PREPARATION OF 21,26,27-TRINOR-5α-CHOLEST-23-EN--25→20-OLIDE FROM A PROPARGYL SYNTHONE

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Reaction of 21-nor-5α-pregnan-20-al (*I*) with propargylmagnesium bromide afforded two isomeric 21-nor-5α-chol-23-yn-20-ols (*II* and *IV*) whose absolute configuration at $C_{(20)}$ was determined by chemical correlation with the known 21-nor-5α-cholan-20-ols (*VI* and *VII*). Extension of the side-chain in the compound *II* by one carbon atom gave (20*R*)-21,26,27-trinor-5α-cholest--23-yne-20,25-diol (*XIV*). The isomeric (20*S*)-diol *XX* was obtained by the same procedure from the alcohol *IV*. Alternative synthesis of the diols *XIV* and *XX* by reaction of lithium salt of 1-methoxymethoxy-2-propyne with (20*S*)-20,21-epoxy-5α-pregnane (*XV*) and the (20*R*)-isomer *XXI*, respectively, gave only low yields. The diols *XIV* and *XX* were converted into the respective unsaturated lactones, *i.e.* (20*R*)-21,26,27-trinor-5α-cholest-23-en-25 → 20-olide (*XVII*) and (20*S*)--21,26,27-trinor-5α-cholest-23-en-25 → 20-olide (*XXIII*).

In our recent[1] synthesis of the isomeric 21,26,27-trinor-5α-cholest-23-en-25 → 20--olides (*XVII* and *XXIII*) *via* the corresponding saturated lactones, the double bond was introduced only in the last steps. In this paper we describe another approach in which the lactone ring is synthesized by means of a propargyl synthone, already containing the multiple bond.

Reaction of the aldehyde *I* (ref.[2]) with propargylmagnesium bromide[3] afforded two ethynyl derivatives *II* and *IV* (in 47% and 27% yields, respectively), differing in configuration at $C_{(20)}$, which were separated by column chromatography on silica gel. The less polar compound *II* was hydrogenated to give the known[4] saturated (20*R*)-alcohol *VI* whereas hydrogenation of the more polar isomer *IV* led to the also known[4] saturated (20*S*)-alcohol *VII*. The structure of the ethynyl derivative *II* was further confirmed by the presence of hydroxyl bands at 3 620 and 3587 cm^{-1} and terminal triple bond bands at 3 314 and 2 118 cm^{-1} in its IR spectrum and by the multiplet of the $C_{(20)}$—H at $\delta = 3{\cdot}67$ and triplet of the acetylenic proton at $\delta = 2{\cdot}02$ ($J_{22,24} = 2{\cdot}5$ Hz) in the ^1H NMR spectrum. The spectral data of the ethynyl derivative *IV* were practically the same as those of the compound *II*.

According to the literature[5], the reaction of the aldehyde *I* with propargylmagnesium bromide could give, in addition to the ethynyl derivatives *II* and *IV*, also pro-

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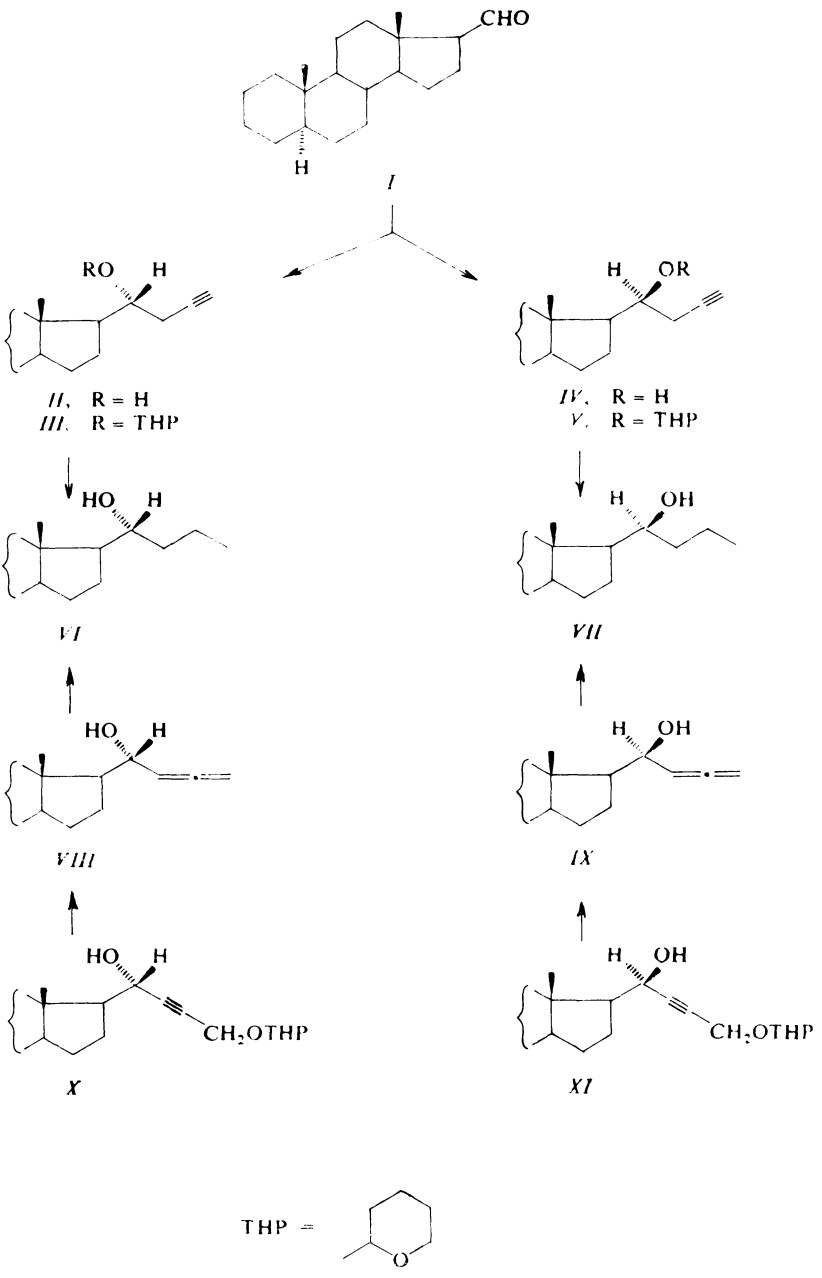
ducts arising from the isomeric allenylmagnesium bromide, *i.e.* the allenyl derivatives *VIII* and *IX*. Authentic samples of these compounds were prepared by rearrange-



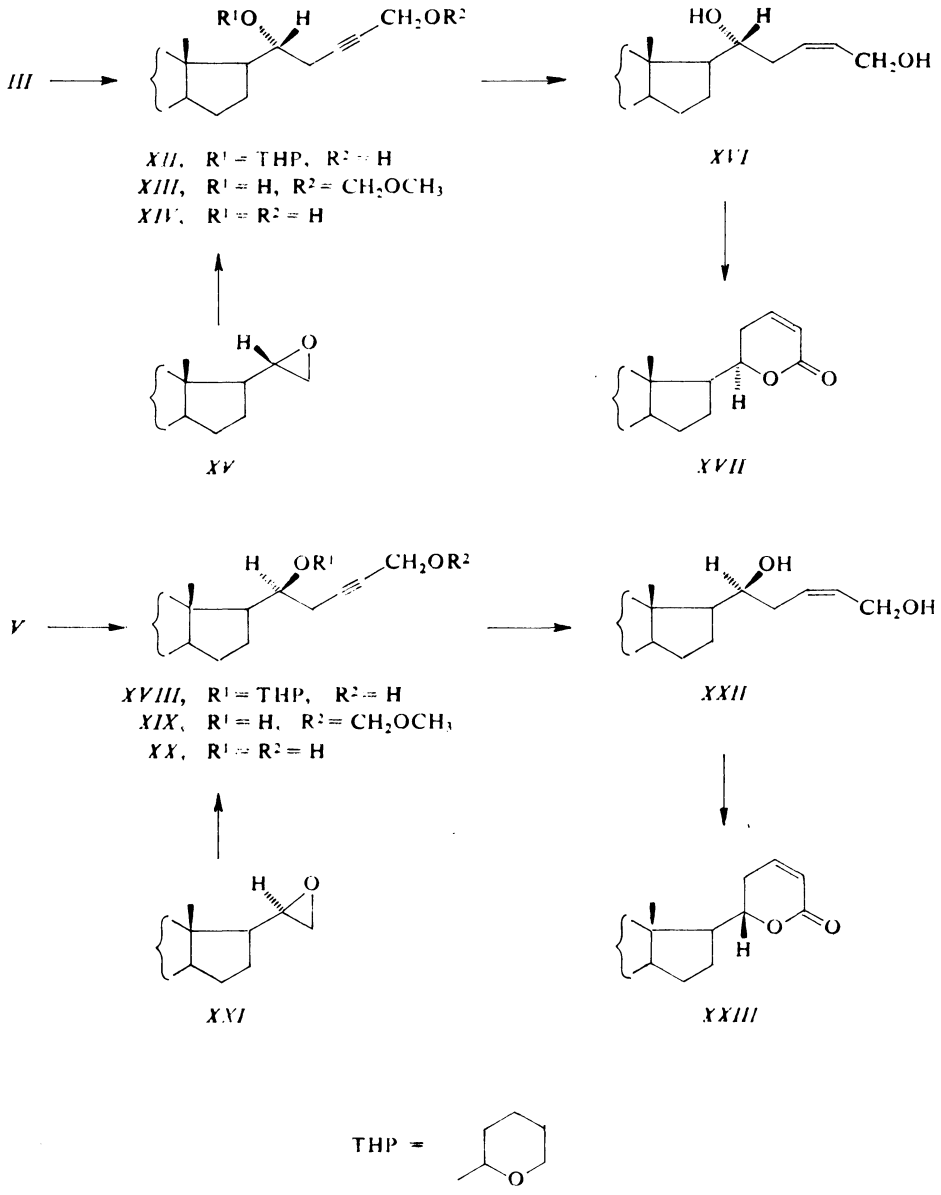
ment[6] of the known[7] 2-alkyne-1,4-diol derivatives *X* and *XI* with lithium aluminium hydride. Compound *X* was thus transformed into the allenyl derivative *VIII* which was hydrogenated to give the already described[4] saturated (20*R*)-alcohol *VI*. The allenyl derivative *IX*, obtained analogously from the compound *XI*, on hydrogenation afforded the saturated alcohol *VII* whose configuration was 20*S* (ref.[4]). The structure of the allenyl derivative *VIII* was confirmed by the IR bands at 1 956 and 847 cm^{-1}, characteristic for the $C{=}C{=}CH_2$ grouping, and by the hydroxyl bands at 3 615 and 3 485 cm^{-1}. Beside the multiplet of the $C_{(20)}$—H proton at $\delta = 4{\cdot}08$, its ^1H NMR spectrum displayed signals of the allenic protons. After decoupling of the $C_{(20)}$—H signal, it was possible to determine the magnitude of $J_{22,24}$ (6·6 Hz) which agreed with the values given[8] for an allenic system. Both thin-layer chromatography and ^1H NMR spectra showed that in the reaction of the aldehyde *I* with propargylmagnesium bromide no allene derivatives *VIII* and *IX* were formed.

During the further transformations of the side chain, the hydroxyl in position 20 was protected with the tetrahydropyranyl group. Reaction of the alcohol *II* with dihydropyran, catalyzed with *p*-toluenesulfonic acid, gave a mixture of two tetrahydropyranyl ethers *III*, differing in configuration at $C_{(2)}$ of the tetrahydropyran ring. These isomers were separable by thin-layer chromatography on silica gel or by column chromatography on alumina. Their ^1H NMR spectra differed mainly in the $C_{(18)}$ methyl signal shifts which enabled us to determine that the crude mixture contained about 47% of the less polar isomer. The mixture of the stereoisomeric ethynyl derivatives *III* was treated with ethylmagnesium bromide to give the corresponding Grignard compounds which on reaction with paraformaldehyde[9] were converted into the alcohol *XII*. According to thin-layer chromatography as well as ^1H NMR spectrum the product *XII* was again a mixture of two isomers with different configuration at the $C_{(2)}$ carbon of the tetrahydropyran ring. Removal of the protecting group afforded the diol *XIV*. The molecular ion M^+ 358 in the mass spectrum proved the attachement of the CH_2OH grouping to the ethynyl derivative *II*. The structure *XIV* was further confirmed by the ^1H NMR spectrum, exhibiting the $C_{(20)}$—H signal as a multiplet at $\delta = 3{\cdot}65$ and the $C_{(25)}$—H_2 signal as a broad singlet at $\delta = 4{\cdot}24$.

The alcohol *IV* was converted by the same procedure into a mixture of the tetrahydropyranyl ethers *V* which, according to the ^1H NMR spectra, consisted of two isomers (7 : 8), unseparable by thin-layer chromatography. The compound *V* was converted *via* the intermediate *XVIII* into the diol *XX* whose ^1H NMR and mass spectra were very similar to those of the $C_{(20)}$-epimeric diol *XIV*.

We tried also to synthesize the diols *XIV* and *XX* from the corresponding epoxides *XV* and *XXI* (ref.[2]) which, unlike the aldehyde *I*, represent compounds with an already existing chiral center at $C_{(20)}$. Heating the lithium salt of 1-methoxymethoxy-2-propyne[10] with the epoxide *XV* (configuration 20*S*) in tetrahydrofuran in the presence of hexamethylphosphoric triamide[11] afforded a low yield (17%) of the ethynyl derivative *XIII* which was deblocked to give the diol *XIV*, most of the epoxide *XV*

(70%) being recovered from the reaction mixture. The epoxide *XXI* (configuration 20*R*) was transformed in the same way and the same yield into the ethynyl derivative *XIX* and further into the diol *XX*. The low yields are probably due to an instability of the organometallic reagent at the temperature employed.



Hydrogenation of the (20*R*)-diol *XIV* over P2 nickel in the presence of 1,2-diaminoethane[12] led to the *cis*-olefinic diol *XVI* which was oxidized and cyclized[13] with silver carbonate on Celite to give the unsaturated lactone *XVII* of configuration 20*R*. The overall yield was 9% based on the aldehyde *I* and 5% based on the epoxide *XV*. The structure of the lactone was confirmed by comparison with an authentic sample[1]. The (20*S*)-diol *XX* was analogously converted *via* the *cis*-olefinic diol *XXII* into the unsaturated lactone *XXIII*, identical with an authentic sample[1], the yield being 6% in both cases (starting from *I* or *XXI*).

If we compare the described method using multiple-bond synthones for preparation of the unsaturated lactones *XVII* and *XXIII* with the older method[1], introducing the unsaturation only into the pentanolide grouping, we can conclude that the method, employing the epoxides *XV* and *XXI*, affords lower yields whereas the formaldehyde extension method gives markedly higher yields, the number of reaction steps being the same.

EXPERIMENTAL

Melting points were determined on a Kofler block. Optical rotations were measured in chloroform at 25°C on a Perkin–Elmer 141 MC instrument. The infrared spectra were recorded on a Perkin–Elmer 580 spectrometer; wavenumbers are given in cm^{-1}. Unless stated otherwise, the ^1H NMR spectra were measured in deuteriochloroform with tetramethylsilane as internal reference on Tesla BS-467 (60 MHz) instrument. Chemical shifts are given in ppm (δ-scale); coupling constants (J) and widhts of multiplets (W) are given in Hz. All values were obtained by first order analysis. The mass spectra were recorded on an AEI MS 901 instrument. Silica gel according to Pitra (60–120 μm) and neutral aluminum oxide (Reanal, grade II) were used for column chromatography, silica gel according to Stahl (Woelm) was used for thin-layer chromatography (TLC). Plates with 200 × 200 × 0·7 mm silica gel layer were used for preparative thin-layer chromatography. Prior to evaporation *in vacuo* (about 2 kPa), solutions of the compounds in organic solvents were dried over anhydrous sodium sulfate. Analytical samples were dried at 50°C and 26 Pa for 12 h. The identity of samples prepared on different routes was checked by comparison of their IR and ^1H NMR spectra, by TLC and mixture melting point determination. Reactions with organometallic reagents and complex hydrides were carried out in an argon atmosphere.

(20*R*)-21-Nor-5α-chol-23-yn-20-ol (*II*)

Mercuric chloride (15 mg) was added to magnesium turnings (420 mg; 17·3 mmol) in ether (20 ml), the mixture was cooled to 0°C and propargyl bromide (1·78 g; 15 mmol) was added during 1 h. After stirring for 1 h at 0°C, the mixture was filtered from the unreacted magnesium. To this solution of propargylmagnesium bromide a solution of the aldehyde *I* (ref.[2], 1·45 g; 5 mmol) in ether (20 ml) was added at 0°C. The mixture was set aside at +5°C for 12 h, diluted with ether (200 ml), washed with saturated aqueous solution of ammonium chloride (3×) and with water, dried and taken down. Chromatography on a column of silica gel (190 g) in light petroleum–benzene–ether (49 : 49 : 2) gave 720 mg (44%) of the ethynyl derivative *II*, m.p. 138–141°C (ether-light petroleum), $[\alpha]_D$ +13° (*c* 1·6). IR spectrum (tetrachloromethane): 3 620, 3 587 (OH), 3 314, 2 118 (C≡C—H). ^1H NMR spectrum: 3·67 m (1 H, $C_{(20)}$—H), 2·31 m (2 H, $C_{(22)}$—H),

2·02 t (1 H, $C_{(24)}$—H, $J_{22,24} = 2·5$), 0·77 s (3 H, $C_{(19)}$—H), 0·74 s (3 H, $C_{(18)}$—H). For $C_{23}H_{36}O$ (328·5) calculated: 84·09% C, 11·04% H; found: 83·81% C, 11·01% H. The column was then eluted further to obtain the derivative *IV* (*vide infra*).

(20*R*)-20-((2*R* and/or *S*)-2-Tetrahydropyranyloxy)-21-nor-5α-chol-23-yne (*III*)

A solution of the hydroxy derivative *II* (540 mg; 1·64 mmol) in dichloromethane (12 ml) was mixed with dihydropyran (0·16 ml; 1·75 mmol) and *p*-toluenesulfonic acid monohydrate (3 mg). After standing at room temperature for 3 h, the mixture was diluted with light petroleum (50 ml) and applied on a column of alumina (50 g). Elution with light petroleum–ether (98 : 2) afforded 590 mg (87%) of a mixture of diastereoisomeric ethers *III*. Thin-layer chromatography in light petroleum–ether (95 : 5) showed two compounds of R_F 0·50 and 0·40. ^{1}H NMR spectrum: 4·70 m (1 H, —O—CH—O— in the tetrahydropyranyloxy group), 1·93 m (1 H, $C_{(24)}$—H), 0·77 bs (4·4 H, $C_{(18)}$—H and $C_{(19)}$—H), 0·65 s (1·6 H, $C_{(18)}$—H). Part of this mixture (410 mg) was chromatographed on a column of alumina (80 g). Elution with light petroleum–ether (95 : 5) afforded 100 mg of the less polar diastereoisomer (R_F 0·50), m.p. 117–119°C (hexane), $[\alpha]_D$ −49° (*c* 1·9). IR spectrum (tetrachloromethane): 3 310, 2 117 (C≡C—H). ^{1}H NMR spectrum: 4·76 bs, (1 H, —O—CH—O—in the tetrahydropyranyloxy group), 2·23 m (1 H, $C_{(22)}$—H), 2·54 m (1 H, $C_{(22)}$—H), 1·91 t (1 H, $C_{(24)}$—H, $J_{22,24} = 2$), 0·76 s (3 H, $C_{(19)}$—H), 0·73 s (3 H, $C_{(18)}$—H). For $C_{28}H_{44}O_2$ (412·7) calculated: 81·50% C, 10·75% H; found: 81·30% C, 10·74% H. Further elution with the same solvent system afforded 200 mg of a mixture of both isomers and 100 mg of pure more polar isomer (R_F 0·40), m.p. 105–108°C (hexane), $[\alpha]_D$ +13° (*c* 1·7). IR spectrum (tetrachloromethane): 3 315, 2 117 (C≡C—H). ^{1}H NMR spectrum: 4·65 m (1 H, —O—CH—O— in the tetrahydropyranoxy group), 2·73 m (1 H, $C_{(22)}$—H), 2·41 m (1 H, $C_{(22)}$—H), 1·95 t (1 H, $C_{(24)}$—H, $J_{22,24} = 2$), 0·77 s (3 H, $C_{(19)}$—H), 0·65 s (3 H, $C_{(18)}$—H). For $C_{28}H_{44}O_2$ (412·7) calculated: 81·50% C, 10·75% H; found: 81·34% C, 10·54% H.

(20*S*)-21-Nor-5α-chol-23-yn-20-ol (*IV*)

Further elution of the column in the preparation of the ethynyl derivative *II* with light petroleum–benzene–ether (48 : 48 : 4) gave 450 mg (27%) of the compound *IV*, m.p. 128–131°C (ether), $[\alpha]_D$ +7° (*c* 2·6). IR spectrum (tetrachloromethane): 3 622, 3 588 (OH), 3 314, 2 118 (C≡C—H). ^{1}H NMR spectrum: 3·68 m (1 H, $C_{(20)}$—H, $W \approx 25$), 2·40 m (2 H, $C_{(22)}$—H), 2·03 t (1 H, $C_{(24)}$—H, $J_{22,24} = 2·5$), 0·76 s (3 H, $C_{(19)}$—H), 0·65 s (3 H, $C_{(18)}$—H). For $C_{23}H_{36}O$ (328·6) calculated: 84·09% C, 11·04% H; found: 83·79% C, 11·25% H.

(20*S*)-20-((2*R* and/or *S*)-2-Tetrahydropyranoloxy)-21-nor-5α-chol-23-yne (*V*)

Dihydropyran (0·2 ml; 2·19 mmol) and *p*-toluenesulfonic acid monohydrate (4 mg) were added to a solution of the hydroxy derivative *IV* (310 mg; 0·94 mmol) in dichloromethane (10 ml). After standing at room temperature for 3 h, the mixture was diluted with light petroleum (40 ml) and applied on a column of alumina (40 g). Elution with light petroleum–ether (98 : 2) gave 317 mg (81%) of a mixture of diastereoisomeric ethers *V*, unseparable by thin-layer chromatography (one spot of R_F 0·40 in light petroleum–ether, 95 : 5). IR spectrum (tetrachloromethane): 3 313, 2 127 (C≡C—H). ^{1}H NMR spectrum: 4·81 bs (0·45 H, —O—CH—O— in the tetrahydropyranyloxy group), 4·64 bs (0·55 H, —O—CH—O— in the tetrahydropyranyloxy group), 1·96 m (1 H, $C_{(24)}$—H), 0·77 s (3 H, $C_{(19)}$—H), 0·65 s (1·4 H, $C_{(18)}$—H), 0·61 s (1·6 H, $C_{(18)}$—H). For $C_{28}H_{44}O_2$ (412·7) calculated: 81·50% C, 10·75% H; found: 81·86% C, 10·87% H.

(20*R*)-21-Nor-5α-cholan-20-ol (*VI*)

A) The ethynyl derivative *II* (80 mg; 0·24 mmol) in ethyl acetate (10 ml) was hydrogenated over palladium on charcoal (30 mg; 10%) for 2 h at ordinary pressure. The catalyst was filtered off, the solvent evaporated *in vacuo* and the residue crystallized from ether. Yield 65 mg (80%) of *VI*, m.p. 145—147°C, $[\alpha]_D$ +16° (*c* 2·0), identical with an authentic sample[4].

B) The allenyl derivative *VIII* (80 mg; 0·24 mmol) was hydrogenated under conditions described under *A*), affording 61 mg (75%) of *VI*, m.p. 143—146°C, $[\alpha]_D$ +19° (*c* 2·0), identical with an authentic sample[4].

(20*S*)-21-Nor-5α-cholan-20-ol (*VII*)

A) The compound *IV* (80 mg; 0·24 mmol) was hydrogenated as described for the derivative *II* (see preparation of *VI*, procedure *A*). Crystallization from acetone afforded 63 mg (78%) of *VII*, m.p. 99—101°C, $[\alpha]_D$ +6° (*c* 2·0), identical with an authentic sample[4].

B) The allene *IX* (80 mg; 0·24 mmol) was hydrogenated as described under *A*), yielding 64 mg (79%) of *VII*, m.p. 96—98°, $[\alpha]_D$ +8° (*c* 2·0), identical with an authentic sample[4].

(20*R*)-21-Nor-5α-chola-22,23-dien-20-ol (*VIII*)

Lithium aluminium hydride (100 mg; 2·6 mmol) was added at −20°C to a stirred solution of the ethynyl derivative *X* (ref.[7], 200 mg, 0·47 mmol) in ether (10 ml). After 2 h at −20°C the mixture was poured into a saturated aqueous ammonium chloride solution, the product was taken up in ether and the organic layer washed with ammonium chloride solution. The residue was chromatographed on a silica gel column (25 g) in light petroleum–ether (95 : 5), affording 75 mg (49%) of *VIII*, m.p. 111—114°C (hexane); $[\alpha]_D$ +4° (*c* 1·6). IR spectrum (tetrachloromethane): 3 615, 3 485 (OH), 1 956, 847 (C=C=CH_2). ^{1}H NMR spectrum (Varian XL-200, 200 MHz): 5·21 m (1 H, $C_{(22)}$—H), 4·83 m (2 H, $C_{(24)}$—H), 4·08 m (1 H, $C_{(20)}$—H, $W \approx 25$), 0·82 s (3 H, $C_{(19)}$—H), 0·80 s (3 H, $C_{(18)}$—H). For $C_{23}H_{36}O$ (328·6) calculated: 84·09% C, 11·04% H; found: 83·84% C, 10·94% H.

(20*S*)-21-Nor-5α-chola-22,23-dien-20-ol (*IX*)

The title compound was prepared from the ethynyl derivative *XI* (ref.[7], 200 mg; 0·47 mmol) as described for preparation of the compound *VIII* from *X*. Chromatography of the residue on a silica gel column (27 g) in light petroleum–ether (90 : 10) gave 84 mg (55%) of *IX*, m.p. 140 to 142°C (ether); $[\alpha]_D$ +65° (*c* 2·4). IR spectrum (tetrachloromethane): 3 615, 3 470 (OH), 1 954, 844 (C=C=CH_2). ^{1}H NMR spectrum (Varian XL-200, 200 MHz): 5·21 m (1 H, $C_{(22)}$—H), 4·81 m (2 H, $C_{(24)}$—H), 4·06 t (1 H, $C_{(20)}$—H, $J \approx 8$), 0·79 s (3 H, $C_{(19)}$—H), 0·67 s (3 H, $C_{(18)}$—H). For $C_{23}H_{36}O$ (328·6) calculated: 84·09% C, 11·04% H; found: 84·27% C, 11·32% H.

(20*R*)-21,26,27-Trinor-5α-cholest-23-yne-20,25-diol (*XIV*)

A) An ethereal solution of ethylmagnesium bromide (2 ml, c 1 mol l^{-1}) was added to a solution of the ethynyl derivative *III* (310 mg; 0·75 mmol) in ether (4 ml) and after stirring for 1 h at room temperature, paraformaldehyde (200 mg) was added. The mixture was stirred for 1 week at room temperature, decomposed with saturated aqueous ammonium chloride solution and the product was taken up in ether. The ethereal solution was washed with an ammonia chloride solution and taken down *in vacuo*, leaving 300 mg of the crude alcohol *XII* which consisted of two diastereoisomers of R_F 0·48 and 0·42 (thin-layer chromatography in light petroleum–ether (1 : 1)). ^{1}H NMR

spectrum: 4·70 m (1 H, —O—CH—O— in the tetrahydropyranyloxy group), 4·25 bs (2 H, $C_{(25)}$—H), 0·77 bs (4·2 H, $C_{(19)}$—H and $C_{(18)}$—H), 0·64 s (1·8 H, $C_{(18)}$—H). A mixture of the crude product *XII* (250 mg; about 0·56 mmol), methanol (12 ml), benzene (3 ml), water (1 ml) and *p*-toluenesulfonic acid monohydrate (50 mg; 0·26 mmol) was stirred at room temperature for 5 h and taken down *in vacuo*. The product was extracted with ether, the extract washed with a solution of potassium hydrogen carbonate and water, dried, taken down and the residue chromatographed on a column of silica gel (22 g). Elution with benzene–ether (90 : 10) afforded 150 mg (67% based on *III*) of the diol *XIV*, m.p. 141–143°C, $[\alpha]_D$ +23° (*c* 1·4). IR spectrum (tetrachloromethane): 3 350 (OH). ^{1}H NMR spectrum: 4·24 bs (2 H, $C_{(25)}$—H), 3·65 m (1 H, $C_{(20)}$—H, $W \approx 20$), 2·33 m (2 H, $C_{(22)}$—H), 0·74 s (3 H, $C_{(19)}$—H), 0·70 s (3 H, $C_{(18)}$—H). Mass spectrum (*m/z*): 358 M^+, 340 (M – H_2O), 289 (M – $CH_2C{\equiv}CCH_2OH$), 271 (289 – H_2O). For $C_{24}H_{38}O_2$ (358·6) calculated: 80·39% C, 10·68% H; found: 80·72% C, 10·61% H.

B) A solution of 1-butyllithium in hexane (0·62 ml; c 1·6 mol l^{-1}) was added at 0°C to a solution of 1-methoxymethoxy-2-propyne[10] (100 mg; 1 mmol) in tetrahydrofuran (1 ml), the mixture was stirred for 5 min at room temperature and a solution of the epoxide *XV* (ref.[2]; 100 mg; 0·33 mmol) and hexamethylphosphoric triamide (0·05 ml; 0·29 mmol) in tetrahydrofuran (1 ml) was added. After stirring for 8 h at 60°C, the mixture was poured into dilute hydrochloric acid (50 ml, 1 : 4) and the product was taken up in ether. The ethereal extract was washed with potassium hydrogen carbonate solution and water, dried and taken down. The residue was subjected to chromatography on two silica gel plates in benzene–ether (4 : 1). Elution of the corresponding zones afforded the less polar unreacted epoxide *XV* (70 mg; 70%) and the more polar product *XIII* (22 mg; 17%). ^{1}H NMR spectrum: 4·69 s (—O—CH_2—O—), 4·21 t (2 H, $C_{(25)}$—H, $J \approx 2$), 3·63 m (1 H, $C_{(20)}$—H, $W \approx 20$), 3·36 s (—OCH_3), 0·75 s (3 H, $C_{(19)}$—H), 0·71 s (3 H, $C_{(18)}$—H). *p*-Toluenesulfonic acid monohydrate (20 mg; 0·11 mmol) was added to a solution of *XIII* (20 mg; 0·05 mmol) in benzene (2 ml) and methanol (2 ml) and the mixture was stirred fo 10 h at 40°C. After evaporation *in vacuo*, the residue was dissolved in benzene and applied on a column of silica gel (3 g). Elution with benzene–ether (90 : 10) afforded 14 mg (79%) of the diol *XIV*, m.p. 140–142°C (ether); $[\alpha]_D$ +21° (*c* 2·0).

(20*R*)-21,26,27-Trinor-5α-cholest-23-en-25 → 20-olide (*XVII*)

An alkaline solution of sodium borohydride[14] (0·2 ml; c 1 mol l^{-1}) was added to a solution of nickel acetate tetrahydrate (50 mg) in ethanol (5 ml). After stirring for 30 s in a hydrogen atmosphere, solutions of 1,2-diaminoethane in ethanol (0·7 ml; c = 0·58 mol l^{-1}) and the compound *XIV* (130 mg; 0·36 mmol) in ethanol (10 ml) were added. The mixture was stirred under hydrogen for 20 min, diluted with ether (50 ml) and filtered through a column of silica gel (10 g). The column was washed with ether, the eluates were taken down and the residue was chromatographed on a column of silica gel (10 g). Elution with benzene–ether (90 : 10) afforded 100 mg (77%) of the olefin *XVI*; IR spectrum (KBr): 3 405, 3 330 (OH), 3 025, 1 659, 720 (—CH=CH—). Silver carbonate on Celite[13] (2·5 g) was suspended in benzene (40 ml), a part of the benzene (10 ml) was distilled off under stirring and a solution of the diol *XVI* (90 mg; 0·25 mmol) in benzene (20 ml) was added. The stirred mixture was refluxed for 1 h, filtered through Celite, taken down and the residue was chromatographed on a preparative silica gel plate in light petroleum–ether–acetone (80 : 10 : 10) affording 43 mg (37% based on *XIV*) of the unsaturated lactone *XVII*, m.p. 185 to 188°C (light petroleum). ^{1}H NMR spectrum: 6·83 m (1 H, $C_{(23)}$—H, $W \approx 18$), 5·97 dt (1 H, $C_{(24)}$—H, $J_{23,24}$ = 9·5, $J_{22,24}$ = 1·5), 4·30 m (1 H, $C_{(20)}$—H, $W \approx 25$), 2·23 m (2 H, $C_{(22)}$—H), 0·79 s (3 H, $C_{(19)}$—H), 0·75 s (3 H, $C_{(18)}$—H). The product was identical with an authentic sample[1].

(20*S*)-21,26,27-Trinor-5α-cholest-23-yne-20,25-diol (*XX*)

A) The title compound was prepared from the ethynyl derivative *V* (310 mg; 0·75 mmol) by the same procedure as described for the preparation of *XIV* from *III*. The alcohol *XVIII* (320 mg) was isolated as an intermediate, homogeneous according to thin-layer chromatography in light petroleum–ether (1 : 1); R_F 0·45. ^{1}H NMR spectrum: 4·80 bs (0·5 H, —O—CH—O— in the tetrahydropyranyloxy group), 4·63 bs (0·5 H, —O—CH—O— in the tetrahydropyranyloxy group), 4·24 bs (2 H, $C_{(25)}$—H), 0·77 s (3 H, $C_{(19)}$—H), 0·65 s (1·5 H, $C_{(18)}$—H), 0·62 s (1·5 H, $C_{(18)}$—H). Removal of the protecting group gave 147 mg (59% based on *V*) of the diol *XX*, *XX*, m.p. 176–177°C (ether), $[\alpha]_D$ +2° (*c* 1·5). IR spectrum (KBr), cm^{-1}: 3 340 (OH), 2 225 (C≡C). ^{1}H NMR spectrum: 4·25 bs (2 H, $C_{(25)}$—H), 3·65 m (1 H, $C_{(20)}$—H, $W \approx 22$), 2·47 m (2 H, $C_{(22)}$—H), 0·77 s (3 H, $C_{(19)}$—H), 0·65 s (3 H, $C_{(18)}$—H). Mass spectrum (*m/z*): 358 M^+, 340 (M – H_2O), 289 (M – $CH_2C{\equiv}CCH_2OH$), 271 (289 – H_2O). For $C_{24}H_{38}O_2$ (358·6) calculated: 80·39% C, 10·68% H; found: 80·15% C, 10·74% H.

B) The intermediate *XIX* was prepared from the epoxide *XXI* (ref.[2], 100 mg, 0·33 mmol) in the same manner as the ethynyl derivative *XIII* from the epoxide *XV* (see the preparation of *XIV*, procedure *B*). The reaction gave 67 mg (67%) of the unreacted epoxide *XXI* and 22 mg (17%) of the product *XIX*. ^{1}H NMR spectrum: 4·71 s (—O—CH_2—O—), 4·22 t (2 H, $C_{(25)}$—H, $J_{22,25} \approx 2$), 3·67 m (1 H, $C_{(20)}$—H), 3·38 s (OCH_3), 0·77 s (3 H, $C_{(19)}$—H), 0·66 s (3 H, $C_{(18)}$—H). Removal of the protecting group from *XIX* (20 mg, 0·05 mmol) as described for *XIII* afforded 13 mg (73%) of the diol *XX*, m.p. 174–177°C (ether), $[\alpha]_D$ 0° (*c* 2·0).

(20*S*)-21,26,27-Trinor-5α-cholest-23-en-25 → 20-olide (*XXIII*)

The lactone *XXIII* was prepared from the diol *XX* (130 mg; 0·36 mmol) as described for the preparation of *XVII* from *XIV*. The olefinic diol *XXII* (97 mg; 74%) was isolated as intermediate; IR spectrum (KBr): 3 340 cm^{-1} (OH). The residue after work-up of the mixture after oxidation with silver carbonate on Celite was not chromatographed (as in the case of *XVII*) but crystallized from ether. Yield 57 mg (48% based on *XX*) of the unsaturated lactone *XXIII*, m.p. 193–195°C. ^{1}H NMR spectrum: 6·85 m (1 H, $C_{(23)}$—H, $W = 18$), 6·00 d (1 H, $C_{(24)}$—H, $J_{23,24} \approx 10$). 4·32 m (1 H, $C_{(20)}$—H, $W \approx 25$), 2·33 m (2 H, $C_{(22)}$—H), 0·77 s (3 H, $C_{(19)}$—H), 0·68 s (3 H, $C_{(18)}$—H). The product was identical with an authentic sample[1].

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