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A New Route to Precursors of Ecdysteroids Using a Regio- and Stereoselective Hydroboration

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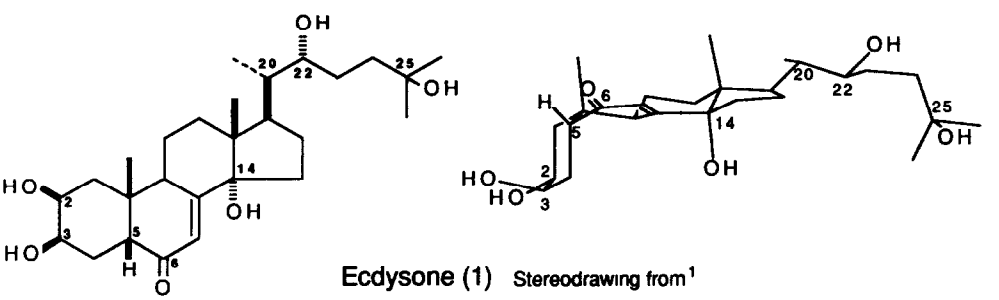
Abstract - We have developed a new route to precursors of ecdysteroids, using a regio- and stereoselective hydroboration Hydroboration of 3,3-(ethylenedioxy)-cholesta-5,7-diene (from 7-dehydrocholesterol in two steps), followed by oxidation with alkaline hydrogen peroxide, produces 3,3-(ethylenedioxy)-5β-cholest-7-en-6β-ol (the same reaction with 7-dehydrocholesterol leads only to the 5α-alcohol (OH-6α), prohibiting the synthesis of 5β-steroids)

Introduction

Ecdysteroids represent a family of polyhydroxylated steroids They serve as hormonal messengers and the parent molecule, ecdysone (**1**), is mostly referred to as the moulting and metamorphosis hormone of insects



Ecdysone (1) Stereodrawing from[1]

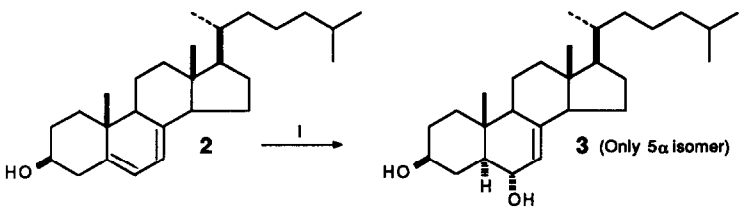
We have been interested for several years in the elucidation of the biosynthetic pathway of ecdysone[2-9] It is well documented that in several insect species like *Locusta* (also *Schistocerca* and *Manduca*), hydroxylation at C-2 is the last step in this biosynthesis[10-12] Therefore all potential precursors of ecdysone have to be synthesized necessarily without a C-2β hydroxyl group, which raises the problem of the A/B ring junction Indeed, in ecdysone, the 5β-epimer is more stable than the 5α-epimer, because of a steric interaction between the 2β-hydroxy group and the 10-methyl[13] In contrast, in 2-deoxyecdysteroids, this steric interaction is absent and the 5α-epimer is the preferred form[14,15]

This instability of the A/B *cis* ring junction (H-5β configuration) resulting from the absence of a 2β-hydroxy group in potential precursor molecules has prompted us to develop a novel approach to the synthesis of molecules with the H-5β configuration The key step in our method is the introduction of this particular configuration by a regio- and stereoselective hydroboration.

Discussion and results

SYNTHESIS OF 3,3-(ETHYLENEDIOXY)-5β-CHOLEST-7-EN-6-ONE

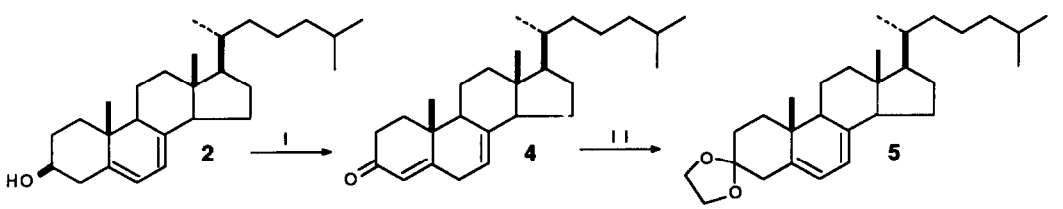
Hydroboration of 7-dehydrocholesterol (**2**) with an excess of borane-tetrahydrofuran complex, takes place by a 1 2 mechanism[16] (cis addition), leading to an allylic boron compound (5α) in which the boron atom is only in the 6α position Oxidation of this organoborane by alkaline hydrogen peroxide produces the corresponding 6α alcohol **3** with an 80% yield (Scheme 1)



Scheme 1 *Reagents and conditions* i, Borane-THF complex (5 eq), THF, 0°C, 2 h, alkaline hydrogen peroxide 30%, 0°C, 1 h, 80%

The stereochemistry of the reaction is determined by the relative accessibility of the two faces of the conjugated diene · the angular methyl groups at the C-10 and C-13 positions shield the β-face of the molecule and this results in an attack on the double bond from the less hindered α-face

Illustrations of this stereochemical preference are given elsewhere for epoxidation and hydrogenation[17] Exceptions have been noted in the epoxidation of 3,3-(ethylenedioxy)-Δ^5-olefin, a substance giving notable yields of the β-epoxide in addition to the α-epoxide[18] From a study of molecular models of this compound, it seems probable that ring B adopts a conformation in which, on the one hand, the β-methyl group at C-10 projects away from the double bond, while on the other the normally unhindered α-face is partially shielded by the axial 3α-oxygen atom of the ketal group

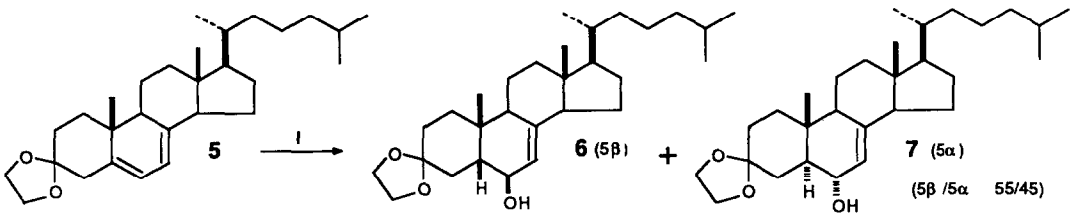


Scheme 2 *Reagents and conditions* i, $Al(OiPr)_3$, cyclohexanone, toluene, reflux, 30 min, 85%, ii, ethylene glycol, para-toluene sulfonic acid, toluene, reflux, 1 h, 65%

Based on these observations, we planned to synthesize 3,3-(ethylenedioxy)-cholesta-5,7-diene (**5**) from 7-dehydrocholesterol (**2**) in two steps as shown in Scheme 2

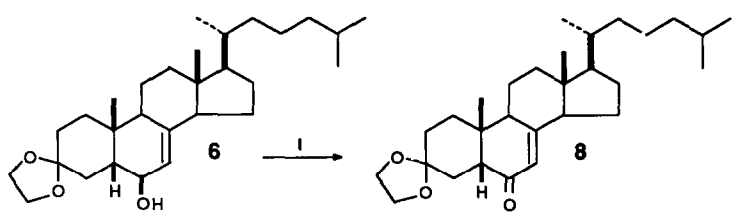
Compound **4** was obtained by reacting 7-dehydrocholesterol (**2**) with aluminium isopropoxide and cyclohexanone in toluene[19] (Oppenauer oxidation) The overall yield of the pure dienone **4** was 85% after chromatography

Treatment of compound **4** with ethylene glycol in toluene[20], containing a catalytic amount of p-toluene sulfonic acid, formed the resulting ketal **5** (65%), with coincident rearrangement of the double bond to the Δ^5 position By carefully monitoring the reaction by TLC, the formation of the less polar isomer 3 3-(ethylenedioxy)-5α-cholesta-6,8(14)-diene (**9**, by-product) could be minimized



Scheme 3 *Reagents and conditions* I, Borane-THF complex (10 eq), THF, 0°C, 4 h, alkaline hydrogen peroxide 30%, 0°C 1 h, 70%

Hydroboration of the ketal **5** with an excess of borane-tetrahydrofuran complex in tetrahydrofuran at 0°C, followed by oxidation with alkaline hydrogen peroxide, produces the two allylic alcohols **6** and **7** in an overall yield of 70%, with a weak diastereoisomeric excess (H-5β, OH-6β (**6**) / H-5α, OH-6α (**7**) 55/45) (Scheme 3) The A/B ring junction (cis or trans) was determined by ^{1}H NMR and ^{13}C NMR (^{1}H NMR δ = 1 07 ppm (CH_3-19, cis), δ = 0 85 ppm (CH_3-19, trans), ^{13}C NMR δ = 25 9 ppm, 36 6 ppm and 47 8 ppm (C-19, C-9 and C-5, cis), δ = 13 4 ppm, 48 5 ppm and 49 5 ppm (C-19, C-9 and C-5, trans)) In addition, mass spectrometry confirmed the identity of the two allylic alcohols As the boranes are well known to perform cis additions, an A/B cis ring junction (H-5β) involves an axial 6β-hydroxyl group, which conduces rapidely to a dehydratation (m/z 444 (100 0) , 426 (40 2)) In the same way, an A/B trans ring junction (H-5α) involves an equatorial, stable, 6β-hydroxyl group (m/z 444 (100 0) , 426 (10 2))



Scheme 4 *Reagents and conditions* I, Manganese dioxide, chloroform, room temperature 30 min, 80%

The oxidation of the allylic alcohol of compound **6** was performed by reacting with manganese dioxide in chloroform at room temperature[21] An overall yield of 80% of the pure 3,3-(ethylenedioxy)-5β-cholest-7-en -6-one (**8**) was obtained after chromatography (Scheme 4)

In order to increase the ratio **6/7** (H-5β, OH-6β / H-5α, OH-6α), hydroboration was performed with substituted borane derivatives

So, ketal **5** was reacted with 9-borabicyclo[3 3 1]nonane (9-BBN, 0 5M in tetrahydrofuran, Aldrich Chemical Company) in refluxing tetrahydrofuran (no reaction at 0°C and at room temperature, very slow reaction at 40°C) The allylic alcohol was obtained in good yield Unfortunately, only the unexpected isomer **7** (H-5α, OH-6α) was isolated Indeed, under these conditions, the desired compound **6** (H-5β, OH-6β) was not observed At higher temperatures, the addition of borane on a double bond is known to be reversible[22] The mechanism appears to involve a partial dissociation of the organoborane into an olefin and a boron-hydrogen moiety, followed by re-addition The process occurs until the boron atom ends up at the least hindered position of the molecule, thereby yielding the most stable of the organoboranes

Elsewhere, treatment of the ketal **5** with other dialkylboranes (disiamylborane, bornane prepared *in situ* with the appropriate olefin (methyl-2-butene-2 or 1,4-pentadiene) and borane-tetrahydrofuran complex in stoechiometric amount) did not produce reactions at 0°C and even at room temperature (these borane-derivatives might be too hindered) 7-Dehydrocholesterol (**2**), taken as a model of a conjugated endocyclic diene, did not react with disiamylborane under the same conditions, but produced slowly the allylic alcohol **3** (H-5α, OH-6α) with bornane, at room temperature (moderate yield)

Alternatively, to increase the ratio **6/7** (H-5β, OH-6β / H-5α, OH-6α), we planned to synthesize the corresponding thioketal (3,3-trimethylenedithio-cholesta-5,7-diene) directly from the dienone **4** In fact, an axial sulfur atom may hinder the α-face of the steroid more than an oxygen atom Unfortunately, treatment of compound **4** with propanedithiol and zinc chloride in chloroform at room temperature[23] produced the Δ^4-thioketal (3,3-trimethylenedithio-cholesta-4,7-diene) in 95% yield (85% with p-toluene sulfonic acid in refluxing toluene) , this reaction did not involve a shift of the double bond to the Δ^5 position

Other types of protection[24] of the dienone **4**, like thiazolidines, imidazolidines or hemithioketals have not yet been examined.

Acknowledgments

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Experimental

Melting points were measured on a Reichert hot stage microscope and are uncorrected $[\alpha]_D$ were measured on a Perkin-Elmer 141 polarimeter in $CHCl_3$ IR spectra were recorded in KBr on a Perkin-Elmer 881 infrared spectrophotometer UV spectra were measured on a Kontron-Uvikon 810 UV-vis spectrophotometer NMR spectra were recorded on a Bruker SY (200 MHz) and a Bruker AM (400 MHz) apparatus with $CHCl_3$ (δ = 7 26 ppm) and C_6H_6 (δ = 7 20 ppm) as internal standards for ^1H NMR, $CDCl_3$ (δ = 77 02 ppm) or CD_2Cl_2 (δ = 53 80 ppm) as internal standards for ^{13}C NMR The chemical shifts are reported in ppm downfield from TMS (*, + = interchangeable assignement) MS were measured on a LKB 9000 S apparatus by direct introduction, or coupled to a GC DB5 column (J W) , an ionization potential of 70 eV was used Microanalyses were performed by the Strasbourg Division

	2#	3#	4#	5§	6§	7§	8#
1	32.0*	30.8*	33 4*	31.8*	31 1*	31 4*	31 1*
2	38.4*	33 6*	34.2*	37.7*	34 4*	33 9*	32 8*
3	70.5	70 6	199.0	109 1	109.4	109.2	107 8
4	40 8*	36.9*	122 8	40 6	36 3*	36 6*	34 1*
5	141 4+	49 0	168 6	141 4+	47 8	49 5	54 5
6	119 6'	68 3	32.9	116.6'	71 3	70 5	201 7
7	116.3'	121 7	115 5	120 1'	118 6	122 5	121 6
8	139 8+	141 3	139 6	139 8+	142 9	141 8	165 1
9	46 3	48 6	46 1	46 5	36 5	48 5	36 0
10	37 0	35 0	38 1	37 3	33 7	36 4	36.0
11	21 2	21 2	22 1	21.6	22 4	21 8	21 9
12	39 2	39 1	39 3	39 8	39 9	39 9	39 1
13	43 0	43 3	43 6	43.4	44 2	44 0	45 4
14	54 5	54 7	55 0	54 9	55 4	55 2	56 1
15	23 0	22 8	22 9	23 5	23 4	23 3	22 6
16	28 1	27 4	27 9	28 5	28 3	28 3	27 8
17	55 9	56 2	56 2	56 5	56 7	56 6	56 3
18	11 8	11 4	11 9	12 0	12 2	12 1	12 4
19	16 3	13 3	21 2	16 4	25 9	13 4	23 6
20	36 2	36 0	36 2	36 6	36 5	36 6	36 0
21	18.9	18 9	18 9	19 1	19 1	19 1	18 8
22	36 2	36,0	36 2	36 6	36 6	36 6	36 0
23	23 9	23 8	24 0	24 3	24 3	24 3	23 9
24	39 5	39 6	39 6	39 9	40 0	39 9	39 5
25	28 0	28 0	28 0	28 5	28 5	28 5	28 0
26	22 6-	22 6-	22 5-	22 7-	22 7-	22 7-	22 6-
27	22 8-	22 8-	22 7-	22 9-	23 0-	23 0-	22 8-
1'				64 6"	64 6	64 4"	64 4
2'				64 7"	64 6	64 6"	64 4

Table 1 : ^{13}C NMR chemical shifts

δ_C (100 MHz, standard Me_4Si) * (or $^+$, $^-$, ', ") interchangeable assignment
Solvents (#) $CDCl_3$ (77 02) or (§) CD_2Cl_2 (53 80)
The assignments were based upon (1) shielding data , (2) by comparison with the spectra of closely related ecdysteroids[a,b] and steroids[c]

References (a) W B Smith, *Org Magn Reson* , 1977, *9*, 644 , (b) See ref 5, 10 and 21
(c) J W Blunt et al, *Org Magn Reson* , 1977, *9*, 439

of the Service Central de Microanalyse of CNRS TLC were run on pre-coated plates of silica gel 60 F 254 (Merck), dipped in a solution of vanillin (1 g) in $EtOH/H_2SO_4$ (95/5, 1 l) and heated on a hot plate to reveal the compounds Medium pressure chromatography (P = 0 5 - 1 1 bar) was conducted on silica gel (40 - 63 µm, Merck) columns All solvents were freshly distilled before use Air- or moisture- sensitive reactions were conducted in flame-dried glassware and under an inert atmosphere

5α-Cholest-7-ene-3β,6α-diol (3)

7-Dehydrocholesterol (2) (400 mg, 1 04 mmol) in anhydrous tetrahydrofuran (30 ml) was treated dropwise at 0°C with 5 ml of borane-tetrahydrofuran complex solution (1 0M solution in tetrahydrofuran, Aldrich Chemical Company) and left at room temperature for 2 hours The solution was then treated with an aqueous sodium hydroxyde solution (5%, 15 ml), followed by a hydrogen peroxide solution (30%, 7 ml) After a further 1 hour at room temperature, the solution was washed twice with water, Fe (II) sulfate solution (10%), brine, dried with sodium sulfate, evaporated under reduced pressure and the residue was chromatographed on silica gel Elution with hexane/ethyl acetate 80/20 gave 5α-cholest-7-ene-3β,6α-diol (3), 335 mg (80%)

3 **Mp** 192°C , $[\alpha]_D^{20}$ + 48 (c = 1 1) , **IR** ν (cm^{-1}) 3337 , 2956 , 1461 , 1374 , 1054 , ^{1}**H NMR** 200 MHz ($CDCl_3$) δ 0 57 (s, 3H, H-18) , 0 84 (s, 3H, H-19) , 0 86 (d, J = 6 59 Hz, 6H, H-26,27) , 0 92 (d, J = 6 20 Hz, 3H, H-21) , 3 57 (m, $w_{1/2}$ = 20 0 Hz, 1H, H-3) , 3 81 (bd, $w_{1/2}$ = 15 0 Hz, 1H, H-6) , 5 18 (bd, $w_{1/2}$ = 5 0 Hz, 1H, H-7) , **MS** m/z 402 (14 8) (M^+, $C_{27}H_{46}O_2$) , 385 (22 9) , 384 (77 0) , 369 (26 5) , 366 (19 0) , 352 (27 9) , 351 (100 0) , 325 (28 2) , 270 (42 6) , 253 (37 1) , **Microanalysis** calc for $C_{27}H_{46}O_2$ (402 6584) C 80 54, H 11 51 , found C 80 38, H 11 52 , ^{13}**C NMR** in table 1

Cholesta-4,7-dien-3-one (4)

A toluene solution (400 ml, freshly distilled) containing 7-dehydrocholesterol (2) (20 0 g, 52 0 mmol), cyclohexanone (60 ml, 0 58 mol, freshly distilled) and molecular sieve 0 4 nm (10 0 g) was stirred at room temperature for 2 hours After the rapid addition of aluminium isopropoxide (6 0 g, 29 3 mmol), the orange-red reaction solution was stirred and boiled under reflux for 30 minutes The solution was cooled to room temperature, washed successively with cold (5°C) 2N hydrochloric acid, cold water, cold aq sat sodium hydrogen-carbonate and cold brine, dried with sodium sulfate and filtered The toluene solution was concentrated to dryness under reduced pressure and the residue was chromatographed on silica gel Elution with hexane/ethyl acetate 95/5 gave cholesta-4,7-dien-3-one (4), 17 0 g (85%)

4 **Mp** 87-89°C , $[\alpha]_D^{23}$ + 33 (c = 1 0) , **UV** λ_{max} (ethanol) 238 nm (ε = 15500) , **IR** ν (cm^{-1}) 1690 , 1630 , 1470 , ^{1}**H NMR** 200 MHz ($CDCl_3$) δ 0 59 (s, 3H, H-18) , 0 86$^+$ (d, J = 6 61 Hz, 3H, H-26) , 0 87$^+$ (d, J = 6 59 Hz, 3H, H-27), 0 93 (d, J = 6 26 Hz, 3H, H-21) , 1 17 (s, 3H, H-19) , 5 18 (m, $w_{1/2}$ = 9 0 Hz, 1H, H-7) , 5 79 (d, J = 1 72 Hz, 1H, H-4) , **SM** m/z 382 (100 0) (M^+, $C_{27}H_{42}O$) , 367 (9 0) , 339 (10 8) , 338 (37 9) , 259 (20 6) , 247 (11 6) , 227 (10 5) , 136 (20 7) , **Microanalysis** : calc for $C_{27}H_{42}O$ (382 3578) C 84 81, H 11 07 , found C 84 78, H 11 18 , ^{13}**C NMR** in table 1

3,3-(Ethylenedioxy)-cholesta-5,7-diene (5)

A mixture of 1 8 g of cholesta-4,7-dien-3-one (4) (4 7 mmol), 20 ml of toluene, 2 ml of ethylene glycol and 20 mg of p-toluenesulfonic acid monohydrate was stirred and refluxed for 1 hour (continuous water-removal adapter) Saturated sodium hydrogen-carbonate solution was added to the cooled mixture and the toluene layer was separated The extract was washed twice with water, brine, dried with sodium sulfate, evaporated under reduce pressure and the residue was chromatographed on silica gel Elution with hexane/ethyl acetate 98/2 gave 3,3-(ethylenedioxy)-5α-cholesta-6,8(14)-diene (9), 25 mg (2%) and 3,3-(ethylenedioxy)-cholesta-5,7-diene (5), 865 mg (65%)

9 ^{1}H NMR 200 MHz ($CDCl_3$) δ 0 75 (s, 3H, H-18) , 0 87 (d, J = 6 69 Hz, 6H, H-26,27) , 0 88 (s, 3H, H-19) , 0 94 (d, J = 6 53 Hz, 3H, H-21) , 3 94 (s, 4H, H-1',2') , 5 50 (dd, J = 5 49 et 9 85 Hz, 1H, H-6) , 6 09 (d, J = 9 82 Hz, 1H, H-7) , SM m/z 426 (100 0) (M^+, $C_{29}H_{46}O_2$) , 311 (24 4) , 211 (20 7) , 185 (18 5) , 157 (23 5) , 145 (20 0) , 99 (18 0)

5 Mp 135 5-137°C , $[\alpha]_D$31 - 14 (c = 2 1) , UV λ_{max} (ethanol) 271 nm (ε = 10600), 282 nm (ε = 11500), 294 nm (ε = 7000) , IR ν (cm^{-1}) 2948 , 1735 , 1650 , 1460 , 1378 , 1100 , 1085 , ^{1}H NMR 200 MHz ($CDCl_3$) δ 0 61 (s, 3H, H-18) , 0 87 (d, J = 6 55 Hz, 3H, H-26,27) , 0 94 (d, J = 6 45 Hz, 3H, H-21) , 1 00 (s, 3H, H-19) , 3 70 (s, 4H, H-1',2') , 5 41* (b, $w_{1/2}$ = 10 0 Hz, 1H, H-6) , 5 57* (b, $w_{1/2}$ = 10 0 Hz, 1H, H-7) , ^{1}H NMR 200 MHz (C_6D_6) δ 0 68 (s, 3H, H-18) , 0 93 (d, J = 6 56 Hz, 3H, H-26,27) , 0 96 (s, 3H, H-19) , 0 99 (d, J = 5 19 Hz, 3H, H-21) , 2 43 (d, J = 15 58 Hz, 1H, H-4) , 2 74 (d, J = 14 97 Hz, 1H, H-4) , 3 58 (s, 4H, H-1',2') , 5 53* (b, $w_{1/2}$ = 10 0 Hz, 1H, H-6) , 5 64* (b, $w_{1/2}$ = 10 0 Hz, 1H, H-7) , SM m/z 426 (43 2) (M^+, $C_{29}H_{46}O_2$) , 411 (6 2) , 364 (5 8) , 327 (5 6) , 325 (8 7) , Microanalysis · calc for $C_{29}H_{46}O_2$ (426 6804) C 81 63, H 10 87 , found C 81 51, H 11 05 , ^{13}C NMR in table 1

3,3-(Ethylenedioxy)-5β-cholest-7-en-6β-ol (6)

3,3-(Ethylenedioxy)-cholesta-5,7-diene (**5**) (400 mg, 0 94 mmol) in anhydrous tetrahydrofuran (30 ml) was treated dropwise at 0°C with 10 ml of borane-tetrahydrofuran complex solution (1 0M solution in tetrahydrofuran, Aldrich Chemical Company) and left at room temperature overnight The solution was then treated with an aqueous sodium hydroxide solution (5%, 20 ml), followed by an hydrogen peroxide solution (30%, 7 ml) After a further 1 hour at room temperature, the solution was washed twice with water, Fe (II) sulfate solution (10%), brine, dried with sodium sulfate, evaporated under reduced pressure and the residue was chromatographed on silica gel Elution with hexane/ethyl acetate 90/10 gave a mixture of 3,3-(ethylenedioxy)-cholest-7-en-5α-ol (**10**), 21 mg (5%), 3,3-(ethylenedioxy)-5β-cholest-7-en-6β-ol (**6**), 150 mg (36%), 3,3-(ethylenedioxy)-5α-cholest-7-en-6α-ol (**7**), 121 mg (29%)

10 ^{1}H NMR 200 MHz ($CDCl_3$) δ 0 54 (s, 3H, H-18) , 0 86 (d, J = 6 54 Hz, 3H, H-26) , 0 87 (d, J = 6 61 Hz, 3H, H-27) , 0 91 (s, 3H, H-19) , 0 92 (d, J = 6 24 Hz, 3H, H-21) , 3 95 (s, 4H, H-1',2') , 5 05 (b, $w_{1/2}$ = 10 0 Hz, 1H, H-7) , SM m/z 444 (100 0) (M^+, $C_{29}H_{48}O_3$) , 426 (45 2) , 411 (34 8) , 364 (45 9) , 329 (47 5) , 328 (32 7) , 121 (60 4)

6 Mp 100-101°C , $[\alpha]_D^{22}$ + 24 (c = 2 9) , IR ν (cm^{-1}) 3502 , 2916 , 2890 , 1662 , 1465 , 1368 , 1273 , 1240 , 1181 , 1105 , 1028 , ^{1}H NMR 200 MHz ($CDCl_3$) δ 0 58 (s, 3H, H-18) , 0 87 (d, J = 6 59 Hz, 6H, H-26,27) , 0 93 (d, J = 6 18 Hz, 3H, H-21) , 1 07 (s, 3H, H-19) , 3 73 (bd, J = 5 00 Hz, 1H, H-6) , 3 93 (s, 4H, H-1',2') , 5 35 (bd, J = 5 00 Hz, 1H, H-7) , MS m/z 444 (100 0) (M^+, $C_{29}H_{48}O_3$) , 426 (40 2) , 382 (23 7) , 367 (45 6) , 329 (24 3) , 149 (22 9) , 99 (56 6) , Microanalysis calc for $C_{29}H_{48}O_3$ (444 6852) C 78 33, H 10 88 , found C 78 28, H 10 91 , ^{13}C NMR in table 1

7 Mp 142-144°C , $[\alpha]_D^{23}$ = + 39 (c = 0 8) , IR ν (cm^{-1}) 3547 , 3477 , 2955 , 2812 , 1467 , 1377 , 1210 , 1182 , 1101 , 1033 , ^{1}H NMR 200 MHz ($CDCl_3$) δ 0 54 (s, 3H, H-18) , 0 85 (s, 3H, H-19) , 0 87 (d, J = 6 05 Hz, 6H, H-26,27) , 0 92 (d, J = 6 21 Hz, 3H, H-21) , 3 78 (bd, J = 7 50 Hz, 1H, H-6) , 3 95 (s, 4H, H-1',2') , 5 18 (bd, J = 1 74 Hz, 1H, H-7) , MS m/z 444 (100 0) (M^+, $C_{29}H_{48}O_3$) , 426 (10 2) , 382 (9 5) , 329 (9 4) , 99 (52 9) , Microanalysis calc for $C_{29}H_{48}O_3$ (444 6852) C 78 33, H 10 88 , found C 78 12, H 11 02 , ^{13}C NMR in table 1

3,3-(Ethylenedioxy)-5β-cholest-7-en-6-one (8)

544 mg (1 2 mmol) of 3,3-(ethylenedioxy)-5β-cholest-7-en-6β-ol (**6**) were dissolved in 40 ml of chloroform and 16 0 g of manganese dioxide (184 mmol, 150 eq, Merck, activated precipitate) were added After 30 min the reaction was stopped, the suspension filtered on celite, the filtrat evaporated under reduced pressure and the residue was chromatographed on silica gel Elution with hexane/ethyl acetate 95/5 gave 3,3-(ethylenedioxy)-5β-cholest-7-en-6-one (**8**), 435 mg (80%)

8 Mp 106-107°C , $[\alpha]_D^{23}$ = + 74 (c = 0 8) , UV λ_{max} (CH_3CN) 192 nm (ε = 5300), 239 nm (ε = 17900) , IR ν (cm^{-1}) 2930 , 1655 , 1618 , 1457 , 1381 , 1363 , 1313 , 1282 , 1261 , 1103 , 1036 , **^{1}H NMR** 200 MHz ($CDCl_3$) δ 0 60 (s, 3H, H-18) , 0 87 (s, 3H, H-19) , 0 87 (d, J = 6 57 Hz, 6H, H-26,27) , 0 93 (d, J = 5 94 Hz, 3H, H-21) , 2 52 (C part of an ABC system, That looks like a dd, $J_{apparent}$ = 3 92 Hz and $J_{apparent}$ = 12 44 Hz, 1H, H-5) , 3 94 (s, 4H, H-1',2') , 5 71 (t, J = 2 21 Hz, 1H, H-7) , MS m/z 442 (60 3) (M^+, $C_{29}H_{46}O_3$) , 413 (27 5) , 328 (10 7) , 167 (20 6) , 99 (100 0) , **Microanalysis** calc for $C_{29}H_{46}O_3$ (442 6794) C 78 68, H 10 47 , found C 78 79 , H 10 51 , **^{13}C NMR** in table 1

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