A Novel Stereospecific Synthesis of 22-Hydroxylated Triterpenes and Steroids: Syntheses of 22*R*-Hydroxylanosterol and 22*R*-Hydroxydesmosterol

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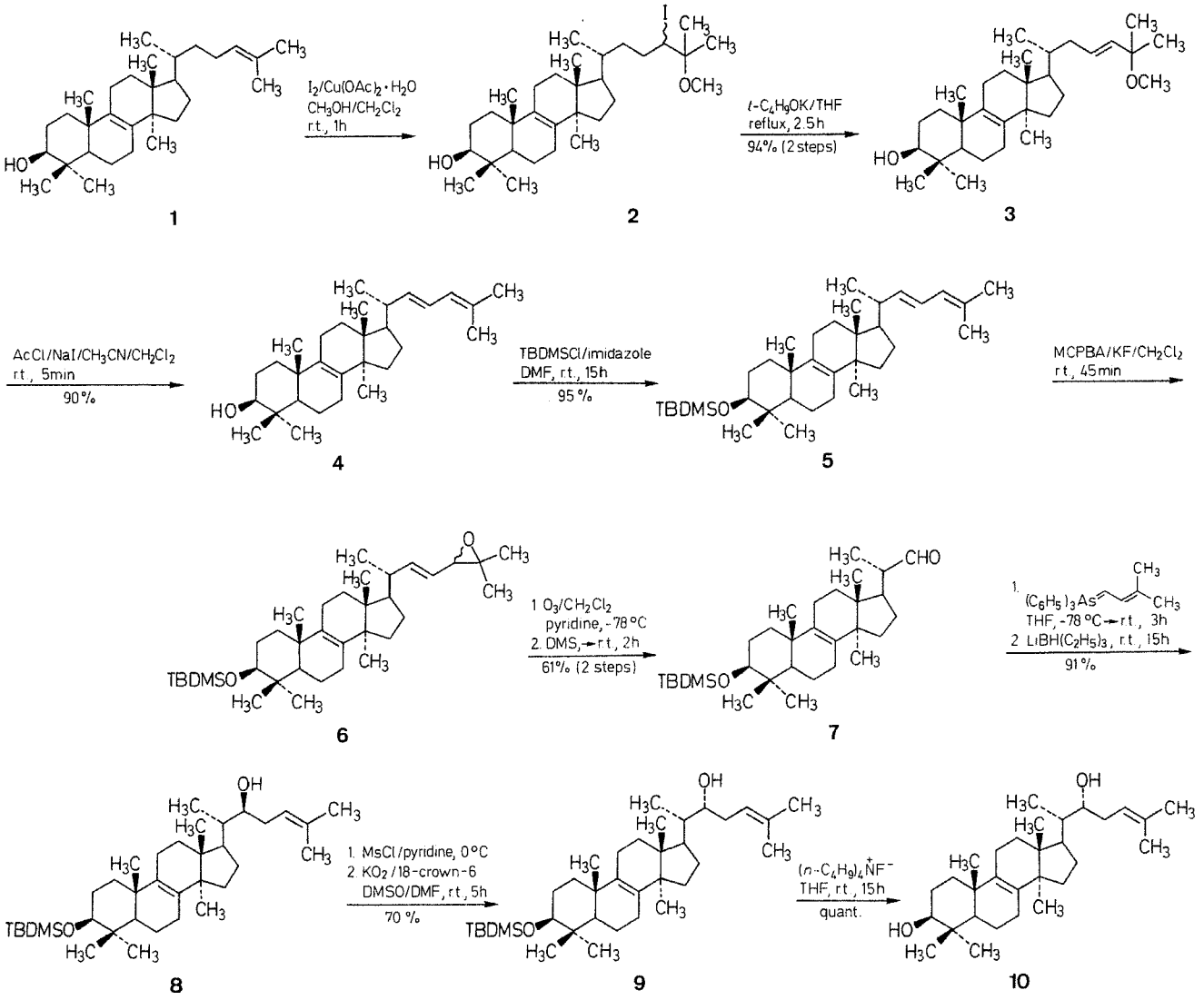
22*R*-Hydroxylanosterol **(10)** is prepared from lanosterol **(1)** with an overall yield of over 30%. The key step of the synthesis is the stereospecific coupling of the aldehyde **7** with an arsenic ylide. The same reaction is used to build the side chain of 22*R*-hydroxydesmosterol **(14)**.

Sterols and triterpenes bearing a hydroxyl group at C-22*R* have been shown[1,2] to be selectively cytotoxic towards tumor cells cultured *in vitro*. Two of these compounds seem to be particularly biologically interesting: 3β,22*R*-dihydroxylanosta-8,24-diene, known as inotodiol **(10)**, which was originally extracted from *Inonotus obliquus*,[3] an anticancer drug described by Soljenitsin in "Cancer Ward", and 22*R*-hydroxydesmosterol **(14)**, a derivative of a biosynthetic precursor of cholesterol.[4] Two syntheses of inotodiol have been reported.[5] They have the disadvantages of being non-stereospecific and low-yielding. We now describe new syntheses of **10** (Scheme A) and **14** (Scheme B), which are stereospecific and high-yielding, and compatible with large scale preparation of products for further biological studies.

Synthesis of inotodiol **(10)** is achieved *via* preparation of diene **4**, cleavage of the side chain, rebuilding of the side chain, and inversion of the configuration in position 22 (Scheme A).

Conjugated diene **4** has been prepared from lanosterol **(1)** by various methods[6] but with a maximum yield of 50%. Our method requires three steps, but the yield is 85%. Commercial lanosterol (containing ~ 50% lanostenol) is transformed into iodo-methoxy-compound **2** by treatment with copper acetate and iodine in a mixture of methanol and dichloromethane. Compound **2** is dehydroiodinated with potassium *tert*-butoxide in refluxing tetrahydrofuran to yield **3** which is treated with acetyl chloride and sodium iodide in a mixture of dichloromethane and acetonitrile. This reagent normally cleaves ethers to yield the corresponding acetates. Ether **3** being α,β-unsaturated, the intermediate iodide behaves like a base and diene **4** forms in 5 minutes, at room temperature, in 90% isolated yield. The use of chlorotrimethylsilane or of *tert*-butylchlorodimethylsilane instead of acetyl chloride also yields **4** almost quantitatively.

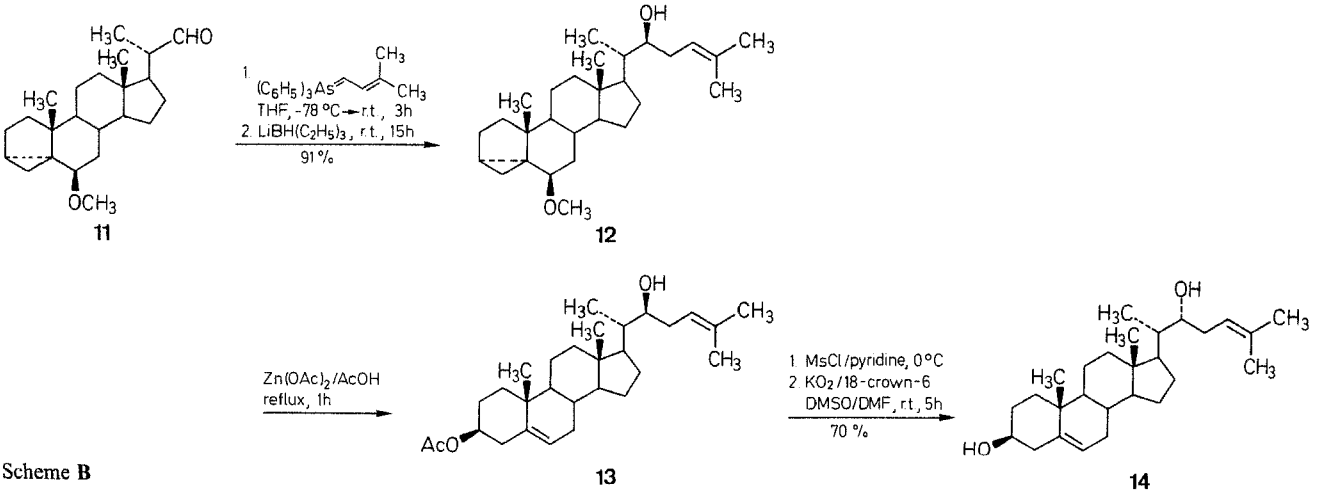
If diene **4** is ozonized directly, both C-22 and C-24 aldehydes form, the latter being slightly predominant. Further ozonization of C-24 aldehyde does not yield the target product, **7** (potassium permanganate was used successfully for this transformation, after protection of the 3-OH). Triene **4** can be mono-epoxidized regiospecifically using 1.05 equivalent of potassium fluoride-*m*-chloroperbenzoic acid complex in dichloromethane, and the epoxide forms the C-22 aldehyde by ozonolysis. The C-22 aldehyde being base sensitive (epimerization at C-20 can occur), it is more convenient to protect the 3-OH before the aldehyde is formed. The diene **4** is protected into its *tert*-butyldimethylsilyl derivative **5** which is epoxidized into **6** as described above and pyridine is added to the solution which is directly treated by ozone at -78 °C. After work-up using dimethyl sulfide, **7** is isolated in over 60% yield. Unreacted α,β-unsaturated epoxide is recovered; so the yield of aldehyde **7** could be increased.



MCPBA = *m*-chloroperbenzoic acid
TBDMS = *t*-butyldimethylsilyl
Ms = methanesulfonyl

Scheme A

Neither Grignard reagents, nor sulfur ylides can be used to build the side chain, because the dimethylallylic moiety rearranges. A sulfone α-anion condenses with aldehyde **7**, but the sulfinate residue does not eliminate; two epimers of 23-(*p*-toluenesulfinoxy)lanosta-8,24-diene-3β,22-diol were isolated and identified, but basic treatment resulted in a reversion of the coupling. Arsenic ylide addition was found to be the solution to form an intermediate α,β-unsaturated epoxide, which could be reduced to **8**. (Methyl-3-but-2-enyl)-triphenylarsonium tetrafluoroborate is treated with *n*-butyllithium to form the ylide which is condensed with aldehyde **7**. The intermediate epoxide can be purified to some extent, evaporating the solution to dryness and



Scheme B

dissolving the residue in dry hexane (triphenylarsine is also soluble), or it can be reduced directly by lithium triethylborohydride into alcohol **8** in 91% yield and over 96% enantiomeric excess.

22*S*-Hydroxylated steroids with a saturated side chain have already been inverted by Corey's method.[7] The alcohol **8** is mesylated in over 95% in pyridine (the use of triethylamine results in dehydration). The mesylate is reacted with potassium superoxide and 18-crown-6 in a mixture of dry dimethylformamide and dimethyl sulfoxide. **9** forms in 70% yield and is deprotected with tetrabutylammonium fluoride to yield **10**. Inotodiol is formed in over 30% yield from lanosterol.

(22*R*)-22-Hydroxydesmosterol **14** is formed using the same sequence of condensation of an aldehyde with an arsenic ylide and inversion of the configuration in position 22 (Scheme **B**). Aldehyde **11** formed from stigmasterol by the classical procedure,[8] is reacted with the arsenic ylide and reduced as described previously to form **12** in 91% yield. Refluxing **12** with zinc acetate in acetic acid yields **13** almost quantitatively. The alcohol **13**, after mesylation, is treated with superoxide which inverts position 22 and lyses the acetate to form **14** in 70% yield.

Melting points were measured on a Reichert hot stage microscope and are uncorrected. $[\alpha]_D^{20}$ were measured on a Perkin-Elmer 141 polarimeter. Microanalyses were performed by the Strasbourg Division of the Service Central de Microanalyses of the CNRS. ^{1}H-NMR spectra were run on a 200 MHz Bruker spectrometer. Mass spectra were recorded on a Thomson-Houston THN208 or on an LKB 9000 spectrometer. TLC were run on pre-coated plates of silica gel 60F254 (Merck) and silica gel (40–63 μ, Merck) was used for column chromatography.

(24ξ)-24-Iodo-25-methoxylanost-8-ene-3β-ol (2):
A mixture of lanosterol and lanost-8-ene-3β-ol (Merck, 14.22 g, 16.6 mmol lanosterol) is dissolved in CH_2Cl_2 (120 mL). Copper(II) acetate monohydrate (2.20 g, 11 mmol) in methanol (200 mL) is added under vigorous stirring. The mixture is protected from light by an aluminium foil, and iodine (4.014 g, 15.81 mmol) in CH_2Cl_2 (80 mL) is added. After 1 h stirring the solution is filtered and the filtrate is stirred with powdered K_2CO_3 (15 g). After 20 min the discolored solution is filtered and evaporated to dryness. The residue is dissolved in CH_2Cl_2 (250 mL) and washed with water (3 × 250 mL). The solution is dried ($MgSO_4$) and evaporated to dryness. The crude product (17.17 g) can be used as such for the next step. A pure sample can be obtained by chromatography on silica using CH_2Cl_2 as eluent; m.p. 157–158 °C (acetone).

$C_{31}H_{53}IO_2$ calc. C 63.69 H 9.14
(584.7) found 63.50 9.27

^{1}H-NMR ($CDCl_3$): δ = 0.70, 0.82, 0.89, 0.99, 1.01 (5s, 5 × 3 H, CH_3); 0.935 (d, 3 H, J = 6.2 Hz, CH_3-21); 1.365 (s, 6 H, CH_3-26 and CH_3-27); 3.22 (s, 3 H, CH_3O); 3.24 (dd, 1 H, J = 5.2 and 10.1 Hz, H-3); 4.08 (m, 1 H, H-24).

MS (CI/NH_3): m/e = 602 ($M + NH_4^+$, 56); 584 (M^+, 27); 553 (46); 476 (100).

25-Methoxylanosta-8,23-diene-3β-ol (3):
The crude mixture obtained from the last step (17.17 g) is dissolved in THF (250 mL). Potassium *t*-butoxide (8 g, 71 mmol) is added and the mixture is refluxed 2.5 h under argon. The mixture is allowed to cool and NH_4Cl (4 g) is added to destroy the excess of base. The solution is filtered, evaporated to dryness and the residue is dissolved in CH_2Cl_2 (250 mL) and washed with water (3 × 250 mL). After drying ($MgSO_4$) and evaporating the solvent, the product is chromatographed on silica gel with CH_2Cl_2 as eluent; yield: 6.79 g (94%, based on iodine); m.p. 167–168 °C (acetone); $[\alpha]_D^{20}$ = + 37° ($CHCl_3$, c = 0.96).

$C_{31}H_{52}O_2$ calc. C 81.52 H 11.48
(456.8) found 81.63 11.58

^{1}H-NMR ($CDCl_3$): δ = 0.04, 0.70, 0.82, 0.87, 0.98, 1.01 (6s, 7 × 3 H, CH_3); 0.91 (d, 3 H, J = 5.8 Hz, CH_3-21); 1.26 (s, 6 H, CH_3-26 and CH_3-27); 3.16 (s, 3 H; CH_3O); 3.24 (dd, 1 H, J = 4.2 and 10.5 Hz, H-3); 5.39 (d, J_{AB} = 16 Hz, 1 H, H-24; 5.54 (ddd, 1 H, J_{AX} = 7.8, J_{AY} = 5.3 Hz, H-23)

MS (CI/NH_3): m/e = 456 (M^+, 39); 442 (51); 425 (100); 409 (39).

Lanosta-8,22,24-triene-3β-ol (4):
To a solution of Ether **3** (4.854 g, 10.6 mmol) in a mixture of CH_3CN (50 mL) and CH_2Cl_2 (50 mL), powdered anhydrous NaI (1.567 g, 10.4 mmol) is added and the solution is stirred under argon. Acetyl chloride (740 µL, 10.4 mmol) is then added dropwise. After 5 min, water (50 mL) is added and the solution is extracted with ether (3 × 100 mL). The ether phase is washed successively with water (3 × 50 mL), saturated brine (50 mL), dried ($MgSO_4$) and evaporated. The crude product can be recrystallized from methanol-acetone or chromatographed on silica gel (eluent: CH_2Cl_2); mixture of isomers; yield: 4.044 g (90%); m.p. 115–117 °C, 118–123 °C (CH_3OH); Lit.[9] 131–133 °C (CH_3OH); $[\alpha]_D^{20}$ = + 55° (c = 0.33).

^{1}H-NMR ($CDCl_3$): δ = 0.65, 0.88, 0.89, 0.90, 0.97 (5s, 5 × 3 H, CH_3); 1.61 and 1.69 (2s, 2 × 3 H, CH_3-26 and CH_3-27); 5.41 (dd, 1 H, J = 8.8 and 14.8 Hz, H-22); 5.76 (d, 1 H, J = 11 Hz, H-24; 6.15 (dd, 1 H, J = 11 and 14.8 Hz, H-23).

3β-(*t*-Butyldimethylsiloxy)lanosta-8,22,24-triene (5):
The trienol **4** (3.2 g, 7.53 mmol), imidazole (1.91 g, 28.1 mmol) and *tert*-butylchlorodimethylsilane (1.67 g, 11.1 mmol) are dissolved in DMF (30 mL). After 15 h water (100 mL) is added and the product is extracted with CH_2Cl_2 (3 × 50 mL). The organic phase is washed with water (3 × 100 mL), dried (Na_2SO_4) and evaporated to dryness. The crude product is chromatographed on silica gel (eluent: hexane) and the isomers are separated; yield: 3.86 g (95%).

Isomer 1: m.p. 157–158 °C (acetone); $[\alpha]_D^{20}$ = + 42° ($CHCl_3$, c = 1.25).

$C_{36}H_{62}OSi$ calc. C 80.23 H 11.60
(539.0) found 80.27 11.77

^{1}H-NMR ($CDCl_3$): δ = 0.04, 0.72, 0.78, 0.88, 0.92, 0.99 (6s, 7 × 3 H, CH_3); 0.90 (s, 9 H, *t*-C_4H_9); 1.02 (d, 3 H, J = 6.6 Hz, CH_3-21); 1.75 (s, 6 H, CH_3-26 and CH_3-27); 3.21 (dd, 1 H, J = 5.5 and 10 Hz, H-3); 5.42 (dd, 1 H, J = 8.5 and 15 Hz, H-22); 5.76 (d, 1 H, J = 10.7 Hz, H-24); 6.16 (dd, 1 H, J = 10.7 and 15 Hz, H-23).

MS (CI, CH_4): m/e = 538 (M^+, 100); 523 (48); 481 (31); 456 (18); 429 (28); 407 (65); 297 (72).

Isomer 2: m.p. 143–150 °C (acetone); $[\alpha]_D^{20}$ = + 21° ($CHCl_3$, c = 2.57).

$C_{36}H_{62}OSi$ calc. C 80.23 H 11.60
(539.0) found 80.29 11.72

^{1}H-NMR ($CDCl_3$): δ = 0.04, 0.67, 0.86, 0.88, 0.92, 0.98 (6s, 7 × 3 H, CH_3); 0.90 (s, 9 H, *t*-C_4H_9); 1.02 (d, 3 H, J = 6.6 Hz, CH_3-21); 1.75 (s, 6 H, CH_3-26 and CH_3-27); 3.21 (dd, 1 H, J = 4.6 and 10.5 Hz, H-3); 5.42 (dd, 1 H, J = 8.5 and 15 Hz, H-22); 5.76 (d, 1 H, J = 10.7 Hz, H-24); 6.16 (dd, 1 H, J = 10.7 and 15 Hz, H-23).

MS (CI, CH_4): m/e = 538 (M^+, 100); 523 (43); 481 (30); 456 (27); 429 (70); 407 (43); 297 (16).

(24ξ)-24,25-Epoxy-3β-(*t*-butyldimethylsiloxy)lanosta-8,22-diene (6):
The oxidation complex is prepared by stirring 90% *m*-chloroperbenzoic acid (212 mg, 1.11 mmol) with KF (73.7 mg, 1.27 mmol) in CH_2Cl_2 (20 mL) under argon. After stirring for 5 min, triene **5** (600 mg, 1.11 mmol, mixture of isomers) in CH_2Cl_2 (20 mL) is added and allowed to react for 45 min. KF (75 mg, 1.29 mmol) is added and the solution is stirred for 1 h before it is filtered. The solution of epoxide is used as such in the next step. By evaporation, a crude product (662 mg, yield ~ 100%) can be obtained, which is pure enough for ^{1}H-NMR and mass spectrometry:

^{1}H-NMR ($CDCl_3$): δ = 0.04, 0.66, 0.71, 0.88, 0.98, 1.05 (6s, 11 × 3 H, CH_3); 1.27 and 1.33 (2s, 2 × 3 H, CH_3-26 and CH_3-27); 3.13 (d, 1 H, J = 8 Hz, H-24); 3.2 (m, 1 H, H-3); 5.22 (dd, 1 H, J = 8 and 15 Hz, H-22); 5.75 (dd, 1 H, J = 8 and 15 Hz, H-23).

MS (CI, CH_4): m/e = 554 (M^+, 100); 538 (60); 497 (63); 481 (28).

3β-(*t*-Butyldimethylsiloxy)pentanorlanost-8-ene-22-al (7):
The solution of allylic epoxide **6** previously prepared as described above is diluted with CH_2Cl_2 (total volume 40 mL) and pyridine (140 µL) is added. Ozone is passed through the solution at −78 °C and the reaction is followed by TLC. When the starting material has almost completely disappeared, dimethyl sulfide (2 mL) is added and the solution is allowed to reach room temperature in about 2 h. The solution is evaporated to dryness and the residue is chromatographed on silica gel

using hexane/CH_2Cl_2 (88:12) as eluent; yield: 332 mg (61%); m.p. 133–137°C; $[\alpha]_D^{20} = +25°$ ($CHCl_3$, $c = 1.35$). Unreacted epoxide (141 mg) is recovered.

$C_{31}H_{54}O_2Si$ (486.9) calc. C 76.48 H 11.18 found 76.39 11.35

^{1}H-NMR ($CDCl_3$): $\delta = 0.04$, 0.75, 0.78, 0.91, 0.92, 0.99 (6s, 7 × 3 H, CH_3); 0.90 (s, 9 H, t-C_4Hg); 1.11 (d, 3 H, $J = 6.8$ Hz, CH_3-21); 3.21 (dd, 1 H, $J = 5.5$ and 10.1 Hz, H-3); 9.58 (d, 1 H, $J = 3.3$ Hz, H-22).

MS (CI, CH_4): $m/e = 486$ (M^+, 57); 429 (100); 401 (36).

(Methyl-3-but-2-enyl)triphenylarsonium Bromide:

To a solution of triphenylarsine (7.7 g, 25.1 mmol) in acetonitrile (100 mL) is added bromo-1-methyl-3-butene-2 (5 g, 90% pure, 30.2 mmol) under an argon atmosphere. The mixture is protected from light with an aluminium foil. After 22 h, the solution is evaporated to dryness and the residue is triturated in ether (50 mL). The ether phase is filtered and the solid is dissolved in CH_2Cl_2 (100 mL) and washed with water (3 × 25 mL). The solution is concentrated to 30 mL and the salt is precipitated with ether (50 mL), filtered and washed with ether (30 mL); yield: 7.5 g (~ 55%); m.p. 146°C (subl).

^{1}H-NMR ($CDCl_3$): $\delta = 1.38$, 1.69 (2s, 2 × 3 H, CH_3); 4.65 (d, 2 H, J, 2 H, CH_2); 5.3 (t, 1 H, $J = 8$ Hz, CH); 7.8 (m, 15 H, Ph).

(Methyl-3-but-2-enyl)triphenylarsonium Tetrafluoroborate:

To a solution of (methyl-3-but-2-enyl)triphenylarsonium bromide (1.51 g, 3.32 mmol) in CH_2Cl_2 (20 mL) is added a solution of silver tetrafluoroborate (645 mg, 1 equiv) in water (20 mL) is added and the mixture is stirred vigourously for 10 min. The silver chloride formed is filtered off, the filtrate is allowed to settle and the organic phase is washed with saturated brine (5 mL) and evaporated to dryness. Trituration of the residue with ether affords crystals; yield: 1.4 g (91%); m.p. 149–151°C.

This salt is more soluble in THF than the corresponding bromide and gives better yields in the reaction of coupling with aldehydes.

(22*S*)-22-Hydroxy-3β-(*t*-butyldimethylsiloxy)lanosta-8,24-diene (8):

To a stirred suspension of (methyl-3-but-2-enyl)triphenylarsonium tetrafluoroborate (630 mg, 1.36 mmol) in THF (10 mL) at −30°C is added a solution of 2.4 molar BuLi in THF dropwise until a slight colour persists, and then one equivalent of BuLi (565 µL) is added at once. After stirring for 5 min, the red solution is cooled to −78°C and aldehyde **7** (590 mg, 1.21 mmol) in THF (6 mL) is added dropwise. The reaction mixture remains slightly colored. The temperature is allowed to reach room temperature in 3 h. The solution is then cooled to 0°C and a molar solution of lithium triethylborohydride in THF (5 mL, 5 mmol) is added. After 15 h the solution is evaporated, and the residue is dissolved in hexane (50 mL) and washed with water (3 × 30 mL). After drying ($MgSO_4$), the solution is evaporated to dryness and chromatographed on silica gel, with cyclohexane and cyclohexane/ethyl acetate (97:3) successively as eluents; yield: 614 mg (91%); m.p. 178–180°C (EtOH); $[\alpha]_D^{20} = +23°$ ($CHCl_3$, $c = 4.1$).

$C_{36}H_{64}O_2Si$ (557.0) calc. C 77.63 H 11.58 found 77.57 11.77

^{1}H-NMR ($CDCl_3$): $\delta = 0.04$, 0.65, 0.70, 0.78, 0.99, 1.01 (6s, 7 × 3 H, CH_3); 0.87 (d, 3 H, $J = 6.6$ Hz, CH_3-21); 0.90 (s, 9 H, t-C_4H_9); 1.65 and 1.74 (2s, 2 × 3 H, CH_3-26 and CH_3-27); 3.21 (dd, 1 H, $J = 5.4$ and 10.2 Hz, H-3); 3.68 (t, 1 H, $J = 3.4$ Hz, H-22); 5.16 (t, 1 H, $J = 8.1$ Hz, H-24).

MS (CI, CH_4): $m/e = 556$ (M^+, 100); 541 (36); 499 (30); 486 (43); 429 (12).

(22*R*)-22-Hydroxy-3β-(*t*-butyldimethylsiloxy)lanosta-8,24-diene (9):

To the alcohol **8** (320 mg, 0.575 mmol) dissolved in pyridine (4 mL) and mesyl chloride (1 mL, 12.9 mmol) is added at 0°C under stirring. After 5 h, ice and water (20 mL) are added and the solution is extracted with ether (3 × 10 mL). The ether phase is washed with water (3 × 5 mL) and saturated brine (5 mL), and evaporated to dryness. The slightly yellow mesylate crystallizes; yield: 348 mg (95%).

The mesylate formed is checked by ^{1}H-NMR: The H-22 shifts to 4.8–4.9 ppm and the methyl of CH_3SO_3R appears at 2.99 ppm. The crude mesylate (161 mg, 0.253 mmol) and 18-crown-6 (217 mg, 0.82 mmol) are dissolved in a 1:1 mixture of DMSO and DMF (7 mL). Potassium superoxide (76 mg, 1.07 mmol) is added and the solution is stirred under argon. After 5 h, superoxide has almost completely dissolved and the reaction is over. Water (20 mL) and a few drops of 1 normal solution of HCl are added and the solution is extracted with ether (3 × 20 mL). The ether phase is washed with water (3 × 20 mL) and saturated brine (10 mL), dried ($MgSO_4$) and evaporated to dryness. The crude product is chromatographed on silica gel using hexane/ethyl acetate (95:5) as eluent; yield: 103.5 mg (73%); m.p. 189–190°C; $[\alpha]_D^{20} = +28°$ ($CHCl_3$, $c = 1.08$).

$C_{36}H_{64}O_2Si.CH_3OH$ (589.0) calc. C 77.45 H 11.64 found 77.43 11.76

^{1}H-NMR ($CDCl_3$): $\delta = 0.04$, 0.68, 0.73, 0.78, 0.87, 0.98 (6s, 7 × 3 H, CH_3); 0.87 (d, 3 H, $J = 6.6$ Hz, CH_3-21); 0.90 (s, 9 H, t-C_4H_9); 1.66 and 1.75 (2s, 2 × 3 H, CH_3-26 and CH_3-27); 3.21 (dd, 1 H, $J = 5.3$ and 10.2 Hz, H-3); 3.67 (m, 1 H, H-22); 5.22 (m, 1 H, H-24).

MS (EI, 70 eV): $m/e = 556$ (M^+, 100); 541 (17); 499 (38); 486 (25), 429 (100); 409 (21).

(22*R*)-3β,22-Dihydroxylanosta-8,24-diene (10):

The protected compound **9** (15 mg, 0.027 mmol) is stirred with a molar solution of tetrabutylammonium fluoride in THF (1 mL) at room temperature. After 15 h, water (10 mL) is added and the solution is extracted with CH_2Cl_2 (3 × 10 mL). The organic phase is washed with water (3 × 10 mL), dried ($MgSO_4$), and evaporated to dryness; yield: 12 mg (quantitative); m.p. 185–186°C (aq. CH_3OH); Lit.[5] 189–191.5° (CH_3OH); $[\alpha]_D^{20} = +34°$ ($c = 0.34$, $CHCl_3$); Lit.[5] +59° ($c = 0.8$)

$C_{30}H_{50}O_2 \cdot CH_3OH$ (474.7) calc. C 78.43 H 11.47 found 78.38 11.49

^{1}H-NMR ($CDCl_3$): $\delta = 0.73$, 0.82, 0.88, 0.99, 1.01 (5s, 5 × 3 H, CH_3); 0.98 (d, 3 H, $J = 6.6$ Hz, CH_3-21); 1.66 and 1.76 (2s, 2 × 3 H, CH_3-26 and CH_3-27); 3.23 (m, 1 H, H-3); 3.68 (m, 1 H, H-22); 5.19 (m, 1 H, H-24).

MS (EI, 70 eV): $m/e = 442$ (M^+, 58); 427 (29); 409 (16); 372 (100); 357 (83); 339 (33).

(22*S*)-22-Hydroxy-6β-methoxy-3α, 5α-cyclocholest-24-ene (12):

Arsenic ylide (1.11 mmol) is prepared as described previously and reacted with aldehyde **11** (344 mg, 1 mmol). When the mixture has reached room temperature, the clear, almost colorless solution is evaporated to dryness and the residue is triturated with hexane (30 mL), filtered and the filtrate is evaporated to dryness. ^{1}H-NMR of the residue shows that only triphenylarsine and the intermediate epoxide are present.

^{1}H-NMR ($CDCl_3$): $\delta = 0.44$ (dd, 1 H, $J = 5$ and 8 Hz, H-3), 0.73 (s, 3 H, CH_3-18); 1.06 (s, 3 H, CH_3-19); 1.8 (brs, 6 H, CH_3-26 and CH_3-27); 2.73 (m, 1 H, H-6); 3.32 (s, 3 H, CH_3O); 3.35 (dd, 1 H, H-22); 3.62 (dd, 1 H, $J = 4.5$ and 9 Hz, 1 H, H-23), 5.02 (d, 1 H, $J = 9$ Hz, H-24).

The crude epoxide is dissolved in THF (15 mL) and reduced to the alcohol 12 with lithium triethylborohydride as described previously. Chromatography with hexane/ethylacetate (95:5) affords alcohol **12** as a colorless oil; yield: 376 mg (91%).

^{1}H-NMR ($CDCl_3$): $\delta = 0.44$ (dd, 1 H, $J = 5$ and 8 Hz, H-3), 0.75 (s, 3 H, CH_3-18); 0.97 (d, 3 H, $J = 6.7$ Hz, CH_3-21), 1.03 (s, 3 H, CH_3-19), 1.66 and 1.75 (2s, 2 × 3 H, CH_3-26 and CH_3-27); 2.78 (t, 1 H, $J = 2.7$ Hz, H-6); 3.33 (s, 3 H, CH_3O); 3.65 (m, 1 H, H-22); 5.17 (m, 1 H, H-24).

MS (EI, 70 eV) $m/e = 414$ (M^+, 1); 399 (1); 388 (1); 382 (5); 344 (35); 329 (24); 313 (100).

(22*S*)-3β-Acetoxy-22-hydroxycholesta-5,24-diene (13):

A mixture of the *i*-ether **12** (160 mg, 0.386 mmol) and zinc acetate (1.59 g, 8.66 mmol) are refluxed for 1 h in acetic acid (15 mL). Water (60 mL) is added and the solution is extracted with dichloromethane (3 × 50 mL). The organic phase is washed with 5% aqueous $NaHCO_3$ (2 × 20 mL) and water (3 × 30 mL). The organic layer is dried ($MgSO_4$) and evaporated to dryness to give **13**; yield: 174 mg (100%, contains traces of diacetate); m.p. 120–121°C (MeOH–H_2O); $[\alpha]_D^{22} = -56°$ ($CHCl_3$, $c = 3.6$).

$C_{29}H_{46}O_3$ (442.7) calc. C 78.68 H 10.47 found 78.80 10.57

^{1}H-NMR ($CDCl_3$): $\delta = 0.70$ (s, 3 H, CH_3-18); 0.945 (d, 3 H, $J = 6.2$ Hz, CH_3-21); 1.03 (s, 3 H, CH_3-19); 1.65 and 1.74 (2s, 2 × 3 H, CH_3-26 and CH_3-27); 2.04 (s, 3 H, $COCH_3$); 3.68 (dd, 1 H, $J = 4.8$ and 8.9 Hz, H-22); 4.6 (m, 1 H, H-3); 5.17 (t, 1 H, $J = 6.7$ Hz, H-24); 5.39 (d, 1 H, $J = 3.7$ Hz, H-7).

MS (EI, 70 eV): $m/e = 382$ (19); 312 (100).

(22*R*)-3β, 22-Dihydroxycholesta-5,24-diene (14):

The crude alcohol **13** (100 mg, 0.226 mmol) in pyridine (4 mL) is treated with mesylchloride (1 mL). Work-up as described previously yields the mesylate which is treated with potassium superoxide (45 mg, 0.633 mmol) and 18-crown-6 (511 mg, 1.93 mmol) in a 1:1 mixture of DMF and DMSO (10 mL) (cf. procedure described previously). Work-up and chromatography with hexane/EtOAc (85:15) affords 22*R*-hydroxydesmosterol **(14)**; yield: 63 mg (70%); m.p. 184–186°C (aq CH_3OH): Lit.[4] 182–184°C; $[\alpha]_D^{20} = -35°$ ($CHCl_3$, $c = 1.3$); Lit.[4] $-37°$ ($c = 2.00$).

$C_{27}H_{44}O_2.1.5CH_3OH$	calc.	C 76.30	H 11.23
(448.7)	found	76.19	11.07

^{1}H-NMR ($CDCl_3$): $\delta = 0.72$ (s, 3H, CH_3-18); 0.975 (d, 3H, $J = 6.7$ Hz, CH_3-21); 1.02 (s, 3H, CH_3-19); 1.66 and 1.75 (2s, 2 × 3H, CH_3-26 and CH_3-27); 3.52 (m, 1H, H-3); 3.64 (m, 1H, H-22); 5.18 (t, 1H, $J = 7.7$ Hz, H-24); 5.36 m (d, 1H, $J = 5.3$ Hz, H-7).

MS (EI, 70 eV): $m/e = 400$ (M^+, < 1); 382 (< 1); 364 (< 1); 312, 330 (100).

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