5α-PREGNA-1,20-DIEN-3-ONE AND RELATED COMPOUNDS FROM A SOFT CORAL

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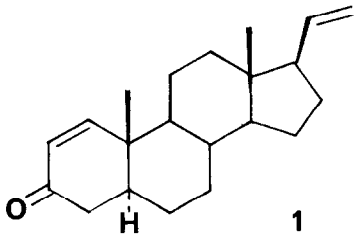
ABSTRACT

Four unusual pregnane derivatives, 5α-pregna-1,20-dien-3-one (1), 1,4,20-pregnatrien-3-one (3), 5α-pregn-20-en-3α-ol 3-acetate (4), and 5α-pregn-20-en-1α,3α-diol 3-acetate (6) have been isolated from an unidentified soft coral from Canton Island.

The alcyonaceans (soft corals) are a rich source of sesquiterpenes [1] and cembrane diterpenes [2]. Several polyhydroxylated steroids have recently been isolated from soft corals [3]. We wish to report the structural elucidation of four pregnane derivatives which were isolated, together with a complex mixture of common 3β-hydroxysterols, from an unidentified [4] soft coral collected at Canton Island.

The ether-soluble material from a methanol extract of soft coral was chromatographed on Florisil to obtain four steroids having the pregnane skeleton. The major pregnane derivative was shown to be 5α-pregna-1,20-dien-3-one (1). The ketone 1, mp 127-8°, had the molecular formula $C_{21}H_{30}O$. The uv absorption at 229 nm (ε = 9,630) and ir band at 1686 cm^{-1} both suggested the presence of an α,β-unsaturated ketone. The pmr spectrum contained signals at δ 7.16 (d, 1H, J = 10 Hz) and 5.86 (d, 1H, J = 10 Hz) for the protons on the conjugated olefin. Assuming a normal steroid skeleton, these signals can arise only from a 1-en-3-one system. A complex series of signals at δ 5.77 (m, 1H, J = 17, 11, 7 Hz), 5.00 (m, 1H, J = 11, 2.5, 1 Hz), 4.98 (m, 1H. J = 17, 2.5, 1 Hz), and 1.98 (m) were assigned to the protons of a vinyl group at C-17. Due to the small

difference in chemical shift between the protons at C-21, the spectrum was analyzed using an ITRCAL program to obtain the chemical shifts and coupling constants. The methyl group signals at δ 1.01 (C-19) and 0.62 (C-18) were at the expected positions for the dienone 1 [5]. The cmr spectrum was also compatible with that structure.



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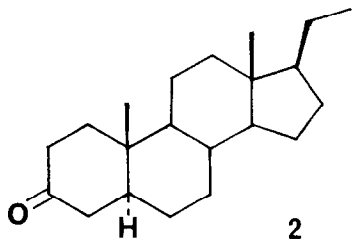

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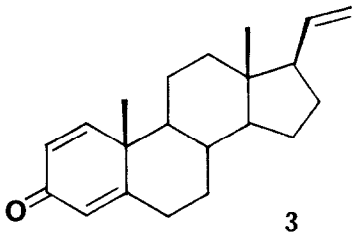

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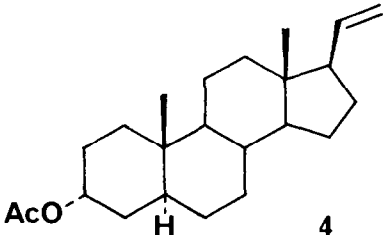
Hydrogenation of 1 over 2% palladium on charcoal gave a saturated ketone, mp 113-4°, which was identical in all respects to 5α-pregnan-3-one (2) [6]. The stereochemistry of 1 must therefore be as shown, with a 17β-vinyl group. The structure of 5α-pregna-1,20-dien-3-one (1) was confirmed by synthesis [7]. Comparison of the CD curves of synthetic and natural material showed that the two samples had the same absolute configuration.

1,4,20-Pregnatrien-3-one (3) was isolated as one of three minor products. The trienone 3, mp 167-8°, had the molecular formula $C_{21}H_{28}O$. The uv absorption at 244 nm (ε = 12,770) and the ir bands at 1654, 1622

and 1604 cm^{-1} were indicative of a cross-conjugated dienone. The pmr spectrum contained signals at δ 0.66 (3H) and 1.23 (3H) due to the methyl groups, 4.95 (m, 1H), 5.00 (m, 1H) and 5.75 (m, 1H) for the vinyl group, and 6.07 (bs, 1H), 6.23 (dd, 1H) and 7.08 (d, 1H). We observed a 2 Hz coupling constant between the protons at C-2 (δ 6.23) and C-4 (δ 6.07), a typical coupling constant for the two α-protons in a cross-conjugated dienone.

Hydrogenation of the dienone 3 over 2% palladium on charcoal gave 5α-pregnan-3-one (2). Oxidation of the α,β-unsaturated ketone 1 with DDQ in refluxing benzene [8] gave the cross-conjugated dienone 3, together with recovered starting material.

The least polar of the minor constituents was shown to be 5α-pregn-20-en-3α-ol 3-acetate (4). The acetate 4, mp 129-130°, had the molecular formula $C_{23}H_{26}O_2$. The ir band at 1730 cm^{-1}, together with a pmr signal at δ 2.05 (s, 3H), suggested the presence of an acetoxy group. The pmr spectrum also contained signals at δ 0.59 (s, 3H) and 0.80 (s, 3H) due to the methyl groups, 4.98 (m, 1H), 5.00 (m, 1H) and 5.56 (m, 1H) for the vinyl group, and 5.02 (m, 1H) due to the 3β proton.



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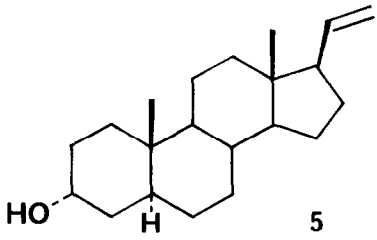

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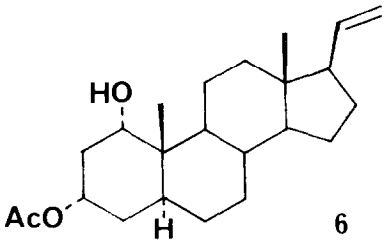
The acetate 4 was reduced with lithium aluminum hydride in ether to obtain the corresponding alcohol 5, which was in turn oxidized to a ketone with Jones reagent. The ketone was hydrogenated over 2% palladium on

charcoal to obtain 5α-pregnan-3-one (2). The pmr spectrum of the alcohol 5 contained a broad multiplet ($W_{1/2}$ (D_2O added) = 10 Hz) for the 3β proton, indicating that the proton must be equatorial [9]. Thus the corresponding acetate must be 5α-pregn-20-en-3α-ol 3-acetate (4).

The remaining minor product was identified as 5α-pregn-20-en-1α,3α-diol 3-acetate (6). The crystalline acetoxy alcohol, mp 104-5°, had the molecular formula $C_{23}H_{36}O_3$. The ir spectrum indicated the presence of hydroxyl (3550 cm^{-1}) and acetate (1745 cm^{-1}) groups. The pmr spectrum contained methyl signals at δ 0.57 (s, 3H), 0.81 (s, 3H) and 2.07 (s, 3H, acetate) and signals at 2.45 (d, 1H, J = 9 Hz, OH), 3.67 (br d, 1H, J = 9, 2.5, 2.5 Hz) due to the 1β proton, 5.30 (m, 1H) for the 3β proton, and 4.97, 4.99 and 5.77 ppm assigned to the vinyl group.



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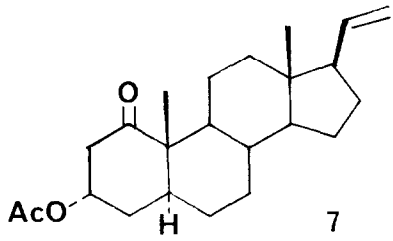

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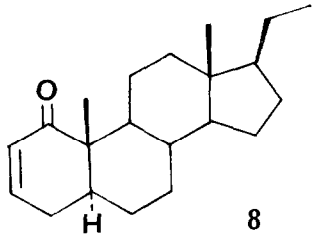

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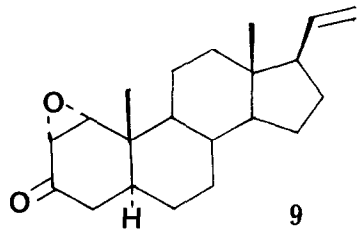

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Oxidation of the acetoxy alcohol 6 with chromium trioxide in pyridine gave an acetoxy ketone 7. The pmr spectrum contained signals at δ 2.30 (dt, 1H, J = 13, 2.5, 2.5 Hz) and 2.94 (dd, 1H, J = 13, 4.5 Hz) due to the protons at C-2. Both signals were coupled to the 3β proton signal at δ 5.08 (m, 1H).

The acetoxy ketone 7 was treated with potassium t-butoxide in t-butanol to obtain an α,β-unsaturated ketone 8, which was not identical to 1. The pmr spectrum contained olefinic signals at δ 5.82 (dt, 1H, J = 10, 2, 2 Hz, C-2) and 6.64 (dt, 1H, J = 10, 2, 4 Hz, C-3).

In order to confirm the structure of the α,β-unsaturated ketone 8, it was synthesized from the known α,β-unsaturated ketone 1 by standard procedures. The α,β-unsaturated ketone 1 was treated with hydrogen peroxide in aqueous dioxan to obtain a mono-epoxide 9. The epoxide 9 was treated with hydrazine hydrate at 100°C and the resulting allylic alcohol oxidized with Jones reagent to obtain the α,β-unsaturated ketone 8 in 35% overall yield [10].

In addition to the four pregnane derivatives, the soft coral also contained a "normal" array of 3β-hydroxy sterols, which were not investigated further. We were unable to find either sesquiterpenes or cembrane diterpenes, the typical secondary metabolites of soft corals, in this sample.

EXPERIMENTAL

Melting points were measured on a Fisher-Johns apparatus and are reported uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on Varian HR-220 and CFT-20 instruments respectively. Infrared and ultraviolet spectra were recorded on Perkin-Elmer models 136 and 124 spectrophotometers respectively. Optical rotations were measured on a Perkin-Elmer 141 polarimeter, using a 10 cm cell thermostated at 20°C. Low resolution mass spectra were recorded on a Hewlett-Packard 5930-A mass spectrometer. High resolution mass measurements were obtained

from the Analytical Facility at California Institute of Technology. All solvents used were either spectral grade or redistilled from glass prior to use.

COLLECTION, EXTRACTION AND CHROMATOGRAPHIC SEPARATION

The unidentified soft coral was collected by SCUBA (-6 m) at Canton Island (2°50'S, 171°42'W) in October 1976. The air-dried coral (335 g) was twice homogenized in methanol, the slurry filtered, and the solvent removed to yield a deep-red semi-solid. The crude extract was partitioned between ether and water to obtain an ether extract which was dried over sodium sulfate and the solvent evaporated to yield a red gum (4.25 g). The solid residues were exhaustively Soxhlet extracted, using methanol, and the extract was treated as before to obtain additional crude extract (1.25 g).

The combined crude extracts (5.5 g, 1.64% dry weight) were applied to a column (50 cm x 4 cm dia.) containing Florisil (100/120 mesh) in hexane, and the material was eluted with solvents of increasing polarity from hexane to methanol. Elution with 50% diethyl ether in hexane gave a fraction (469 mg) which was rechromatographed on alumina (II), using 5% ethyl acetate in ether as eluant, to obtain 5α-pregn-20-en-3α-ol 3-acetate (4) (80 mg, 0.024% dry weight). The material (1.26 g) which was eluted with 2% ethyl acetate in ether was rechromatographed on silica gel, using chloroform as eluant, to obtain 5α-pregna-1,20-dien-3-one (1) (506 mg, 0.15% dry weight) and 5α-pregn-20-en-1α,3α-diol 3-acetate (6) (146 mg, 0.44% dry weight). A fraction which was eluted with 5% ethyl acetate in ether was rechromatographed on silica gel, using chloroform as eluant, to obtain 1,4,20-pregnatrien-3-one (3) (151 mg, 0.45% dry weight).

(5α,14α,17β)-Pregna-1,20-dien-3-one (1) was obtained as white needles from methanol, mp 127-128°C; $[\alpha]_D^{20}$ + 39.5° (c = 1.1, $CHCl_3$); CD $[\theta]_{337}$ = 4770 (MeOH); λ_{max} (EtOH) 229 nm (9,630); ν_{max} 1686, 1644 cm^{-1}; ^1H nmr, δ ($CDCl_3$) 0.62 (s, 3H), 1.01 (s, 3H), 1.98 (m, 1H), 2.21 (dd, 1H, J = 17, 4 Hz), 2.41 (dd, 1H, J = 17, 14 Hz), 4.98 (m, 1H, J = 17, 2.5, 1.3 Hz), 5.00 (m, 1H, J = 11, 2.5, 1 Hz), 5.77 (m, 1H, J = 17, 11, 7 Hz), 5.86 (d, 1H, J = 10 Hz), 7.16 (d, 1H, J = 10 Hz); ^{13}C nmr, δ ($CDCl_3$) 211.9 (s), 158.4 (d), 139.5 (d), 127.4 (d), 114.7 (t), 55.8 (d), 55.3 (d), 50.3 (d), 44.4 (d), 43.7 (s), 41.0 (t), 37.4 (t), 35.8 (t), 31.4 (t), 27.7 (t), 27.2 (t), 24.6 (t), 20.8 (t), 13.0 (2q); MS, m/e (rel. abundance) 298 (17), 283 (22), 122 (100), 91 (71), 79 (91). High resolution mass measurement, found 298.231 ± 0.010, $C_{21}H_{30}O$ requires 298.230.

(14α,17β)-1,4,20-Pregnatrien-3-one (3) was obtained as white needles from aqueous acetone, mp 167-168°C; $[\alpha]_D^{20}$ +36.9° (c = 1.0, $CHCl_3$); λ_{max} (EtOH) 244 nm (12,770); ν_{max} 1654, 1622, 1604 cm^{-1}; ^1H nmr, δ ($CDCl_3$) 0.66 (s, 3H), 1.23 (s, 3H), 4.95 (m, 1H, J = 17, 2.5, 1.3 Hz), 5.00 (m, 1H, J = 11, 2.5, 1 Hz), 5.75 (m, 1H, J = 17, 11, 7 Hz), 6.07 (br s, 1H), 6.23 (dd, 1H, J = 10, 2 Hz), 7.08 (d, 1H, J = 10 Hz); ^{13}C nmr, δ ($CDCl_3$) 186.1 (s), 169.0 (s), 155.7 (d), 139.0 (d), 127.2 (d), 123.6 (d), 114.7 (t), 54.9 (d), 54.4 (d), 52.5 (d), 43.5 (2s), 36.9 (t), 35.5 (d), 33.5 (t), 32.7 (t), 26.9 (t), 24.7 (t), 22.3 (t), 18.5 (q), 12.7 (q); MS, m/e (rel. abundance) 296 (4), 122 (100), 91 (36), 79 (33). High resolution mass measurement, found 296.215 ± 0.010, $C_{21}H_{28}O$ requires 296.214.

(5α,14α,17β)-Pregn-20-en-3α-ol 3-acetate (4) was isolated as white needles from methanol, mp 129-130°C; $[\alpha]_D^{20}$ +9.4° (c = 0.8, $CHCl_3$); ν_{max} 1730, 1642 cm^{-1}; ^1H nmr, δ ($CDCl_3$) 0.59 (s, 3H), 0.80 (s, 3H), 1.96 (m, 1H), 2.05 (s, 3H), 4.98 (m, 1H, J = 17, 2.5, 13 Hz), 5.00 (m, 1H, J = 11, 2.5, 1 Hz), 5.02 (m, 1H), 5.56 (m, 1H, J = 17, 11, 7 Hz); ^{13}C nmr, δ ($CDCl_3$) 171.5 (s), 139.8 (d), 114.4 (t), 70.02 (d), 55.7, 55.3, 54.5, 43.5, 40.0, 37.5, 35.8, 35.4, 32.9 (2C), 32.0, 28.3, 27.1, 26.0, 24.6, 21.4, 20.3, 12.8 (q), 12.27 (q); MS, m/e (rel. abundance) 344 (25), 284 (4), 215 (42), 79 (64), 43 (100). High resolution mass measurement, found 344.270 ± 0.010, $C_{23}H_{36}O_2$ requires 344.271.

(5α,14α,17β)-Pregn-20-en-1α,3α-diol 3-acetate (6) was obtained as white crystals from aqueous acetone, mp 104-105°; $[\alpha]_D^{20}$ +51.1° (c = 1.06, $CHCl_3$); ν_{max} 3550, 1745, 1639 cm^{-1}; ^1H nmr, δ ($CDCl_3$) 0.57 (s, 3H), 0.81 (s, 3H), 2.04 (m, 1H), 2.07 (s, 3H), 2.45 (d, 1H, J = 9 Hz, exchanges in D_2O), 3.67 (m, 1H, J = 2.5, 2.5 Hz, D_2O added), 4.97 (m, 1H, J = 17, 2.5, 1.3 Hz), 4.99 (m, 1H, J = 11, 2.5, 1 Hz), 5.30 (m, 1H, J = 3, 3, 3, 3 Hz), 5.77 (m, 1H, J = 16, 11, 7 Hz); ^{13}C nmr δ ($CDCl_3$) 167.4 (s), 139.7 (d), 114.3 (t), 71.5 (d), 70.8 (d), 55.5 (d), 55.3 (d), 47.1 (d), 43.5 (s), 40.2 (s), 37.2 (t), 35.4 (t), 32.9, 32.5, 31.9, 31.6, 28.2, 27.0, 24.7, 21.4 (q), 19.6 (t), 12.8 (q), 12.3 (q); MS, m/e (rel. abundance) 360 (5), 300 (6), 282 (21), 79 (74), 43 (100). High resolution mass measurement, found 360.267 ± 0.010, $C_{23}H_{36}O_3$ requires 360.266.

Hydrogenation of 5α-Pregna-1,20-dien-3-one (1)

A solution of 5α-pregna-1,20-dien-3-one (1) (40 mg, 0.13 mmol) in ether (20 ml) containing 2% palladium on charcoal catalyst (5 mg) was stirred under an atmosphere of hydrogen for 8 hours at room temperature. The catalyst was removed by filtration through celite and the solvent evaporated *in vacuo* to yield 5α-pregnan-3-one (2) as a white solid (38 mg, 95% theoretical). Recrystallization from methanol gave white needles, mp 113-114°C (Lit. 115°C [6]); $[\alpha]_D^{20}$ +36° (c = 0.85, $CHCl_3$); ν_{max} 1718 cm^{-1}; ^1H nmr, δ ($CDCl_3$) 0.56 (s, 3H), 1.00 (s, 3H), 2.04 (m, 2H), 2.29 (m, 2H); ^{13}C nmr, δ ($CDCl_3$) 211.9, 55.8, 54.3, 53.1, 46.8, 44.7, 42.2, 38.7, 38.2, 38.0, 35.8, 35.5, 31.9, 29.3, 29.0, 28.2, 24.5, 23.1, 13.3, 12.6, 11.5; MS, m/e (rel. abundance) 302 (3), 232 (29), 231 (26), 81 (72), 55 (100). High resolution mass measurement, found 302.258 ± 0.010, $C_{21}H_{34}O$ requires 302.261.

Hydrogenation of 1,4,20-Pregnatrien-3-one (3)

A solution of 1,4,20-pregnatrien-3-one (3) (3 mg, 0.007 mmol) in ether was hydrogenated according to the procedure above to obtain 5α-pregnan-3-one (2 mg), mp 113-114°; $[\alpha]_D^{20}$ + 25° (c = 0.2, $CHCl_3$).

Conversion of 5α-pregna-1,20-dien-3-one (1) to 1,4,20-pregnatrien-3-one (3)

A solution of 5α-pregna-1,20-dien-3-one (5 mg, 0.017 mmol) and DDQ (4 mg, 0.018 mmol) in dry benzene (3 ml) was boiled under reflux for 36 hours. The reaction mixture was cooled to 10°C, filtered, and the resulting solution washed with 2% aqueous sodium hydroxide solution (2 x 10 ml). The organic phase was dried over anhydrous magnesium sulfate and the solvent evaporated to yield a pale yellow solid. The solid was chromatographed on a silica gel plate to obtain starting material (3 mg, 60% recovery) and 1,4,20-pregnatrien-3-one (2 mg, 40% theoretical); $[\alpha]_D^{20}$ +39° (c = 0.2, $CHCl_3$), identical in all respects to the natural material.

5α-Pregn-20-en-3α-ol (5)

Lithium aluminum hydride (5 mg, 0.1 mmol) was added to a stirred solution of 5α-pregn-20-en-3α-ol 3-acetate (4) (10 mg, 0.03 mmol) in diethyl ether (2 ml) and the reaction mixture was stirred at room temperature for 10 minutes. A 5% aqueous sodium hydroxide solution (2 ml) was added dropwise and the resulting mixture was extracted with ether (3 x 5 ml). The combined extracts were dried over anhydrous magnesium sulfate and the solvent evaporated in vacuo to yield a white solid (9 mg, 99% theoretical). 5α-Pregn-20-en-3α-ol (5) was recrystallized from acetone as white needles, mp 156-158°C; ^{1}H nmr, δ ($CDCl_3$) 0.58 (s, 3H), 0.78 (s, 3H), 1.97 (m, 1H), 4.06 (br s, 1H), 4.98 (m, 1H, J = 17, 2.5, 1.3 Hz), 5.00 (m, 1H, J = 11, 2.5, 1 Hz), 5.78 (m, 1H, J = 17, 11, 7 Hz); MS, m/e (rel. abundance) 302 (52), 284 (45), 269 (38), 215 (84), 79 (100). High resolution mass measurement, found 302.263 ± 0.010, $C_{21}H_{34}O$ requires 302.261.

Conversion of 5α-pregn-20-en-3α-ol (5) to 5α-pregnan-3-one (2)

One equivalent of Jones reagent [11] was added dropwise to a stirred solution of the alcohol 5 (9 mg, 0.03 mmol) in acetone (1 ml) at 5°C. After 5 minutes, the organic material was partitioned between hexane and water. The organic extracts were dried over anhydrous magnesium sulfate and the solvent evaporated in vacuo to yield a ketone (8 mg, 99% theoretical). A solution of the crude ketone in diethyl ether was hydrogenated as in previous experiments to obtain 5α-pregnan-3-one (2) (8 mg, 89% theoretical), $[\alpha]_D^{20}$ +32° (c = 0.8, $CHCl_3$), identical in all respects to an authentic sample.

5α-Pregna-2,20-dien-1-one (8).

a) From 5α-pregn-20-en-1α,3α-diol 3-acetate (6)

A solution of chromium trioxide (2 mg, 0.02 mmol) in dry pyridine (1 ml) was added to the hydroxy acetate 6 (5 mg, 0.014 mmol) and the solution was stirred at 22°C for 8 hours. The reaction mixture was partitioned between ether (3 x 5 ml) and 5N hydrochloric acid (10 ml). The ether phase was dried over anhydrous magnesium sulfate and the solvent evaporated in vacuo to obtain the acetoxy ketone 7 (5 mg) as an oil; ^{1}H nmr, δ ($CDCl_3$) 0.59 (s, 3H), 1.16 (s, 3H), 2.01 (s, 3H), 2.30 (dt, 1H, J = 13, 2.5, 2.5 Hz), 2.94 (dd, 1H, J = 13, 4.5 Hz), 4.95 (m, 1H, J = 17, 2.5, 1.3 Hz), 4.97 (m, 1H, J = 11, 2.5, 1 Hz), 5.08 (m, 1H), 5.77 (m, 1H, J = 17, 11, 7 Hz); MS m/e (rel. abundance) 358 (3), 298 (18), 79 (100).

A solution of potassium t-butoxide (3 mg, 0.026 mmol) in t-butanol (2 ml) was added to the crude acetoxy ketone, and the reaction mixture was stirred at 22°C for 2 hours. The product was partitioned between ether and water, neutralizing any excess base with CO_2. The ether extract was dried over anhydrous magnesium sulfate and the solvent evaporated in vacuo to obtain 5α-pregna-2,20-dien-1-one (8) (3 mg, 75% theoretical), $[\alpha]_D^{20}$ +9.1° (c = 0.3, $CHCl_3$) which was identical to the authentic sample obtained below.

b) From 5α-pregna-1,20-dien-3-one (1)

Hydrogen peroxide (2 ml of 30% solution) was added to a solution of 5α-pregna-1,20-dien-3-one (40 mg, 0.14 mmol) in dioxan (2 ml) and the reaction mixture stirred at 22°C for 12 hours. Excess hydrogen peroxide was destroyed by addition of 15% aqueous sodium thiosulfate solution (10 ml) and the organic material extracted with carbon tetrachloride

(25 ml). The organic phase was dried over anhydrous magnesium sulfate and the solvent evaporated in vacuo to yield the epoxide 9 (35 mg, 83% theoretical); ^{1}H nmr, δ ($CDCl_3$) 0.62 (s, 3H), 0.89 (s, 3H), 3.26 (d, 1H, J = 4 Hz), 3.57 (d, 1H, J = 4 Hz), 5.01 (m, 1H, J = 17, 2.5, 1.3 Hz), 5.03 (m, 1H, J = 11, 2.5, 1 Hz), 5.79 (m, 1H, J = 17, 11, 7 Hz). High resolution mass measurement, found 314.225 ± 0.010, $C_{21}H_{30}O_2$ requires 314.224.

The epoxide 9 (25 mg, 0.08 mmol) was heated in hydrazine hydrate (5 mg, 0.15 mmol) at 100°C for 20 minutes. The reaction mixture was cooled and partitioned between water and hexane. The organic extracts were dried over anhydrous magnesium sulfate, and the solvent was evaporated in vacuo to yield a yellow solid (20 mg) which consisted of a mixture of two alcohols. An excess of Jones reagent was added to a stirred solution of the crude alcohol mixture (20 mg) in acetone (2 ml) at 5°C. After 30 minutes, the organic material was extracted with diethyl ether (5 x 15 ml). The combined organic extracts were dried over anhydrous magnesium sulfate, and the solvent was evaporated in vacuo to yield a yellow oil. The oil was chromatographed on a silica gel plate to obtain 5α-pregna-2,20-dien-1-one (8) as a white solid (8 mg, 32% theoretical; $[\alpha]_D^{20}$ +12.2° (c = 0.8, $CHCl_3$); λ_{max} (MeOH) 222 nm (9,670); ν_{max} 1682, 1640 cm^{-1}; ^{1}H nmr, δ ($CDCl_3$) 0.61 (s, 3H), 1.07 (s, 3H), 4.93 (m, 1H, J = 17, 2.5, 1.3 Hz), 4.95 (m, 1H, J = 11, 2.5, 1 Hz), 5.79 (m, 1H, J = 17, 11, 7 Hz), 5.82 (dt, 1H, J = 10, 2, 2 Hz), 6.64 (dt, 1H, J = 10, 4, 4 Hz); MS, m/e (rel. abundance) 298 (21), 283 (22), 122 (79), 91 (99), 79 (100). High resolution mass measurement, found 298. 228 ± 0.010, $C_{21}H_{30}O$ requires 298.230.

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