3H, 19-CH_3), 1.02 (*d*, J 5, 3H, 21-CH_3), 3.40-3.65 (*m*, 1H, H-3), 5.01 (*dd*, $J_{22\text{-}23}$ 15.7, J 8.2, 1H, H-22 or H-23), 5.16 (*dd*, $J_{22\text{-}23}$ 15.7, J 8.2, 1H, H-22 or H-23), 5.35 (*d*, J 5.2, 1H, H-6). **MS**: m/z (%), 412 (M^+, 45), 397 (M^+-CH_3, 5), 394 (M^+-H_2O, 32), 379 (7), 369 (13), 351 (20), 300 (18), 271 (23), 255 (44), 159 (27), 145 (27), 133 (28), 123 (19), 105 (28), 97 (34), 83 (75), 81 (62), 69 (58), 55 (100), 43 (41), 41 (37). A stirred solution of **15** (20.6 g), *p*-toluenesulfonic acid monohydrate (0.2 g) in acetic acid (200 ml) and acetic anhydrid (60 ml) was refluxed for 1 h then cooled to 20°C. Following addition of water (200 ml), the mixture was extracted with diethyl ether (3x). The combined organic layers were washed with a saturated solution of sodium hydrogencarbonate (1x), water (2x), dried over sodium sulfate, filtered and concentrated under reduced pressure to give **16** as a colorless solid (22.24 g, 98%). **mp**: 141-143°C (CH_2Cl_2-MeOH, plates, lit. 140[21], 143[32]). **EA**: calc. for $C_{31}H_{50}O_2$: 81.88% C, 11.83% H; found: 81.97% C, 11.99% H. **Rf**: 0.46 (silicagel-$AgNO_3$, CH_2Cl_2). **^{1}H-NMR**: 0.69 (*s*, 3H, 18-CH_3), 0.76-0.86 (*m*, 9H, 26-CH_3, 27-

CH_3, 29-CH_3), 1.02 (*s*, 3H, 19-CH_3), 1.02 (*d*, J 6.6, 3H, 21-CH_3), 2.03 (*s*, 3H, 2'-CH_3), 4.5-4.7 (*m*, 1H, H-3), 5.00 (*dd*, $J_{22\text{-}23}$ 15.1, J 8.1, 1H, H-22 or H-23), 5.16 (*dd*, $J_{22\text{-}23}$ 15.1, J 8.1, 1H, H-22 or H-23), 5.37 (*d*, J 4.1, 1H, H-6).

17: Stigmast-5-en-3β-ol acetate. Useful literature: refs. 21,22. CAUTION, the reaction mixtures must be purged with argon before and after hydrogenation to avoid explosion (H_2 and O_2). To a solution of (22E)-stigmasta-5,22-dien-3β-ol acetate **16** (20.5 g) in anhydrous ethyl acetate (350 ml) was added a catalytic amount of platinum dioxide and the mixture was hydrogenated with stirring for 3 h. The catalyst was removed by filtration (3x). Concentration of the filtrate under reduced pressure gave **17** as a colorless solid (17.62 g, 86%). **mp** 117-120°C (CH_2Cl_2-MeOH, lit. 125[21]). Purity: 91% (GC). **EA**: calc. for $C_{31}H_{52}O_2$: 81.52% C, 11.48% H; found: 81.88% C, 11.61% H. **R_f**: 0.63 (silicagel-$AgNO_3$, CH_2Cl_2). **^{1}H-NMR**: 0.68 (*s*, 3H, 18-CH_3), 0.79-0.88 (*m*, 9H, 26-CH_3, 27-CH_3, 29-CH_3), 0.92 (*d*, J 6.4, 3H, 21-CH_3), 1.02 (*s*, 3H, 19-CH_3), 2.03 (*s*, 3H, 2'-CH_3), 4.5-4.7 (*m*, 1H, H-3), 5.38 (*d*, J 4.6, 1H, H-6).

18: Stigmast-5-en-3β-ol. Useful literature: ref. 21. A stirred mixture of the acetate **17** (17 g, 37.22 mmol), potassium hydroxide (20.88 g, 372.2 mmol) in methanol (300 ml) was refluxed 1 h and cooled to 20°C. Following addition of ice (200 g), the mixture was extracted with diethyl ether (3x). The combined organic layers were washed with water (4x), dried over sodium sulfate, filtered and concentrated under reduced pressure to give **18** as a colorless solid (13.81 g, 89%). **mp**: 137-138°C (CH_2Cl_2-MeOH, needles, litt. 133[21],138[32]). Purity: 90% (GC). **EA**: calc. for $C_{29}H_{50}O$: 83.99% C, 12.15% H; found: 83.22% C, 12.29% H. **R_f**: 0.17 (silicagel, CH_2Cl_2). **^{1}H-NMR**: 0.68 (*s*, 3H, 18-CH_3), 0.809 (*d*, J 6.8, 3H, 26-CH_3 or 27-CH_3), 0.831 (*d*, 6.8, 3H, 26-CH_3 or 27-CH_3), 0.841 (*t*, J 7.2, 3H, 29-CH_3), 0.92 (*d*, J 6.4, 3H, 21-CH_3), 1.01 (*s*, 3H, 19-CH_3), 3.40-3.65 (*m*, 1H, H-3), 5.35 (*d*, J 5.4, 1H, H-6). **MS**: m/z (%), 414 (M^+, 30), 399 (M^+-CH_3, 10), 396 (M^+-H_2O, 100), 381 (33), 329 (9), 303 (11), 286 (7), 275 (16), 265 (24), 213 (18), 159 (22), 145 (37), 133 (19), 121(23), 105 (32), 95 (31), 81 (45), 57 (40), 55 (44), 43 (68), 41 (34).

20: Pregn-4-en-3-one. Useful literature: refs. 7,23,34. A mixture of pregn-5-en-3β-ol **6** (9.6 g, 31.74 mmol), aluminium *tert*-butylate (11.73 g, 47.60 mmol) in anhydrous acetone (70 ml) and toluene (170 ml) was refluxed for 9 h then cooled to 20°C. Following slow addition of water (30 ml) and 10% sulfuric acid (60 ml, 10%), the organic layer was separated. The aqueous layer was extracted with toluene (3x). The combined organic layers were washed with water (3x), dried over sodium sulfate, filtered and concentrated under reduced pressure to give a yellow oil (7.89 g). Chromatography (CC, ethyl acetate-hexane 15% v/v) gave an unidentified solid (0.51 g) then the enone **20** as a pale-yellow solid (7.3 g, 77%). **mp:** 102-103°C (MeOH, lit. 101[34], 102[7]). **EA**: calc. for $C_{21}H_{32}O$: 83.94% C, 10.73% H; found: 83.85% C, 10.53% H. **R_f** (silicagel): 0.64 (ethyl acetate-hexane 30:70 v/v), 0.85 (Et_2O). **^{1}H-NMR**: 0.62 (*s*, 3H, 18-CH_3), 1.19 (*s*, 3H, 19-CH_3), 2.2-2.6 (*m*, 4H, H-2 and H-6), 5.73 (*d*, J 1.7, 1H, H-4). **MS** (10 eV): m/z (%), 300 (M^+, 87), 275 (M^+-CH_3, 7), 258 (43), 229 (8), 215 (13), 177 (46), 163 (19), 136 (24), 124 (100).

21: Cholest-4-en-3-one. Useful literature: ref. 23. Prepared from **19** as for **20**. Pale-yellow solid (77%). **mp**: 73-77°C (toluene-acetone, lit. 77[23]). **EA**: calc. for $C_{27}H_{44}O$: 84.31% C, 11.53% H; found: 84.15% C, 11.71% H. **R_f**: 0.50 (silicagel, ethyl acetate-hexane 30% v/v). **^{1}H-NMR**: 0.70 (*s*, 3H, 18-CH_3), 0.859 (*d*, J 6.5, 6H, 26-CH_3, 27-CH_3), 0.905 (*d*, J 6.5, 3H, 21-CH_3), 1.17 (*s*, 3H, 19-CH_3), 2.2-2.6 (*m*, 4H, H-2, H-6), 5.52 (*s* , 1H, H-4). **MS**: m/z (%), 384 (M^+, 61), 369 (M^+-CH_3, 9), 342 (22), 327 (5), 299 (8), 271 (8), 261 (25), 229 (40), 147 (19), 135 (21), 124 (100), 107 (20), 95 (28), 81 (22), 69 (19), 55 (40), 43 (45), 41.

22: Stigmast-4-en-3-one. Useful literature: refs. 21,23. Prepared from **18** as for **20**. Pale-yellow solid (78%). **mp**: 80-81°C (CH_2Cl_2-MeOH, lit. 80[21]). **R_f**: 0.66 (silicagel, ethyl acetate-hexane 30% v/v). **EA**: calc. for $C_{29}H_{48}O$: 84.40% C, 11.72% H; found: 84.61% C, 11.81%. **^{1}H-NMR**: 0.71 (*s*, 3H, 18-CH_3), 0.807 (*d*, J 6.8, 3H, 26-CH_3 or 27-CH_3), 0.830 (*d*, J 6.8, 26-CH_3 or 27-CH_3), 0.839 (*t*, J 7.3, 3H, 29-CH_3), 0.912 (*d*, J 6.4, 3H, 21-CH_3), 1.18 (*s*, 3H, 19-CH_3), 2.2-2.6 (*m*, 4H, H-2 and H-6), 5.72 (*s*, 1H, H-4). **MS**: m/z (%), 412 (M^+, 71), 397 (M^+-CH_3, 8), 370 (23), 355 (6), 327 (7), 289 (21), 288 (14), 171 (11), 229 (38), 187 (7), 147 (19), 135 (20), 124 (100), 107 (19), 95 (26), 81 (20), 69 (21), 57 (27), 55 (40), 43 (61), 41 (29).

23: 2α-Methylpregna-3,5-diene. Useful literature: refs. 18-20. A mixture of the alcohol **25** (1.90 g, 6.00 mmol) and *p*-toluenesulfonic acid monohydrate (1.37 g, 7.20 mmol) in dry toluene (50 ml) was stirred for 1.5 h under argon. Following addition of a saturated solution of sodium hydrogencarbonate (10 ml) and water (20 ml), the organic layer was separated. The aqueous layer was extracted with toluene (2x). The combined organic layers were washed with water (3x), dried over sodium sulfate, filtered and concentrated under reduced pressure to give the diene **23** (1.6 g, 89%) as a colorless solid. **mp**: 83-85°C (CH_2Cl_2-MeOH). **EA**: calc. for $C_{22}H_{34}$: 88.52% C, 11.48% H, found: 88.51% C, 11.51 % H. **R_f** (silicagel): 0.82 (hexane), 1.00 (CH_2Cl_2). **^{1}H-NMR**: 0.61 (*s*, 3H, 18-CH_3), 0.97 (*s*, 9H, 19-CH_3), 0.998 (*d*, J 7.1, 3H, CH_3-2α), 5.35-5.50 (*m*, 2H, H-3, H-6), 5.89 (*dd*, $J_{3,4}$ 9.9, J 2.6, H-4). **MS**: m/z (%), 298 (M^+, 100), 283 (M^+-CH_3, 30), 176 (22), 163 (46), 159 (26), 121 (36), 119 (38), 105 (48), 95 (30), 91 (31), 81 (35), 67 (22), 55 (36), 41 (38).

24: 2α-Methylpregn-4-en-3-one. Useful literature: refs. 24,25. To a stirred solution of isopropylcyclohexylamine (2.13 ml, 12.94 mmol) in anhydrous tetrahydrofuran (5 ml) at 0°C under argon was added dropwise a solution of butyllithium (12.44 mmol) in hexane (7.8 ml) and a solution of pregn-4-en-3-one **20** (2.99 g, 9.95 mmol) in tetrahydrofuran (13 ml). After 0.5 h, methyl iodide (2.48 ml, 39.8 mmol) was added, then the mixture was warmed to 17°C and stirred for 3 h. Following slow addition of water (30 ml) the organic layer was separated. The aqueous layer was extracted with diethyl ether (2x). The combined organic layers were washed with water (3x), dried over sodium sulfate, filtered and concentrated under reduced pressure to give a mixture of 2ξ-methylpregn-4-en-3-ones (74% of 2β- based on **GC**) as a yellow oil which solidified upon standing (3.2 g). A stirred solution of these epimers (3.2 g) in methanol (530 ml) was treated with potassium hydroxide (1.07 g), refluxed for 3 h, cooled to 17°C and concentrated to 100 ml under reduced pressure. Following addition of water (70 ml) the mixture was extracted with diethyl ether (3x). The combined organic layers were washed with water (3x), dried over sodium sulfate, filtered and concentrated under reduced pressure to give the enone **24** (3.00 g, 96%) as a pale-yellow solid. **mp**: 117-119°C (MeOH). **EA**: calc. for $C_{22}H_{34}O$: 84.02% C, 10.90% H; found: 84.29% C, 11.11% H. **R_f** (silicagel): 0.46 (CH_2Cl_2), 0.80 (ethyl acetate-hexane 30% v/v). **^{1}H-NMR**: 0.61 (*s*, 3H, 18-CH_3), 1.10 (*d*, J 6.6, 3H, CH_3-2α), 1.21 (*s*, 3H, 19-CH_3), 2.2-2.6 (*m*, 3H, H-2, H-6), 5.70 (*d*, J 1.4, 1H, H-4). **MS**: m/z (%), 314 (M^+, 84), 299 (M^+-CH_3, 11), 285 (M^+-C_2H_5, 8), 272 (16), 258 (77), 243 (19), 230 (27), 219 (50), 177 (58), 163 (23), 138 (100), 135 (31), 121 (21), 107 (35), 93 (34), 81 (40), 67 (34), 55 (50), 41 (52).

25: 2α-Methylpregn-4-en-3β-ol. Useful literature: ref. 17. To a stirred suspension of lithium aluminium hydride (1.11 g, 29.25 mmol) in anhydrous diethyl ether (30 ml) was added dropwise a solution of the enone **24** (2.3 g, 7.313 mmol) in diethyl ether (30 ml) at -78°C. After 2 h the mixture was warmed to 0°C and quenched slowly with ethyl acetate (20 ml), methanol (50 ml) and water (30 ml). Following addition of diethyl ether (50 ml), the organic layer was separated. The aqueous layer was extracted with diethyl ether (2x). The

combined organic layers were washed with water (3x), dried over sodium sulfate, filtered and concentrated under reduced pressure to give the enol **25** as a colorless solid (2.26 g, 98%). **mp**: 160-161.5°C (MeOH, needles). **EA**: calc. for $C_{22}H_{36}O$: 83.48% C, 11.46% H; found: 83.57% C, 11.71% H. R_f: 0.27 (silicagel, CH_2Cl_2). **^{1}H-NMR**: 0.58 (*s*, 3H, 18-CH_3), 1.042 (*d*, J 6.1, 3H, CH_3-2α), 1.050 (*s*, 3H, 19-CH_3), 3.66 (*d*, J 8.7, 1H, H-3), 5.22 (*s*, 1H, H-4). **MS**: m/z (%), 316 (M^+, 2), 298 (M^+-H_2O, 2), 283 (21), 269 (7), 173 (16), 163 (25), 132 (24), 120 (73), 119 (59), 105 (89), 95 (35), 91 (30), 81 (32), 67 (22), 55 (34), 41 (37).

26: Cholesta-3,5-diene. Useful literature: ref. 28. To a stirred solution of the tosylate **27** (10 g, 18.49 mmol) in anhydrous toluene (30 ml) was added a solution of potassium *tert*-butylate (14.03 g, 125 mmol) in dimethylsulfoxide (250 ml). After 6 h the precipitate was separated by filtration, washed with methanol (0°C) to give the diene **26** as colorless needles (5.85 g, 86 %). **mp**: 75-77°C (lit. 78[28],79[19]). **EA**: calc. for $C_{27}H_{44}$: 87.97% C, 12.03% H; found: 87.75% C, 12.03% H. R_f (silicagel): 0.71 (hexane), 1.00 (CH_2Cl_2). **MS**: m/z (%), 368 (M^+, 100), 353 (M^+-CH_3, 14), 260 (14), 255 (17), 247 (26), 213 (13), 159 (16), 147 (39), 145 (34), 133 (16), 121 (19), 107 (25), 93 (25), 91 (25), 81 (47), 67 (22), 55 (31), 43 (40).

27: Cholest-5-en-3β-ol *p*-toluenesulfonate. Useful literature: ref. 27. A solution of *p*-toluenesulfonyl chloride (10.85 g, 56.90 mmol) and cholest-5-en-3β-ol **19** (cholesterol, 20 g, 51.73 mmol) in pyridine (50 ml) was stirred 12 h. Following addition of water (100 ml), the mixture was extracted with diethyl ether (3x). The combined organic layers were washed with water (3x), dried over sodium sulfate, filtered and concentrated under reduced pressure to give **27** as a colorless solid (24.58 g, 88%). **mp**: 128-130°C (CH_2Cl_2-MeOH, lit. 132[27]). **EA**: calc. for $C_{34}H_{52}O_3S$: 75.51% C, 9.69% H; found: 75.66% C, 9.59% H. R_f: 0.84 (silicagel, CH_2Cl_2). **^{1}H-NMR**: 0.65 (*s*, 3H, 18-CH_3), 0.856 (*d*, J 6.8, 6H, 26-CH_3, 27-CH_3), 0.892 (*d*, J 7.7, 3H, 21-CH_3), 0.96 (*s*, 3H, 19-CH_3), 1.56 (*s*, 3H, *p*-CH_3), 4.20-4.45 (*m*, 1H, H-3), 5.29 (*d*, J 3.7, 1H, H-6), 7.33 (*d*, J 8.2, 2H, *m*-H), 7.80 (*d*, J 8.4, 2H, *o*-H).

28: 2,17-Dimethyl-18,19-dinor-17α-pregna-1,3,5,7,9,11,13,15-octaene. Useful literature: ref. 26. A stirred mixture of the diene **23** (0.9 g, 3.015 mmol) and 9,10-phenanthrenedione (phenanthraquinone, 4.2 g, 20.20 mmol) in anhydrous anisole (41 ml) was refluxed for 24 h in the dark under argon, cooled to 60°C and filtered over alumina eluting with cyclohexane. CAUTION, overnight heating was performed in a sand bath (no oil bath). Concentration of the filtrate under reduced pressure (azeotropic distillation with toluene) gave a dark yellow oil (2 g). Flash chromatography[35] (silicagel, hexane) of this oil gave a yellow oil (0.7 g) at R_f = 0.6-0.7 (silicagel, ethyl acetate-hexane 5% v/v) which was analysed by **GC** and **GC-MS**: major components of this oil are $C_{21}H_{20}$ (10%), $C_{21}H_{22}$ (9%), $C_{21}H_{24}$ (25%), $C_{22}H_{22}$ (9%), $C_{22}H_{22}$ (20%), $C_{22}H_{24}$ (4%), $C_{22}H_{26}$ (3%), $C_{22}H_{26}$ (17%) and $C_{22}H_{32}$ (3%). A stirred mixture of this oil (0.7 g, *ca* 2.5 mmol) and chloranil (4.12 g, 16.75 mmol) in dry xylene (32 ml) was refluxed for 24 h in the dark under argon, cooled to 60°C and filtered over alumina eluting cyclohexane. Concentration of the filtrate under reduced pressure gave a yellow oil (0.56 g). Flash chromatography[35] (silicagel, hexane) of this oil gave a yellow oil which solidified upon standing (53 mg). R_f: 0.3-0.4 (silicagel, hexane). The major components of this oil are (**GC**, **GC-MS**): $C_{18}H_{18}$ (8%), $C_{21}H_{20}$ (29%), $C_{21}H_{19}Cl$ (7%), $C_{22}H_{22}$ (28%), $C_{22}H_{22}$ (2%), $C_{22}H_{21}Cl$ (4%), $C_{22}H_{21}Cl$ (22%). **HPLC** of this oil gave the octaene **28** (14 mg, 1.7%) as a colorless solid. **mp**: 148-149°C (CH_2Cl_2-MeOH). R_f: 0.41 (silicagel, hexane), 0.77 (silicagel-$AgNO_3$, CH_2Cl_2). **^{1}H-NMR**: 0,65 (*t*, J 7.4, 3 H, 21-CH_3), 1.40 (*s*, 3H, CH_3-17), 1.70-2.05 (*m*, 2H, 20-CH_2), 2.63 (*s*, 3H, CH_3-2), 6.54 (*d*, J 5.6, 1H, H-16), 7.31 (*d*, J 5.7, 1H, H-15), 7.40 (*dd*, J_{3-4} 8.0, J 1.3, 1H, H-3), 7.57 (*d*, J 8.3, 1H, H-12), 7.72 (*d*, J 8.9, 1H, H-6), 7.78 (*d*, J

8.1, 1H, H-4), 7.95 (*d*, J 9.0, 1H, H-7), 8.48 (*s*, 1H, H-1), 8.55 (*d*, J 8.4, 1H, H-11). **MS**: m/z (%), 272 (M^+, 100), 257 (M^+-CH_3, 78), 243 (M^+-C_2H_5, 40), 239 (17), 228 (33), 226 (13), 215 (5), 202 (3), 136 (4), 129 (7), 121 (7), 119 (10), 113 (7), 107 (4), 101 (3).

29: 3,17-Dimethyl-18,19-dinor-17α-pregna-1,3,5,7,9,11,13,15-octaene. Prepared from **12** as for **28**. Phenanthraquinone dehydrogenation: $C_{21}H_{24}$ (6%), $C_{21}H_{26}$ (3%), $C_{22}H_{24}$ (6%), $C_{22}H_{26}$ (72%), $C_{22}H_{28}$ (13%). Chloranil dehydrogenation : $C_{21}H_{20}$ (2%), $C_{22}H_{22}$ (88%), $C_{22}H_{22}$ (2%), $C_{22}H_{24}$ (8%). **HPLC** of this mixture gave the octaene **29** as a colorless solid (25 mg, 0.5%). **mp**: 108-112°C ($CHCl_3$-MeOH). **R_f**: 0.42 (silicagel, hexane), 0.76 (silicagel-$AgNO_3$, CH_2Cl_2). **^{1}H-NMR**: 0.66 (*t*, J 7.4, 3H, 21-CH_3), 1.40 (*s*, 3H, CH_3-17), 1.75-2.10 (*m*, 2H, 20-CH_2), 2.57 (*s*, 3H, CH_3-3), 6.54 (*d*, J 5.6, 1H, H-16), 7.31 (*d*, J 5.6, 1H, H-15), 7.47 (*dd*, $J_{1\text{-}2}$ 8.4, J 1.9, 1H, H-2), 7.58 (*d*, J 8.4, 1H, H-12), 7.68 (*s*, 1H, H-4), 7.70 (*d*, J 9.2, 1H, H-6), 8.00 (*d*, J 8.9, 1H, H-7), 8.53 (*d*, J 8.2, 1H, H-11), 8.59 (*d*, J 8.6, 1H, H-1). **MS**: m/z (%) : 272 (M^+, 89), 257 (M^+-CH_3, 100), 243 (M^+-C_2H_5, 48), 242 (24), 239 (23), 228 (36), 226 (18), 215 (12), 136 (8), 120 (8), 113 (9).

30: 6,17-Dimethyl-18,19-dinor-17α-pregna-1,3,5,7,9,11,13,15-octaene. Prepared from **4** as for **28**. Phenanthraquinone dehydrogenation: $C_{21}H_{20}$ (8%), $C_{21}H_{22}$ (16%), $C_{21}H_{24}$ (38%), $C_{22}H_{22}$ (8%), $C_{22}H_{26}$ (10%), $C_{22}H_{32}$ (15%), unidentified compound (5%). Chloranil dehydrogenation: $C_{21}H_{20}$ (27%), $C_{21}H_{19}Cl$ (38%), $C_{22}H_{22}$(9%), $C_{22}H_{21}Cl$ (20%), unidentified compounds (6%). **HPLC** of this mixture gave the pure octaene **30** as a colorless oil which solidified upon standing (15 mg, 1.7%). **R_f**: 0.39 (silicagel,hexane), 0.75 (silicagel-$AgNO_3$, CH_2Cl_2). **^{1}H-NMR**: 0.65 (*t*, J 7.4, 3H, 21-CH_3), 1.40 (*s*, 3H, CH_3-17), 1.70-2.07 (*m*, 2H, 20-CH_2), 2.78 (*s*, 3H, CH_3-6), 6.53 (*d*, J 5.6, 1H, H-16), 7.32 (*d*, J 5.6, 1H, H-15), 7.54 (*d*, J 8.3, 1H, H-12), 7.55-7.73 (*m*, 2H, H-2, H-3), 7.87 (*s*, 1H, H-7), 8.01-8.12 (*m*, 1H, H-4), 8.53 (*d*, J 8.4, 1H, H-11), 8.68-8.79 (*m*, 1H, H-1). **MS**: m/z (%), 272 (M^+, 100), 257 (M^+-CH_3, 78), 243 (M^+-C_2H_5, 40), 239 (18), 228 (36), 226 (13), 215 (6), 202 (3), 136 (3), 128 (5), 121 (8), 119 (10), 114 (8), 101 (5).

31: 3,17-Dimethyl-18,19-dinor-17α-cholesta-1,3,5,7,9,11,13,15-octaene. Prepared from **13** as for **28**. Phenanthraquinone dehydrogenation: $C_{27}H_{34}$ (4%), $C_{27}H_{36}$ (32%), $C_{27}H_{38}$ (12%), $C_{28}H_{34}$ (4%), $C_{28}H_{36}$ (1%), $C_{28}H_{36}$ (8%), $C_{28}H_{38}$ (23%), $C_{28}H_{40}$ (4%), $C_{28}H_{44}$ (12%). Chloranil dehydrogenation: $C_{27}H_{32}$ (44%), $C_{28}H_{34}$ (46%), $C_{28}H_{34}$ (3%), unidentified compound (7%). **HPLC** of this mixture gave the octaene **31** as a colorless solid (174 mg, 6.5%). **mp**: 144-145°C (CH_2Cl_2-MeOH). **R_f**: 0.33 (silicagel, hexane), 0.46 (silicagel-$AgNO_3$, CH_2Cl_2). **^{1}H-NMR**: 0.57 (*d*, J 6.7, 3H, 21-CH_3), 0.876 (*d*, J 6.5, 3H, 26-CH_3 or 27-CH_3), 0.880 (*d*, J 6.5, 3H, 26-CH_3 or 27-CH_3), 1.39 (*s*, 3H, CH_3-17), 2.56 (*s*, 3H, CH_3-3), 6.53 (*d*, J 5.6, 1H, H-16), 7.32 (*d*, J 5.6, 1H, H-15), 7.46 (*dd*, $J_{1\text{-}2}$ 8.5, J 1.5, 1H, H-2), 7.57 (*d*, J 8.4, 1H, H-12), 7.67 (*s*, 1H, H-4), 7.69 (*d*, J 9.1, 1H, H-6), 7.99 (*d*, J 8.9, 1H, H-7), 8.50 (*d*, J 8.3, 1H, H-11), 8.57 (*d*, J 8.5, 1H, H-1). **MS**: m/z (%), 356 (M^+, 47), 341 (M^+-CH_3, 5), 271 (M^+-C_6H_{13}, 100), 256 (6), 244 (47), 243 (28), 228 (25), 71 (5), 57 (11), 43 (16), 41 (8).

32: 3,17-Dimethyl-18,19-dinor-17α-stigmasta-1,3,5,7,9,11,13,15-octaene. Prepared from **14** as for **28**. Phenanthraquinone dehydrogenation: $C_{29}H_{38}$ (7%), $C_{29}H_{40}$ (7%), $C_{30}H_{38}$ (6%), $C_{30}H_{40}$ (7%), $C_{30}H_{42}$ (39%), $C_{30}H_{48}$ (34%). Chloranil dehydrogenation: $C_{29}H_{36}$ (9%), $C_{30}H_{38}$ (71%), $C_{30}H_{38}$ (11%), $C_{30}H_{37}Cl$ (9%). **HPLC** of this mixture gave the octaene **32** as a colorless solid (6.2 mg, 2.2%). **mp**: 110-111°C ($CHCl_3$-MeOH). **R_f**: 0.42 (silicagel, hexane), 0.75 (silicagel-$AgNO_3$, CH_2Cl_2). **^{1}H-NMR**: 0.55 (*d*, J 6.8, 3H, 21-CH_3), 0.821 (*d*, J 6.8, 3H, 26-CH_3 or 27-CH_3), 0.858 (*t*, J 7.4, 3H, 29-CH_3), 0.868 (*d*, J 6.8, 3H,

26-CH_3 or 27-CH_3), 1.40 (*s*, 3H, CH_3-17), 2.56 (*s*, 3H, CH_3-3), 6.54 (*d*, J 5.6, 1H, H-16), 7.33 (*d*, J 5.6, 1H, H-15), 7.46 (*dd*, J_{1-2} 8.4, J 1.5, 1H, H-2), 7.57 (*d*, J 8.3, 1H, H-12), 7.67 (*s*, 1H, H-4), 7.69 (*d*, J 9.1, 1H, H-6), 7.99 (*d*, J 8.9, 1H, H-7), 8.51 (*d*, J 8.6, 1H, H-11), 8.57 (*d*, J 8.6, 1H, H-1). **MS**: m/z (%), 384 (M^+, 51), 379 (M^+-CH_3, 2), 271 (M^+-C_8H_{17}, 100), 256 (6), 244 (35), 243 (20), 228 (20), 85 (10), 71 (13), 69 (3), 57 (15), 55 (7), 43 (34), 41 (8).

33: 3,17-Dimethyl-18,19-dinor-17α-cholesta-1,3,5,7,9,11,13-heptaene. Prepared from **31** as for **1**. Colorless solid (98%). **mp**: 140-142°C (CH_2Cl_2-MeOH). **R_f**: 0.38 (silicagel, hexane), 0.85 (silicagel-$AgNO_3$, CH_2Cl_2). **^{1}H-NMR**: 0.75 (*d*, J 6.7, 3H, 21-CH_3), 0.88 (*d*, J 6.5, 6H, 26-CH_3, 27-CH_3), 1.34 (*s*, 3H, CH_3-17), 1.7-2.4 (*m*, 2H, 16-CH_2), 2.56 (*s*, 3H, CH_3-3), 3.26 (*t*, J 7.4, 2H, 15-CH_2), 7.41 (*d*, J 8.6, 1H, H-12), 7.46 (*dd*, J_{1-2} 8-9, J 1.5, 1H, H-2), 7.66 (*s*, 1H, H-4), 7.68 (*d*, J 8.6, 1H, H-6 or H-7), 7.75 (*d*, J 9.2, 1H, H-7 or H-6), 8.52 (*d*, J 8.3, 1H, H-11), 8.57 (*d*, J 8.4, 1H, H-1). **MS**: m/z (%), 358 (M^+, 4), 245 (M^+-C_8H_{17}, 100), 230 (7), 229 (6), 215 (7), 57 (2), 55 (1), 43 (5), 41 (3).

34: 3,17-Dimethyl-18,19-dinor-17α-stigmasta-1,3,5,7,9,11,13-heptaene. Prepared from **32** as for **1**. Colorless solid (99%). **mp**: 109-110°C (CH_2Cl_2-MeOH). **R_f**: 0.48 (silicagel, hexane), 0.93 (silicagel-$AgNO_3$, CH_2Cl_2). **^{1}H-NMR**: 0.72 (*d*, J 6.7, 3H, 21-CH_3), 0.814 (*d*, J 6.7, 3H, 26-CH_3 or 27-CH_3), 0.847 (*d*, J 6.7, 3H, 26-CH_3 or 27-CH_3), 0.847 (*t*, J 7.3, 3H, 29-CH_3), 1.33 (*s*, 3H, CH_3-17), 1.7-2.4 (*m*, 2H, 16-CH_2), 2.54 (*s*, 3H, CH_3-3), 3.24 (*t*, J 7.4, 2H, 15-CH_2), 7.39 (*d*, J 8.6, 1H, H-12), 7.41-7.47 (*m*, 1H, H-2), 7.64 (*s*, 1H, H-4), 7.66 (*d*, J 8.6, 1H, H-6 or H-7), 7.72 (*d*, J 9.2, 1H, H-7 or H-6), 8.50 (*d*, J 8.3, 1H, H-11), 8.55 (*d*, J 8.4, 1H, H-1). **MS**: m/z (%), 386 (M^+, 4), 245 (M^+-$C_{10}H_{21}$, 100), 230 (7), 229 (5), 216 (3), 215 (6), 57 (1), 55 (1), 43 (5), 41 (2).

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