On reduction of α,β-unstaurated ketones and the respective allylic alcohols, bearing a phenylsulfonyl or phenylsulfanyl group in the α position. Hydroxy group-controlled stereoselective reduction of 3α- and 3β-hydroxy-4-(phenylsulfonyl)cholest-4-ene

Karol Michalak, Wiaczesław Stepanenko and Jerzy Wicha *

Institute of Organic Chemistry, Polish Academy of Sciences, POB 58, 01-224 Warsaw, Poland

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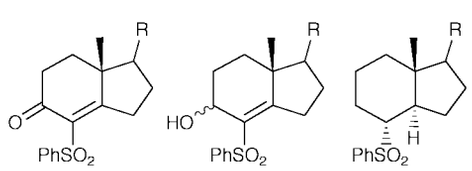
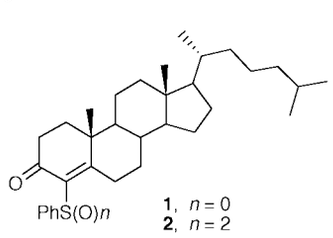
Reduction reactions of cholest-4-en-3-one derivatives bearing the phenylsulfonyl or phenylsulfanyl group at C-4 with various metal hydrides are studied. Lithium aluminohydride reduction of 4-(phenylsulfonyl)cholest-4-en-3β-ol **13a** and 4-(phenylsulfonyl)cholest-4-en-3α-ol **15a** occurs with saturation of the double bond and deoxygenation to give 4β-phenylsulfonyl-5β-cholestane **8** and 4α-phenylsulfonyl-5α-cholestane **7a**, respectively. Reduction of 4-(phenylsulfonyl)cholest-4-en-3-one **2** with lithium aluminohydride yields compound **8**. Reduction of compounds **2**, **13a** and **15a** with other metal hydrides affords mixtures of diastereomeric products. Metal hydride reductions of 4-(phenylsulfanyl)cholest-4-en-3-one **1** affect the carbonyl group only. Catalytic hydrogenation of compound **2** gives a mixture of 5α- and 5β- dihydro derivatives. Mechanistic and stereochemical aspects of the reduction reactions are discussed.

Introduction

Metal hydride reduction reactions of α,β-unsaturated ketones,[1,2] α-phenylsulfonyl ketones[3] and vinyl sulfones[4–6] have been extensively studied. However, there are no reports on the reduction of α,β-unsaturated ketones bearing in the α-position a phenylsulfonyl or a phenylsulfanyl group. In such derivatives relative rates of reduction of the carbonyl group and the double bond may differ from those in the parent compound, and, consequently, the steric outcome of the reaction may be different. Some consecutive reactions due to the presence of the sulfur-containing group may also occur. Recently, we have shown[7,8] that the complex hydrindane derivative **i** with oxo and vinyl sulfone functions, in reaction with lithium aluminohydride was transformed stereoselectively into product **iii** with *trans*-fused hydrindane rings. We have also noted that the steric course of the carbon–carbon double-bond reduction doesn't depend upon the orientation of the hydroxy group (α or β) in the intermediate **ii**. It was thought of interest to examine in some detail the reduction of easily available α,β-unsaturated ketones **1** and **2**, and the corresponding 3-hydroxy derivatives that are likely immediate products of the carbonyl compounds' reduction. It was expected that we would gain insight into the multistep reduction mechanism and, eventually, develop stereoselective approaches to *trans*- and *cis*-decalin derivatives.

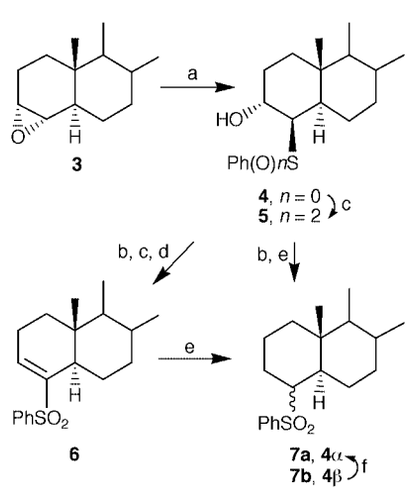


R = oxygen substituent or modified steroid side chain



Results and discussion

Sulfide **1** was prepared by treatment of 4β,5-epoxy-5β-cholestan-4-one[9] with thiophenol and potassium hydroxide in ethanol.[10] Sulfone **2** was obtained by oxidation of sulfide **1** with MCPBA. In order to prepare some reference compounds, the known[11,12] 3α,4α-epoxy-5α-cholestane **3** (Scheme 1) was



Scheme 1 *Reagents and yields*: (a) PhSH, EtOH, 83% yield; (b) MsCl, Et_3N, CH_2Cl_2; (c) MCPBA, 100%; (d) DBU, PhH, 95% in 2 steps; (e) Et_3BLiH, 99%; (f) *tert*-BuOK–*tert*-BuOH, 100%.

allowed to react with sodium thiophenolate in ethanol to give diaxial hydroxy sulfide **4**, by analogy to the procedure developed for related hydrindane derivatives.[13] Compound **4** was treated consecutively with mesyl chloride, MCPBA, and DBU to afford vinylic sulfone **6**. Reduction of **6** with Et_3BHLi and chromatographic separation of the products afforded

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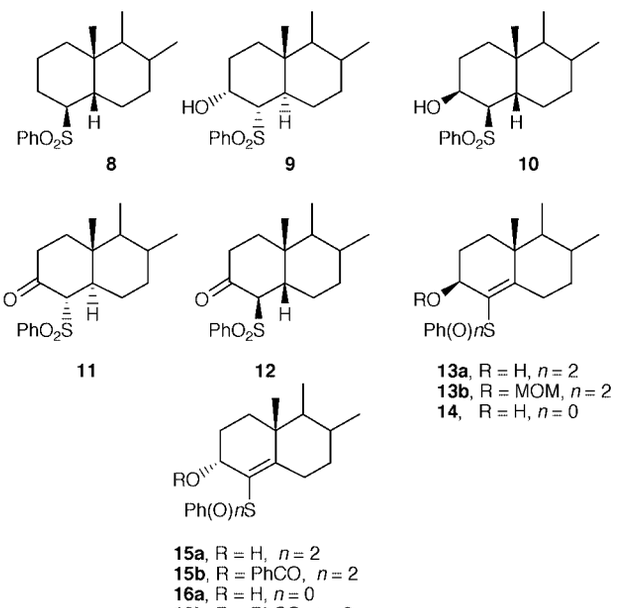
4α- and 4β-phenylsulfonyl derivatives **7a** and **7b** in 79 and 20% yield, respectively. Alternatively, oxidation of hydroxy sulfide **4** with MCPBA provided sulfone **5**, which on treatement with mesyl chloride and then with Et_3BHLi gave a mixture of **7a** and **7b**. Compound **7b** with an axially oriented phenylsulfonyl group was transformed into its epimer **7a** quantitatively with potassium *tert*-butoxide in *tert*-butyl alcohol.[14]

Reduction of sulfone **2** with an excess of $LiAlH_4$ in THF at room temperature afforded saturated sulfone **8** with *cis* configuration at the ring junction, isolated in 78% yield. The structure of compound **8** was confirmed by its reduction with sodium amalgam, which afforded 5β-cholestane.

Reduction of compound **2** with $NaBH_4$ in methanol afforded a mixture of hydroxy sulfones **9** (5α-H) and **10** (5β-H) (83% yield). The mixture could not be separated by either chromatography or crystallization; however, a sample of pure compound **9** was isolated by precipitation. Oxidation of the crude mixture of **9** and **10** with Jones reagent followed by chromatography afforded oxo sulfones **11** and **12** in 58% and 41% yield, respectively. Configuration at C-5 in compounds **11** and **12** was established by their reduction to 5α- and 5β-cholestan-3-one, respectively.



The configuration around C-3 and C-4 in compound **9** follows from the results of nuclear Overhauser effects (NOE) experiments involving C-19, C-4 and C-3 protons (see Experimental section). Configuration around C-3 and C-4 in **10** was deduced from the ^1H NMR spectrum of the mixture of **9** and **10** in which the signals of the C-3 proton (δ 3.91, broad singlet) and the C-4 proton (δ 3.15, doublet of doublets, $J = 12.1$ and 2.0 Hz) in **10** could be seen. It was assumed that the value $J = 2$ Hz corresponds to C-3–C-4 proton coupling (*cis*) and that the value $J = 12.1$ Hz reflects coupling of C-4 and C-5 protons in a *trans* configuration (4α,5β). The assignment of structures of **9** and **10** was corroborated by the ^1H NMR spectrum of previously prepared hydroxy sulfone epimer **5** which differs from that of **9** in the orientation of the phenylsulfonyl group. It is noteworthy that in both alcohols **9** and **10** the hydroxy group occupies an axial position whereas the sulfonyl group is in an equatorial position.

Next, reduction of **2** with $NaBH_4$ in THF in the presence of DMPU as a polar co-solvent was examined. Treatment of **2** with $NaBH_4$ in THF–DMPU (a suspension) at room temperature afforded a mixture of hydroxy sulfones **9** and **10** in 74% yield in a ratio of ≈5.5 : 1, and oxo sulfone **12** in 23% yield. Oxo sulfone **12** resisted further reduction under the reaction conditions. It is noteworthy that isomeric oxo sulfone **11** was smoothly reduced under analogous conditions to give alcohol **9**. This experiment shows that the reduction reaction occurs along two mechanistic paths: (1) with reduction of the carbonyl group preceding the reduction of the carbon–carbon double bond and (2) with reduction of the carbon–carbon double bond occurring first, followed by reduction of the carbonyl group (or providing a saturated ketone **12**). In practical terms, selectivity with regard to the ring-junction configuration was poor, providing, in total, 5α and 5β isomers in the ratio 65 : 35.

Reduction of **2** with a system, CuCN–*n*-BuLi–DIBAH, that is known to reduce steroidal and related 4-en-3-ones selectively to the corresponding 5α-H saturated ketones,[15,16] afforded a mixtute of ketones **11** (39%) and **12** (22%) and unsaturated alcohol **13a** (10%). Reduction of **2** with DIBAH in methylene dichloride affected the carbonyl group only and yielded quantitatively alcohol **13a**.

Allylic alcohol **13a** was thought to be a likely intermediate in reduction of phenylsulfonyl enone **2** to sulfone **8** by means of LiAlH. Since a directive effect of the hydroxy group appeared to be possible it was of interest to compare the steric courses of reduction of epimeric alcohols **13a** and **15a**. Accordingly, alcohol **13a** was subjected to the Mitsunobu inversion which afforded 3α-hydroxy sulfone **15a** in 64% overall yield, *via* benzoate **15b**. In parallel experiments **15a** was prepared from 3β-hydroxy sulfide **14** (see below) *via* **16b** and **16a** in a somewhat better overall yield (68%).

Reduction of 3β-hydroxy sulfone **13a** with $LiAlH_4$ afforded 5β-H sulfone **8** in 78% yield. Reduction of 3α-hydroxy sulfone **15a** with $LiAlH_4$ afforded 5α-H sulfone **7a** in 82% yield.

In light of the clear directing effect exerted by the hydroxy group in the reduction of hydroxy sulfone **13a**, it was of interest to examine the effect of an alkoxy group. To this end, the methoxymethyl derivative **13b**, prepared from **13a** in the usual way, was treated with $LiAlH_4$. Three products, **8**, **7a** and **7b**, were obtained; a ratio of 5α- to 5β-H products was estimated as ≈1 : 1. The above results for the reduction reactions of vinylic sulfones **2**, **13a** and **15a** are compiled in Table 1.

Reduction of sulfide **1** with various reducing agents afforded mixtures of 3-hydroxy-4-(phenylsulfanyl)cholest-4-enes **14** and **16a**. Some results are shown in Table 2. No carbon–carbon double-bond reduction was observed. Only Luche reduction[17] ($NaBH_4$–$CeCl_3$) was virtually selective with respect to 3β-hydroxy derivative **14**.

Catalytic hydrogenation of sulfone **2** in the presence of 10% palladium on carbon was examined for completeness of our study. Compound **2** was practically unchanged under hydrogenation conditions in EtOH at room temperature. However, at reflux temperature the reaction was complete in *ca.* 5 h to yield *trans* and *cis* products, **11** and **12** in the ratio 6.5 : 1. Hydrogenation of **2** in EtOH at room temperature in the presence of CF_3COOH afforded **11** and **12** in the ratio 5.5 : 1. Our attempts to achieve stereoselective reduction of the carbon–carbon double bond in **2** by varying the solvent in the catalytic hydrogenation reaction failed.

The above described experiments allow for some mechanistic comments. It is likely that reduction of **2** to 5β-H saturated sulfone **8** commences with hydride ion addition to the carbonyl group from the α-side to form intermediate **iv**, Scheme 2. Further reduction occurs with intramolecular hydride ion delivery and elimination of the metal-bonded oxygen atom. The intermediate vinylic sulfone **v** with *cis* ring junction undergoes further reduction to **8**. This mechanism is corroborated by stereoselective reduction of the allylic alcohol with β-oriented hydroxy group, **13a** (Table 1, entry 2). Intramolecular hydride anion delivery presumably occurs in a similar fashion in reduction of 3α-hydroxy derivative **15a** (*via* intermediate **vi**) to yield 5α-H sulfone **7a** (Table 1, entry 3). The importance of the hydroxy group for stereoselective introduction of the hydrogen at C-5 is also shown by the reduction of the MOM ether **13b** in which a mixture of 5α- and 5β-H products was formed

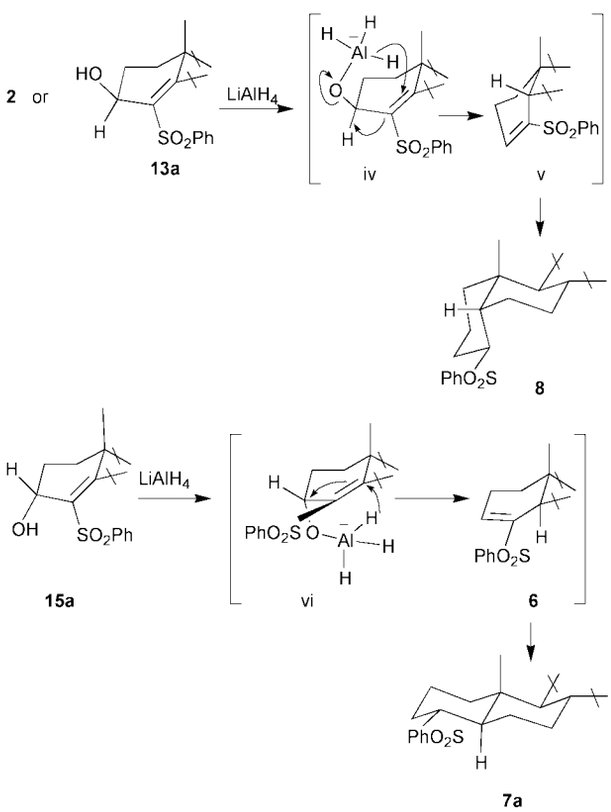
Table 1 Reduction of oxo sulfone **2** and hydroxy sulfones **13a** and **15a** with metal hydrides

Entry	Compound	Reducing system	Product (yield %), ratio	5α : 5β
1	**2**	$LiAlH_4$–THF	**8** (78)	5β-H only
2	**13a**	$LiAlH_4$–THF	**8** (78)	5β-H only
3	**15a**	$LiAlH_4$–THF	**7a** (82)	5α-H only
4	**13b**	$LiAlH_4$–THF	**8**, **7a**, **7b**	1 : 1
5	**2**	$NaBH_4$–MeOH	**9**, **10** (83)	3 : 2
6	**2**	$NaBH_4$–THF–DMPU	**9**, **10** (74) and **12** (23)	2 : 1
7	**2**	CuCN–*n*-BuLi–DIBAH	**11** (39), **12** (22), **13a** (10)	2 : 1
8	**2**	DIBAH–CH_2Cl_2	**13a** (100)	

Table 2 Reduction of oxo sulfide **1** with metal hydrides

Entry	Reducing agent	Solvent	Temp.	Product (yield %, ratio)
1	DIBAH	CH_2Cl_2–hexane	−78 °C	**14** (69) and **16a** (21)
2	L-Selectride	THF	−78 °C	**14** and **16a** (79, 82 : 18)[a]
3	$NaBH_4$–$CeCl_3$	THF–MeOH	−78 °C to rt	**14** (91)[b]
4	$LiAlH_4$	THF	rt	**14** and **16a** (91, 84 : 16)

[a] Ratio of products was determined by ^{1}H NMR spectroscopy. [b] Some **15a**, less than 5%, could be detected by ^{1}H NMR analysis.



Scheme 2

(Table 1, entry 4). The hydroxy group-directing effect has not been observed in the reduction of a related hydrindane system.[7] This difference suggests that in the hydrindane system reduction of the vinyl sulfone unit occurs by intermolecular hydride anion delivery. It is noteworthy that $LiAlH_4$ reduction of the carbon–carbon double bond at the ring junction in a hydrindane-related vinylic sulfone lacking an oxygen function afforded the *trans*-hydrindane derivative only.[6] $NaBH_4$–methanol reduction of **2** affording a mixture of **9** and **10** shows little selectivity with respect to the configuration at the ring junction (Table 1, entry 5).

In conclusion, it was shown that readily available sulfonyl ketone **2** may be stereoselectively transformed into 5α- or 5β-cholestane derivatives, **7** or **8**. Reduction of the sulfur-containing α,β-unsaturated ketones **1** and **2**, and of the respective alcohols, has been scrutinized. Some mechanistic suggestions regarding the multistep reduction have been made.

Experimental

Mps were determined on a Kofler hot-stage melting point apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were performed for samples in $CDCl_3$ on a Varian Gemini 200 MHz spectrometer using residual $CHCl_3$ as an internal standard (δ 7.26 and 77.0, respectively). Signal multiplicities in ^{13}C spectra were assigned using DEPT sequence and are given in brackets. *J*-Values are given in Hz. Mass spectra were taken at an ionizing voltage of 70 eV; peak (*m*/*z*) relative intensities are given in parentheses. Air-sensitive reactions were performed in oven- or flame-dried glassware under argon. Bulk solution of $LiAlH_4$ (1 M) was prepared using freshly purchased reagent (Aldrich) and Na/K alloy-dried THF. Organic extracts were dried over Na_2SO_4 and the solvents were evaporated on a rotary evaporator.

4-(Phenylsulfanyl)cholest-4-en-3-one 1

This compound was prepared from 4β,5-epoxy-5β-cholestan-3-one[9] following the described procedure;[10] mp 105 °C (Found: C, 80.62; H, 9.70. Calc. for $C_{33}H_{48}OS$: C, 80.43; H, 9.82%); λ_{max}(EtOH)/nm 321.3, 250.4, 202.5; ν_{max}(KBr)/cm^{-1} 1679, 1581, 1557; δ_H 7.24–7.02 (5 H, m, ArH), 3.62 (1 H, dtd, *J* 14.5, 3.0, 0.5), 2.54 (2 H, dd, *J* 9.9, 4.5), 2.23 (1 H, td, *J* 14.2, 5.3), 1.29 (3 H, s, 19-H_3), 0.91 (3 H, d, $J_{20,21}$ 6.5, 21-H_3), 0.86 (6 H, d, $J_{25,26\text{ and }25,27}$ 6.6, 26- and 27-H_3), 0.71 (3 H, s, 18-H_3); δ_C 194.1, 177.9, 137.23, 128.7, 126.9, 125.1, 56.0, 55.7, 54.2, 42.3, 41.6, 39.5, 39.4, 36.0, 35.6, 35.2, 34.6, 34.4, 32.0, 31.0, 28.1, 27.9, 24.0, 23.7, 22.7, 22.5, 21.1, 18.6, 18.3, 11.9. Physical constants were in agreement with those described, with the exception of ^{1}H NMR signal at δ 3.62 (1 H) which has been not recorded in the original characterization.

4-(Phenylsulfonyl)cholest-4-en-3-one 2

To a stirred solution of sulfide **1** (604 mg, 1.23 mmol) in CH_2Cl_2 (10 cm^3) was added MCPBA (60%; 734 mg, 2.55 mmol) in portions. After 2 h, the mixture was partitioned between aq. Na_2SO_3 and CH_2Cl_2. The organic solution was washed with water and the solvent was evaporated. The residue was crystallized from acetone–hexane to give *sulfone* **2** (528 mg, 82%), mp 146–148 °C; λ_{max}(EtOH)/nm 253.3, 221.7, 199.6; ν_{max}(KBr)/cm^{-1} 1688; δ_H 8.02–7.92 (2 H, m, ArH), 7.58–7.42 (3 H, m, ArH), 4.32 (1 H, dt, *J* 14.1, 2.8), 2.38–0.82 (26 H, m) over-

lapping with 1.25 (3 H, s, 19-H_3), 0.89 (3 H, d, $J_{20,21}$ 7.0, 21-H_3), 0.85 (6 H, d, $J_{25,26\text{ and }25,27}$ 7.0, 26- and 27-H_3), 0.70 (3 H, s, 18-H_3); δ_C 192.0 (C-3), 181.2 (C-4 or -5), 142.6 (C-5 or -4), 136.1 (C-*ipso*), 132.7 (C-*o*), 128.4 (C-*m*), 127.7 (C-*p*), 55.9, 55.5, 54.7, 42.8, 42.3, 39.4, 39.3, 36.0, 35.6, 35.1, 34.1, 33.4, 32.6, 28.1, 27.9, 27.6, 23.9, 23.7, 22.7, 22.5, 21.3, 18.5, 18.4, 11.9 (C-18); *m*/*z* (EI) 524.332 34 (M^+, 22%. $C_{33}H_{48}O_3S$ requires *M*, 524.332 41), 509 [$(M - CH_3)^+$, 2)], 460 [$(M - SO_2)^+$, 100], 445 (13), 383 [$(M - SO_2Ph)^+$, 83].

4β-Phenylsulfanyl-5α-cholestan-3α-ol 4

To anhydrous EtOH (30 cm^3) was added sodium (214 mg, 9.3 mg-atom). After the reaction was complete, thiophenol (0.94 cm^3, 9.15 mmol) was added, followed by 3α,4α-epoxy-5α-cholestane **3**[11,12] (1.80 g, 4.6 mmol). The mixture was heated under reflux for 24 h, cooled and partitioned between water and benzene. The organic extract was washed with water and evaporated. The residue was chromatographed on SiO_2 (10 g; hexane–EtOAc, 9:1) to give *compound* **4** (1.93 g, 83%), mp 133 °C (from EtOH); δ_H 7.41–7.12 (5 H, m, ArH), 4.02 (1 H, br d, $J_{3,4}$ 2.2, 3-H_3), 3.17 (1 H, br dd, $J_{3,4}$ 2.2, $J_{4,5}$ 2.2, 4-H_3), 0.97 (3 H, s, 19-H_3), 0.91 (3 H, d, $J_{20,21}$ 7.1, 21-H_3) overlapping with 0.87 (6 H, d, $J_{25,26\text{ and }25,27}$ 6.7, 26- and 27-H_3), 0.66 (3 H, s, 18-H_3); δ_C 137.9 (C-*i*), 130.5 (C-*o*), 120.9 (C-*m*), 126.3 (C-*p*), 70.2 (C-3), 56.7, 56.5, 56.2, 55.1, 42.8, 42.5, 39.9, 39.5, 36.5, 36.2, 35.8, 35.3, 32.3, 31.6, 28.2, 28.0, 27.5, 24.3, 24.2, 23.9, 22.8, 22.6, 20.5, 18.7, 13.7 (C-19), 12.0 (C-18); *m*/*z* (EI) 496.373 12 (M^+, 84%. $C_{33}H_{52}OS$ requires *M*, 496.373 89), 386 (14), 369 (100), 353 (5), 287 (8), 273 (8), 257 (7), 243 (10), 229 (7), 215 (11), 189 (7), 175 (10), 161 (24), 147 (12), 135 (18), 121 (10), 107 (15).

4β-Phenylsulfonyl-5α-cholestan-3α-ol 5

To a solution of sulfide **4** (598 mg, 1.2 mmol) in CH_2Cl_2 (20 cm^3) was added MCPBA (60%; 710 mg, 2.47 mmol). The mixture was stirred for 2 h and then partitioned between aq. Na_2SO_3 and CH_2Cl_2. The product was isolated in the usual way to give *sulfone* **5** (627 mg, 98%), δ_H 7.91–7.82 (2 H, m, ArH), 7.65–7.45 (3 H, m, ArH), 4.13 (1 H, br s, 3-H), 3.26 (1 H, d, *J* 5.3, 4-H), 1.19 (3 H, s, 19-H_3), 0.90 (3 H, d, $J_{20,21}$ 7.3, 21-H_3) overlapping with 0.86 (6 H, d, $J_{25,26\text{ and }25,27}$ 6.7, 26- and 27-H_3), 0.66 (3 H, s, 18-H_3); δ_C 141.6 (C-*i*), 133.2 (C-*o*), 129.1 (C-*m*), 127.9 (C-*p*), 70.6 (C-3), 65.2 (C-4), 56.4, 56.2, 55.6, 45.2, 42.4, 39.9, 39.5, 36.2, 35.8, 35.4, 33.3, 31.9, 28.2, 28.0, 27.3, 25.7, 24.2, 23.8, 22.8, 22.6, 20.9, 18.7, 13.4 (C-19), 12.0 (C-18); *m*/*z* (EI) 528.363 67 (M^+, 5%. $C_{33}H_{52}O_3S$ requires *M*, 528.363 71), 510 [$(M - H_2O)$, 8], 495 (4), 445 (3), 387 (23), 369 (100), 355 (17), 341 (3), 313 (2), 287 (6), 257 (6), 247 (10), 229 (23), 215 (33), 201 (8), 175 (10), 161 (20), 147 (21), 135 (27), 121 (23), 107 (28), 95 (38), 81 (47).

4-Phenylsulfonyl-5α-cholest-3-ene 6

To a solution of hydroxy sulfide **5** (306 mg, 0.62 mmol) in CH_2Cl_2 (10 cm^3) was added Et_3N (0.26 cm^3, 1.9 mmol) followed by MsCl (0.09 cm^3, 1.2 mmol). The mixture was set aside for 4 h and then partitioned between hexane and water. The hexane layer was washed consecutively with 3% HCl and water. The solvent was evaporated to give 3ξ-chloro-4β-phenylsulfanyl-5α-cholestane (316 mg, 100%), δ_H 7.38–7.20 (5 H, m, ArH), 4.45 (1 H, br d, $J_{3,4}$ 2.2, 3-H), 3.43 (1 H, br dd, $J_{3,4}$ 2.2, $J_{4,5}$ 2.2, 4-H), 2.59–2.38 (1 H, m), 2.29–2.16 (1 H, m), 1.00 (3 H, s, 19-H_3), 0.92 (3 H, d, $J_{20,21}$ 7.5, 21-H_3), 0.89 (6 H, d, $J_{25,26\text{ and }25,27}$ 6.8, 26- and 27-H_3), 0.67 (3 H, s, 18-H_3); δ_C 136.9 (C-*i*), 130.3 (C-*o*), 129.1 (C-*m*), 126.7 (C-*p*), 62.4 (C-3), 57.1, 56.5, 56.2, 54.8, 42.5, 42.3, 39.8, 39.5, 36.6, 36.2, 35.8, 35.3, 32.1, 31.8, 28.2, 28.0, 27.4, 25.0, 24.2, 23.9, 22.8, 22.6, 20.5, 18.7, 14.3 (C-19), 12.0 (C-18).

To a solution of the crude chloride (226 mg, 0.44 mmol) in CH_2Cl_2 (10 cm^3) was added MCPBA (60%; 256 mg, 0.89 mmol). After 8 h the mixture was partitioned between benzene and aq. Na_2SO_3. The organic layer was washed successively with aq. Na_2SO_3 and water. Evaporation of the solvent gave 3ξ-chloro-4β-phenylsulfonyl-5α-cholestane (239 mg, 100%), δ_H 7.94–7.86 (2 H, m, ArH), 7.69–7.51 (3 H, m, ArH), 4.53 (1 H, br s, 3-H), 3.42 (1 H, br d, $J_{4,5}$ 4.3, 4-H), 2.74–2.56 (1 H, m), 2.41–2.23 (2 H, m), 1.21 (3 H, s, 19-H_3), 0.90 (3 H, d, $J_{20,21}$ 8.1, 21-H_3), overlapping with 0.86 (6 H, d, $J_{25,26\text{ and }25,27}$ 6.6, 26- and 27-H_3), 0.67 (3 H, s, 18-H_3); δ_C 141.1 (C-*i*)(0), 133.6 (C-*o*)(1), 129.3 (C-*m*)(1), 127.7 (C-*p*)(1), 71.4 (C-3)(1), 56.3 (1), 56.2 (1), 55.3 (1), 44.7 (1), 42.4 (0), 39.8 (2), 39.5 (2), 36.1 (2), 35.9 (1), 35.7 (1), 35.4 (1), 33.2 (2), 32.1 (2), 28.2 (2), 28.0 (1), 27.1 (2), 26.6 (2), 24.1 (2), 23.8 (2), 22.8 (C-26 or -27)(3), 22.5 (C-27 or -26)(3), 20.9 (2), 18.6 (C-21)(3), 13.6 (C-19)(3), 12.0 (C-18)(3).

A solution of the later product (239 mg, 0.44 mmol) in benzene (10 cm^3) containing DBU (0.07 cm^3, 0.46 mmol) was heated under reflux for 30 min and then cooled and partitioned between benzene and 3% HCl. The organic layer was washed with water and the solvent was evaporated to give *vinylic sulfone* **6** (220 mg, 99%), δ_H 7.83–7.76 (2 H, m, ArH), 7.60–7.44 (3 H, m, ArH), 7.14 (1 H, br d, $J_{2,3}$ 3.1, 3-H_3), 0.87 (3 H, d, $J_{20,21}$ 5.0, 21-H) overlapping with 0.84 (6 H, d, $J_{25,26\text{ and }25,27}$ 6.3, 26- and 27-H_3), 0.70 (3 H, s, 19-H_3), 0.59 (3 H, s, 18-H_3); δ_C 141.7 (C-4 or -*i*)(0), 141.1 (C-*i* or -4)(0), 140.3 (C-3)(1), 132.6 (C-*o*)(1), 128.8 (C-*m*)(1), 127.1 (C-*p*)(1), 56.1 (1), 56.1 (1), 52.8 (1), 45.8 (1), 42.4 (0), 39.9 (2), 39.4 (2), 36.1 (2), 35.7 (1), 34.8 (1), 32.8 (2), 31.4 (2), 28.2 (2), 27.9 (1), 23.9 (2), 23.8 (2), 23.6 (2), 23.4 (2), 22.8 (C-26 or -27)(3), 22.5 (C-27 or -26)(3), 21.4 (2), 18.6 (C-21)(3), 12.4 (C-19)(3), 12.0 (C-18)(3); *m*/*z* (EI) 510.353 64 (M^+, 63%. $C_{33}H_{50}O_2S$ requires *M*, 510.353 15), 495 (23), 462 (3), 445 (12), 397 (3), 369 (42), 355 (100), 341 (20), 287 (10), 275 (22), 259 (7), 235 (10), 229 (17), 213 (22), 199 (5), 171 (6), 161 (8), 147 (13), 135 (23), 121 (35), 107 (28), 95 (35), 81 (65).

4α-Phenylsulfonyl-5α-cholestane 7a and 4β-phenylsulfonyl-5α-cholestane 7b

(a) To a stirred solution of vinyl sulfone **6** (100 mg, 0.2 mmol) in THF (5 cm^3) was added a solution of $LiEt_3BH$ (0.5 M in THF; 0.25 cm^3, 0.125 mmol). The mixture was set aside for 2 h and then partitioned between CH_2Cl_2 and water. The organic solution was evaporated and the residue was chromatographed on SiO_2 (6 g; hexane–AcOEt, 9:1) to give consecutively **7b** (20 mg, 20%) and then **7a** (79 mg, 79%).

(b) To a solution of hydroxy sulfone **5** (108 mg, 0.2 mmol) in CH_2Cl_2 (5 cm^3), stirred under argon at −20 °C, was added Et_3N (0.09 cm^3, 0.65 mmol) followed by MsCl (0.03 cm^3, 0.39 mmol). After 1 h, water (5 cm^3) was added. The mixture was allowed to warm to room temperature and then was extracted with CH_2Cl_2. The organic extract was dried and evaporated to give the crude mesyl ester. The later product was dissolved in THF (5 cm^3) and treated with $LiEtBH_3$ (0.5 M in THF; 0.7 cm^3, 0.35 mmol). The mixture was stirred at room temperature for 0.5 h, and then was poured into water and extracted with CH_2Cl_2. The organic extract was dried and concentrated. The residue was chromatographed on SiO_2 (10 g; hexane–ethyl acetate, 9:1) to give **7b** (19 mg, 18%), **7a** (80 mg, 76%) and a fraction containing both these components (5 mg, 5%).

Compound **7b** had δ_H 7.96–7.87 (2 H, m, ArH), 7.63–7.48 (3 H, m, ArH), 3.21 (1 H, br t, *J* 5.2, 4-H), 1.23 (3 H, s, 19-H), 0.89 (3 H, d, $J_{20,21}$ 7.0, 21-H_3) overlapping with 0.86 (6 H, d, $J_{25,26\text{ and }25,27}$ 7.0, 26- and 27-H_3), 0.66 (3 H, s, 18-H_3) [lit.,[14] δ_H 3.22 (4-H), 1.24 (19-H_3), 0.68 (18-H_3)].

Compound **7a** had δ_H 7.87–7.78 (2 H, m, ArH), 7.66–7.47 (3 H, m, ArH), 3.04 (1 H, br t, *J* 10.7, 4-H), 2.43 (1 H, dd, *J* 13.6, 2.4), 0.89 (3 H, d, $J_{20,21}$ 5.2, 21-H_3) overlapping with 0.85 (6 H, d, $J_{25,26\text{ and }25,27}$ 7.1, 26- and 27-H_3) overlapping with 0.83 (3 H, s, 19-H_3), 0.63 (3 H, s, 18-H_3); δ_C 139.1 (C-*i*)(0), 133.1 (C-*o*)(1), 128.9 (C-*m*)(1), 128.5 (C-*p*)(1), 64.5 (C-4)(1), 56.3 (1), 56.1 (1), 54.4 (1), 46.7 (1), 42.3 (0), 39.9 (2), 39.5 (2), 37.5 (0),

37.4 (2), 36.1 (2), 35.7 (1), 34.6 (1), 31.4 (2), 28.8 (2), 28.2 (2), 28.0 (1), 25.4 (2), 24.0 (2), 23.8 (2), 22.8 (C-26 or -27)(3), 22.5 (C-27 or -26)(3), 21.1 (2), 20.6 (2), 18.6 (C-21)(3), 13.3 (C-19)(3), 12.0 (C-18)(3) [lit.,[14] δ_H 2.96 (4-H), 1.27 (19-H_3), 0.65 (18-H_3)].

Reduction of 2 with $LiAlH_4$. 4β-Phenylsulfonyl-5β-cholestane 8

To a stirred solution of compound **2** (120 mg, 0.229 mmol) in THF (5 cm^3) was added $LiAlH_4$ (1 M in THF; 3 cm^3, 3.00 mmol) dropwise. The reaction was quenched with MeOH[18] (1 cm^3) and the mixture was poured into 10% aq. tartaric acid. The product was extracted with CH_2Cl_2. The solvent was evaporated and the residue was chromatographed on SiO_2 (6 g; hexane–EtOAc, 50:1, 10:1 and 5:1) to give *compound* **8** (92 mg, 78%), δ_H 7.88–7.78 (2 H, m, ArH), 7.66–7.46 (3 H, m, ArH), 3.55 (1 H, td, *J* 11.1, 3.7, 4-H_3), 2.51–2.37 (1 H, m), 0.99 (3 H, s, 19-H_3), 0.88 (3 H, d, $J_{20,21}$ 6.3, 21-H_3), 0.85 (3 H, d, $J_{25,26}$ 6.6, 26-H_3), 0.85 (3 H, d, $J_{25,27}$ 6.6, 27-H_3), 0.63 (3 H, s, 18-H_3); δ_C 138.9 (C-*i*)(0), 133.1 (C-*o*)(1), 128.8 (C-*m*)(1), 128.5 (C-*p*)(1), 61.1 (C-4)(1), 56.5 (1), 56.3 (1), 43.6 (1), 42.6 (0), 42.1 (1), 40.1 (2), 39.4 (2), 37.1 (0), 36.5 (2), 36.1 (2), 35.7 (1), 35.7 (1), 28.9 (2), 28.3 (2), 28.0 (1), 26.1 (2), 24.1 (C-21)(3), 23.8 (2), 23.1 (2), 22.8 (C-26)(3), 22.5 (C-27)(3), 20.8 (2), 19.5 (2), 18.6 (C-19)(3), 12.0 (C-18)(3); *m*/*z* (EI) 512.368 99 (M^+, 0.5%. $C_{33}H_{52}O_2S$ requires *M*, 512.368 80), 510 (1), 495 (0.3), 447 (0.3), 397 (0.4), 371 (100), 355 (7), 245 (14), 163 (23), 149 (35), 135 (30), 109 (41), 95 (55), 81 (45).

Desulfuration of 8

To a stirred solution of sulfone **8** (30 mg, 0.06 mmol) in THF (2 cm^3) and MeOH (10 cm^3) was added 6% sodium amalgam (310 mg) in portions during 12 h. The mixture was partitioned between hexane and water, and the product was isolated in the usual way. 5β-Cholestane was obtained (21 mg, 96%), δ_H 0.91 (3 H, s, 19-H_3) overlapping with 0.90 (3 H, d, $J_{20,21}$ 6.5, 21-H_3) overlapping with 0.86 (6 H, d, $J_{25,26\text{ and }25,27}$ 6.7, 26- and 27-H_3), 0.64 (3 H, s, 18-H_3); δ_C 56.7, 56.4, 43.8, 42.7, 40.6, 40.3, 39.5, 37.6, 36.2, 35.9, 35.8, 35.4, 28.3, 28.0, 27.6, 27.3, 27.1, 26.6, 24.3, 23.8, 22.8, 22.6, 21.4, 20.9, 18.7, 12.1 (lit.,[19] δ_C 56.6, 56.3, 43.7, 42.7, 40.5, 40.3, 39.5, 37.6, 36.2, 35.9, 35.8, 35.3, 28.3, 28.0, 27.5, 27.2, 27.0, 26.6, 24.3, 23.8, 22.8, 22.5, 21.3, 20.8, 18.6, 12.0).

Reduction of 2 with $NaBH_4$ in MeOH. 4α-Phenylsulfonyl-5α-cholestan-3α-ol 9 and 4β-phenylsulfonyl-5β-cholestan-3β-ol 10

To a stirred solution of ketone **2** (201 mg, 0.38 mmol) in MeOH (20 cm^3) was added $NaBH_4$ (161 mg, 4.2 mmol) in portions during 7 h. The mixture was set aside for 16 h and then was poured into water. The product was extracted with CH_2Cl_2. The extract was evaporated. The residue was chromatographed on SiO_2 (7 g; benzene–EtOAc, 85:15). A mixture of alcohols **9** and **10** was obtained (168 mg, 83%). A sample of *pure isomer* **9** was obtained by dissolution of the mixture in CH_2Cl_2 and precipitation of an amorphous solid with pentane; δ_H 7.96–7.88 (2 H, m, ArH), 7.70–7.51 (3 H, m, ArH), 3.75 (1 H, br s, 3-H_3), 3.10 (1 H, dd, $J_{4,5}$ 11.5, $J_{3,4}$ 1.8, 4-H), 2.38–2.20 (2 H, m), 2.01–0.81 (29 H, m) overlapping with 0.89 (3 H, d, $J_{20,21}$ 6.2, 21-H_3), 0.85 (6 H, d, $J_{25,26\text{ and }25,27}$ 7.3, 26- and 27-H_3) overlapping with 0.84 (3 H, s, 19-H_3), 0.64 (3 H, s, 18-H_3); NOE experiments: Irradiation at δ 0.84 ppm (19-H_3) led to an increase of intensity of the signal at δ 3.1 (3-H) by 1.4% being observed. Irradiation at δ 3.10 (4-H) led to an increase of signals at δ 0.84 by 1.4% and at δ 3.75 ppm (3-H) by 5.2%. Upon irradiation at δ 3.75 an increase of the signal at δ 3.10 by 5.0% was observed; δ_C 139.5 (C-*i*)(0), 133.5 (C-*o*)(1), 129.1 (C-*m*)(1), 128.1 (C-*p*)(1), 67.8 (C-3 or -4)(1), 65.1 (C-4 or 3)(1), 56.2 (1), 56.1 (1), 54.1 (1), 42.3 (0), 40.3 (1), 39.9 (2), 39.5 (2), 37.7 (0), 36.1 (2), 35.8 (1), 34.6 (1), 31.5 (2), 31.2 (2), 28.3 (2), 28.2 (2), 28.0 (1), 25.2 (2), 24.0 (2), 23.8 (2), 22.8 (3), 22.5 (3), 21.2 (2), 18.6 (3), 12.4 (C-19)(3), 12.0 (C-18)(3); *m*/*z* (EI) 528.363 68 (M^+, 8%. $C_{33}H_{52}O_3S$ requires *M*, 528.363 71), 463 (3), 445 (8), 387 (86), 369 (100), 353 (5), 329 (3), 287 (5), 261 (8), 243 (10), 231 (21), 215 (12), 175 (11), 161 (14), 135 (16), 107 (7).

Compound **10**: δ_H selected signals: 3.91 (1 H, br s), 3.15 (1 H, dd, *J* 12.1, 2.0), 1.03 (3 H, s, 19-H_3).

On attempted reduction of **2** with $NaBH_4$ in MeOH at the reflux temp., the enol of **2** [4-(phenylsulfonyl)cholesta-3,5-dien-3-ol] was obtained in 85% yield, λ_{max}(EtOH)/nm 201.3, 222.5, 248.9, 286.8; δ_H 11.25 (1 H, s, OH), 7.84–7.77 (2 H, m, ArH), 7.67–7.43 (3 H, m, ArH), 6.08 (1 H, dd, $J_{6,7a}$ 5.5, $J_{6,7b}$ 2.7, 6-H), 2.50–2.38 (2 H, m), 0.88 (3 H, d, $J_{20,21}$ 6.0, 21-H_3) overlapping with 0.85 (6 H, d, $J_{25,26\text{ and }25,27}$ 6.2, 26- and 27-H), 0.62 (3 H, s, 19-H_3), 0.59 (3 H, s, 18-H_3); δ_C 165.4, 140.8 (C-*i*), 133.1 (C-*o*), 131.8, 128.6 (C-*m*), 127.0 (C-*p*), 122.0, 106.6, 56.6, 56.0, 48.7, 39.6, 39.5, 42.2, 39.6, 39.5, 36.1, 35.9, 35.7, 32.1, 31.8, 30.5, 28.2, 28.0, 27.5, 24.1, 23.8, 22.8, 22.5, 21.1, 18.6, 17.3, 11.8 (C-18); *m*/*z* (EI) 524 (M^+, 19%), 509 (2), 460 (100), 445 (15), 427 (3), 383 (43), 369 (3), 365 (4), 271 (10), 257 (8), 247 (10), 229 (15), 213 (8), 197 (16), 173 (15), 147 (15), 135 (18), 121 (19), 105 (22), 95 (35).

4α-Phenylsulfonyl-5α-cholestan-3-one 11 and 4β-phenylsulfonyl-5β-cholestan-3-one 12

A mixture of **9** and **10**, as described above, (95 mg, 0.18 mmol) was dissolved in acetone (5 cm^3) and treated with Jones reagent until the brown colour persisted (2.7 M; 0.1 cm^3, 0.27 mmol), then some propan-2-ol was added and the solution was partitioned between water and CH_2Cl_2. The organic extract was evaporated. The residue was chromatographed on SiO_2 (10 g; hexane–EtOAc, 92:8) to give consecutively ketones **12** (39 mg, 41%) and **11** (55 mg, 58%).

Compound **12** showed δ_H 7.82–7.75 (2 H, m, ArH), 7.71– 7.50 (3 H, m, ArH), 3.63 (1 H, d, $J_{4,5}$ 6.3, 4-H), 2.76 (1 H, br s), 2.55 (1H, dd, *J* 19.6, 7.1), 2.35–2.13 (1 H, m), 1.12 (3 H, s, 19-H_3), 0.87 (3 H, d, $J_{20,21}$ 6.4, 21-H_3), 0.84 (6 H, d, $J_{25,26\text{ and }25,27}$ 6.0, 26- and 27-H_3), 0.63 (3 H, s, 18-H_3); δ_C 204.3 (C-3), 137.6 (C-*i*), 134.0 (C-*o*), 129.0 (C-*m*), 128.9 (C-*p*), 76.5 (C-4), 56.1, 55.9, 43.5, 42.8, 42.5, 39.5, 39.4, 36.1, 35.7, 35.0, 34.8, 34.6, 32.1, 28.2, 28.0, 26.3, 24.0, 23.8, 22.8, 22.5, 22.3, 21.4, 18.6, 11.9 (C-18); *m*/*z* (EI) 526.348 00 (M^+, 2%. $C_{33}H_{50}O_3S$ requires *M*, 526.348 06), 511 (1), 462 (7), 385 (100), 367 (20), 315 (13), 275 (5), 245 (12), 231 (22), 213 (8), 161 (12), 135 (12), 121 (22), 95 (32).

Compound **11** showed δ_H 7.82–7.74 (2 H, m, ArH), 7.69–7.48 (3 H, m, ArH), 3.49 (1 H, dd, $J_{4,5}$ 9.1, 1.3, 4-H), 2.87–2.53 (3 H, m), 2.45–2.25 (2 H, m), 0.90 (3 H, d, $J_{20,21}$ 6.6, 21-H_3) overlapping with 0.86 (6 H, d, $J_{25,26\text{ and }25,27}$ 7.1, 26- and 27-H_3), 0.74 (3 H, s, 19-H_3), 0.64 (3 H, s, 18-H_3); δ_C 204.5 (C-3), 138.0 (C-*i*), 133.9 (C-*o*), 128.9 (C-*m*), 128.8 (C-*p*), 76.2 (C-4), 58.1, 56.0, 53.8, 45.2, 42.5, 39.8, 39.5, 36.1, 35.9, 35.7, 35.6, 35.0, 34.5, 31.2, 29.1, 28.2, 28.0, 24.1, 23.8, 22.8, 22.5, 21.4, 18.6, 13.7 (C-19), 12.0 (C-18); *m*/*z* (EI) 526.348 00 (M^+, 8%), 462 (28), 444 (2), 392 (12), 385 (53), 369 (27), 353 (3), 315 (5), 271 (7), 245 (20), 229 (100), 215 (22), 187 (10), 161 (10).

Desulfuration of 11

To a mixture of sulfone **11** (45 mg, 0.09 mmol), THF (2 cm^3) and MeOH (10 cm^3) was added 6% sodium amalgam (1.2 g) in portions until starting material was consumed (TLC, 5 days). The mixture was partitioned between hexane and water. The product was isolated in the usual way. 5α-Cholestan-3-one was obtained (26 mg, 79%), identical in all respects with an authentic sample.

Desulfuration of 12

Sulfone **12** (48 mg, 0.09 mmol) treated with sodium amalgam under conditions analogous to those described above afforded 5β-cholestan-3-one (28 mg, 80%).

Reduction of 2 with $NaBH_4$ in a mixture of THF and DMPU

To a stirred mixture of $NaBH_4$ (10 mg, 0.26 mmol), THF (2 cm^3) and 1,3-dimethylperhydropyrimidin-2(1*H*)-one (DMPU) (0.3 cm^3) was added ketone **2** (105 mg, 0.2 mmol) in THF (2 cm^3) at 0 °C. After 1 h (at 0 °C), the mixture was allowed to warm to room temp. and was partitioned between benzene and 3% HCl. The organic extract was washed successively with water and brine, and the solvent was evaporated. The residue was chromatographed on SiO_2 (5g; hexane–EtOAc, 95:5) to give compound **12** (23%) and a mixture of alcohols **9** and **10** (74%) in the ratio 5.5:1 (determined by ^1H NMR after oxidation of the mixture to a mixture of ketones **11** and **12**). In an analogous reaction carried out at −45 °C, ketone **12** (24%) and alcohols **9** and **10** (73%, in the ratio 4.5:1, respectively) were obtained.

Reduction of 11 with $NaBH_4$ in THF–DMPU

A mixture of **11** (48 mg, 0.09 mmol), THF (1 cm^3), DMPU (0.3 cm^3) and $NaBH_4$ (4 mg, 0.1 mmol) was stirred at 0 °C for 1 h, and then worked up in an analogous manner to that described above. Alcohol **9** (47 mg, 97%) was obtained.

Attempted reduction of **12** under analogous conditions failed.

Reduction of 2 with CuCN–*n*-BuLi–DIBAH system [16,20]

To a suspension of CuCN (46 mg, 0.513 mmol) in THF (5 cm^3) was added *n*-BuLi (1.3 M in hexane; 0.39 cm^3, 0.513 mmol) at −20 °C. After 30 min, the mixture was cooled to −50 °C and DIBAH (0.7 M in hexane; 1.833 cm^3, 1.283 mmol) and HMPA (1 cm^3) were added consecutively. Stirring at −50 °C was continued for 2 h, and then ketone **2** (52.5 mg, 0.100 mmol) in THF (1 cm^3) was added. After an additional 3 h, the mixture was allowed to warm to room temp. The reaction was quenched with MeOH (2 cm^3) and the mixture was poured into 10% aq. tartaric acid. The product was isolated with CH_2Cl_2 and chromatographed on SiO_2 (6 g; hexane–EtOAc, 40:1, then 20:1) to give 4-(phenylsulfonyl)cholest-4-en-3β-ol **13a** (5 mg, 10%), **12** (11.5 mg, 22%) and **11** (20.5 mg, 39%). Compound **13a** showed δ_H 7.98–7.90 (2 H, m, ArH), 7.62–7.44 (3 H, m, ArH), 4.75 (1 H, t, $J_{2,3}$ 5.5, 3-H_3), 3.05 (1 H, dt, *J* 13.9, 1.8), 1.06 (3 H, s, 19-H_3), 0.86 (3 H, d, $J_{20,21}$ 4.6, 21-H_3), 0.84 (6 H, d, $J_{25,26\text{ and }25,27}$ 6.6, 26- and 27-H_3), 0.62 (3 H, s, 18-H_3); δ_C 164.0 (C-4), 143.4 (C-5), 136.0 (C-*i*), 132.7 (C-*o*), 128.9 (C-*m*), 128.4 (C-*p*), 65.7 (C-3), 55.9, 55.6, 52.3, 42.4, 41.4, 39.6, 39.4, 36.0, 35.6, 35.2, 32.1, 31.0, 28.1, 27.9, 27.7, 26.6, 23.8, 23.7, 22.8, 22.5, 21.5, 20.5, 18.5, 11.9 (C-18); *m*/*z* (LSIMS) 549.337 77 (M^+ + Na. $C_{33}H_{50}NaO_3S$ requires *m*/*z*, 549.337 84).

Reduction of 2 with DIBAH. 4-(Phenylsulfonyl)cholest-4-en-3β-ol 13a

To a solution of **2** (210 mg, 0.38 mmol) in CH_2Cl_2 (10 cm^3), stirred at −20 °C, was added DIBAH (0.7 M in hexane; 0.65 cm^3, 0.46 mmol). After 1 h (at −20 °C) the reaction was quenched with MeOH (0.1 cm^3). The mixture was warmed to room temp. and partitioned between 3% HCl and CH_2Cl_2. The product was isolated in the usual way. Alcohol **13a** (212 mg, 100%) was obtained.

Reduction of 13a with $LiAlH_4$

A mixture of **13a** (98 mg, 0.19 mmol), THF (3 cm^3) and $LiAlH_4$ (10 mg, 0.26 mmol) was stirred for 2 h at room temp. Work-up with saturated aq. Na_2SO_4 and the usual isolation of product gave **8** (70 mg, 78%).

3β-Methoxymethyl-4-(phenylsulfonyl)cholest-4-ene 13b

To mixture of **13a** (102 mg, 0.19 mmol) in THF (5 cm^3) and HMPA (0.25 cm^3) was added NaH (55% in mineral oil; 51 mg, 1.17 mmol), followed by CH_3OCH_2Cl (90%; 0.06 cm^3, 0.74 mmol) and KI (0.1 mg). The mixture was heated under reflux for 24 h and then cooled and partitioned between water and benzene. The organic layer was washed with water and the solvent was evaporated. The residue was chromatographed on SiO_2 (5 g; hexane–EtOAc, 93:7) to give **13b** (106 mg, 96%), δ_H 7.98–7.88 (2 H, m, ArH), 7.56–7.40 (3 H, m, ArH), 4.95 (1 H, d, *J* 7.0, 3-H), 4.68 (2 H, d, *J* 6.8, OCH_2O), 3.39 (3 H, s, CH_3O), 3.07 (1 H, br d, *J* 12.9), 1.01 (3 H, s, 19-H_3), 0.86 (3 H, d, $J_{20,21}$ 5.4, 21-H_3) overlapping with 0.83 (6 H, d, $J_{25,26\text{ and }25,27}$ 6.5, 26- and 27-H_3), 0.62 (3 H, s, 18-H_3); δ_C 165.2 (C-4)(0), 143.9 (C-5)(0), 133.8 (C-*i*)(0), 132.3 (C-*o*)(1), 128.6 (C-*m*)(1), 126.6 (C-*p*)(1), 97.7 (OCH_2O)(2), 71.5 (C-3)(1), 55.9 (1), 55.8 (1), 55.7 (1), 50.5 (CH_3O)(3), 42.5 (0), 41.1 (0), 39.6 (2), 39.4 (2), 36.0 (2), 35.6 (1), 35.3 (1), 32.8 (2), 28.5 (2), 28.2 (2), 27.9 (3), 27.6 (2), 25.6 (2), 23.9 (2), 23.7 (2), 22.7 (3), 22.5 (3), 21.9 (2), 21.5 (3), 18.5 (3), 12.0 (C-18)(3).

Reduction of 13b with $LiAlH_4$

A mixture of ether **13b** (102 mg, 0.18 mmol), THF (5 cm^3) and $LiAlH_4$ (35 mg, 0.92 mmol) was heated under reflux for 20 min and cooled. The reagent excess was decomposed with water and the mixture was partitioned between 3% HCl and benzene. Product was isolated in the usual way and chromatographed on SiO_2 (5 g; hexane–EtOAc, 9:1). A mixture of sulfones **8**, **7a** and **7b** was obtained (70 mg, 76%) in proportions 5:4:1 by ^1H NMR. Rechromatography of the mixture gave pure products **8** and **7a** and **7b**.

4-(Phenylsulfonyl)cholest-4-en-3α-ol 15a

(a) From 13a. To a solution of alcohol **13a** (113 mg, 0.21 mmol) in CH_2Cl_2 (3 cm^3) was added Ph_3P (265 mg, 1.1 mmol) in CH_2Cl_2 (1 cm^3) at −78 °C. The mixture was stirred for 2 h and then benzoic acid (135 mg, 1.1 mmol) in CH_2Cl_2 (2 cm^3) and diethyl azodicarboxylate (0.175 cm^3, 1.1 mmol) were added. The mixture was set aside at room temp. for 4 h and then partitioned between saturated aq. $NaHCO_3$ and benzene. The organic phase was washed with water and the solvent was evaporated. The residue was chromatographed on SiO_2 (5 g; hexane–EtOAc, 95:5) to give benzoate **15b** (80 mg). This crude product was dissolved in 5% methanolic KOH (3 cm^3) and set aside for 16 h. The usual work-up and chromatography of the product on SiO_2 (5 g; hexane–EtOAc, 8:2) gave alcohol **15a** (72 mg, 64%).

(b) From 16a. To a solution of sulfide **16a** (see below) (59 mg, 0.119 mmol) in CH_2Cl_2 (3 cm^3) was added MCPBA (60%; 70 mg, 0.243 mmol) at 0 °C. The mixture was stirred at room temp. for 1 h and poured into aq. Na_2CO_3. The product was extracted with CH_2Cl_2. The extract was washed successively with aq. $Na_2S_2O_3$ and water, and the solvent was evaporated. The residue was chromatographed on SiO_2 (2 g; hexane–EtOAc, 50:1, 25:1, 10:1) to give alcohol **15a** (61 mg, 97%), δ_H 7.97–7.90 (2 H, m, ArH), 7.63–7.46 (3 H, m, ArH), 4.77 (1 H, s, 3-H_3), 3.15 (1 H, dt, *J* 14.5, 3.3), 1.03 (3 H, s, 19-H_3), 0.87 (3 H, d, $J_{20,21}$ 4.7, 21-H_3) overlapping with 0.85 (6 H, d, $J_{25,26\text{ and }25,27}$ 5.7, 26- and 27-H_3), 0.63 (3 H, s, 18-H_3); δ_C 163.0 (C-4)(0), 143.1 (C-5)(0), 135.6 (C-*i*)(0), 132.7 (C-*o*)(1), 128.9 (C-*m*)(1), 126.7 (C-*p*)(1), 62.9 (C-3)(1), 55.8 (1), 55.4 (1), 54.5 (1), 42.2 (0), 40.9 (0), 39.5 (2), 39.3 (2), 35.9 (1), 35.6 (1), 34.9 (1), 31.2 (2), 30.8 (2), 28.0 (2), 27.9 (1), 27.2 (2), 26.5 (2), 23.8 (2), 23.6 (2), 22.7 (3), 22.4 (2), 21.6 (2), 18.4 (2C)(3), 11.8 (C-18)(3); *m*/*z* (EI) 525 (M^+, 0.3%), 508.3373 [$(M - H_2O)^+$, 99. $C_{33}H_{48}O_2S$ requires *m*/*z*, 508.3375], 493 (19), 444 (54), 429 (9), 395 (44), 385 (8), 367 (82), 351 (8), 261 (81), 247 (62), 159 (33), 147 (80), 135 (71), 119 (42), 109 (54), 105 (100), 95 (82), 91 (52), 81 (71), 69 (45), 55 (50), 43 (45).

Reduction of 15a with $LiAlH_4$

To a solution of alcohol **15a** (70 mg, 0.13 mmol) in THF (2 cm^3)

was added $LiAlH_4$ (10 mg, 0.26 mmol) and the mixture was stirred for 2 h. The reagent excess was decomposed with saturated aq. Na_2SO_4, and the mixture was diluted with CH_2Cl_2 and dried with Na_2SO_4. The solid was filtered off and the solvent was evaporated. The residue was chromatographed on SiO_2 (5 g; hexane–EtOAc, 9 : 1) to give compound **7a** (56 mg, 82%).

Reduction of 1 with DIBAH. 4-(Phenylsulfanyl)cholest-4-en-3β-ol 14 and 4-(phenylsulfanyl)cholest-4-en-3α-ol 16a

To a solution of **1** (450 mg, 0.91 mmol) in CH_2Cl_2 (10 cm^3) was added DIBAH (0.7 M in hexane; 4.4 cm^3, 3.08 mmol) at −78 °C. The mixture was stirred for 1 h at −78 °C and allowed to warm to room temp. The reaction was quenched with MeOH (2 cm^3) and the mixture was poured into 10% aq. tartaric acid. The product was isolated with CH_2Cl_2 and chromatographed on SiO_2 (45 g; hexane–EtOAc, 100 : 1 and 75 : 1) to give alcohols **14** (312 mg, 69%) and **16a** (96 mg, 21%).

Compound **14** showed δ_H 7.31–7.08 (5 H, m, ArH), 4.08–3.86 (1 H, m, 3-H), 3.31–3.18 (1 H, m, 8 lines, 6-αH), 2.90 (1 H, br s, 3-OH), 1.17 (3 H, s, 19-H_3), 0.92 (3 H, d, $J_{20,21}$ 6.6, 21-H_3), 0.87 (6 H, d, $J_{25,26\text{ and }25,27}$ 6.6, 26- and 27-H_3), 0.70 (3 H, s, 18-H_3); δ_C 157.6 (C-5), 136.2 (C-*i*), 128.8 (C-*o*), 127.0 (C-*m*), 125.7 (C-4), 125.3 (C-*p*), 68.0 (C-3), 56.0, 56.0, 54.4, 42.3 (C-13), 40.6 (C-10), 39.7, 39.4, 36.0, 35.6, 35.4, 33.7, 32.7, 29.1, 28.1, 27.9, 27.3, 24.0, 23.7, 22.7, 22.4, 21.2, 19.8, 18.5, 11.9; *m*/*z* (EI) 494.358 35 (M^+, 100%. $C_{33}H_{50}OS$ requires *M*, 494.358 24), 476 [$(M - H_2O)^+$, 94], 461 [$(M - CH_3 - H_2O)^+$, 13], 399 [$(M - Ph - H_2O)^+$, 6], 385 (19), 367 (65), 105 (29), 95 (34), 57 (25).

Compound **16a** showed δ_H 7.31–7.06 (5 H, m, ArH), 4.05–3.98 (1 H, m, 3-H), 3.37–3.23 (1 H, m, 6 lines, 6-αH), 2.27 (1 H, br s, 3-OH), 1.14 (3 H, s, 19-H_3), 0.90 (3 H, d, $J_{20,21}$ 8.6, 21-H_3), 0.87 (6 H, d, $J_{25,26\text{ and }25,27}$ 6.6, 26- and 27-H_3), 0.70 (3 H, s, 18-H_3); δ_C 157.7 (C-5), 136.7 (C-*i*), 128.9 (C-*o*), 127.5 (C-*m*), 125.3 (C-4), 124.4 (C-*p*), 67.5 (C-3), 56.0, 55.9, 54.4, 42.3 (C-13), 40.6 (C-10), 39.8, 39.4, 36.0, 35.7, 35.6, 32.2, 31.5, 28.5, 28.1, 27.9, 26.9, 24.0, 23.7, 22.7, 22.5, 21.6, 18.6, 18.5, 11.9; *m*/*z* (EI) 494.358 41 (M^+, 38%), 476.347 53 [$(M - H_{32}O)^+$, 100. $C_{33}H_{48}S$ requires *m*/*z*, 476.347 67], 461 [$(M - CH_3 - H_2O)^+$, 12], 399 [$(M - Ph - H_2O)^+$, 6], 385 (5), 367 (30), 109 [$(SPh)^+$, 14], 105 (36), 95 (24), 57 (19).

Reduction of 1 with $LiAlH_4$

To a stirred solution of $LiAlH_4$ in THF (1.5 M; 5 cm^3) was added a solution of **1** (150 mg, 0.305 mmol) in THF (3 cm^3) in one portion. After 20 min the reaction was quenched with MeOH (1 cm^3) and the mixture was poured into 10% aq. tartaric acid. The product was extracted with CH_2Cl_2. The extract was washed with water and evaporated. The residue was filtered through SiO_2 (15 g; hexane–EtOAc, 40 : 1) to give a mixture of **14** and **16a** (137 mg, 91%) in the ratio 84 : 16, respectively, by ^1H NMR.

Reduction of 1 with L-Selectride®

To a solution of **1** (105 mg, 0.213 mmol) in THF (7 cm^3) was added L-Selectride® (1 M in THF; 0.25 cm^3, 0.25 mmol) at −78 °C. The mixture was stirred at −78 °C for 1 h. The reaction was quenched with MeOH (0.5 cm^3). The product was isolated as in the above described experiments to give a mixture of **14** and **16a** (83 mg 79%) in the ratio 82 : 18, respectively, by ^1H NMR.

Reduction of 1 with $NaBH_4$–$CeCl_3$ system[17]

To a mixture of **1** (100 mg, 0.203 mmol), $CeCl_3 \cdot 7H_2O$ (41 mg, 0.110 mmol), THF (2 cm^3) and MeOH (3 cm^3) was added $NaBH_4$ (8.5 mg, 0.224 mmol) at −78 °C. After 2 h at −78 °C, the mixture was allowed to warm to room temp. and then was poured into 10% aq. tartaric acid. The product was isolated with CH_2Cl_2 and chromatographed on SiO_2 (10 g; hexane–EtOAc, 60 : 1 and 40 : 1) to give **14** (91 mg, 91%). Inspection of the ^1H NMR spectrum of this product showed the presence of traces (≈3%) of the isomer **16a**.

4-(Phenylsulfanyl)cholest-4-en-3a-yl benzoate 16b

To a solution of alcohol **14** (86 mg, 0.174 mmol), Ph_3P (182 mg, 0.695 mmol) and benzoic acid (78 mg, 0.639 mmol) in THF (1.5 cm^3) was added DEAD (0.11 cm^3, 0.575 mmol) in THF (0.5 cm^3) at −78 °C. The mixture set aside at room temp. for 2 h and the solvent was evaporated. The residue was chromatographed on SiO_2 (5 g; hexane–EtOAc, 100 : 1, 50 : 1 and 20 : 1) to give the *title benzoate* **16b** (77 mg, 76%), δ_H 7.89–7.00 (10 H, m, ArH), 5.51 (1 H, br s, 3-H), 3.51–3.36 (1 H, m, 6 lines, 6-αH), 1.19 (3 H, s, 19-H_3), 0.94 (3 H, d, $J_{20,21}$ 6.4, 21-H_3), 0.89 (6 H, d, $J_{25,26\text{ and }25,27}$ 6.6, 26- and 27-H_3), 0.73 (3 H, s, 18-H_3); δ_C 165.9 (C=O), 160.8 (C-5), 137.0 (C-*i*, SPh), 132.4 (C-*p*, Bz), 130.6 (C-*i*, Bz), 129.5 (C-*o*, Bz), 128.6 (C-*o*, SPh), 128.0 (C-*m*, Bz), 127.6 (C-*m*, SPh), 125.1 (C-*p*, SPh), 120.7 (C-4), 72.1 (C-3), 56.1, 55.9, 54.7, 42.3 (C-13), 40.4 (C-10), 39.7, 39.4, 36.0, 35.6, 35.5, 32.2, 32.1, 28.5, 28.1, 27.9, 25.7, 24.0, 23.7, 22.7, 22.5, 21.6, 18.5, 18.5, 11.9; *m*/*z* (EI) 598.384 14 (M^+, 11%. $C_{40}H_{54}O_2S$ requires *M*, 598.384 45), 476.347 80 ($M^+ - C_6H_5CO_2H$, 100. $C_{33}H_{48}S$ requires *m*/*z*, 476.347 67), 461 [$(M - CH_3 - BzOH)^+$, 21], 367 (24), 122 ($BzOH^+$, 18), 105 ($C_6H_5CO^+$, 100).

4-(Phenylsulfanyl)cholest-4-en-3a-ol 16a from 16b

To a solution of benzoate **16b** (77 mg, 0.129 mmol) in CH_2Cl_2 (3 cm^3) was added DIBAH (0.7 M in hexane; 0.4 cm^3, 0.280 mmol) at −78 °C. The mixture was stirred for 1 h before being allowed to warm to room temp., treated with MeOH (0.5 cm^3), and poured into 10% aq. tartaric acid. The product was isolated with CH_2Cl_2 and chromatographed on SiO_2 (1.5 g; hexane–EtOAc, 100 : 1 and 50 : 1) to give **16a** (59 mg, 92%).

Reduction of 15a with $LiAlH_4$

To a solution of hydroxy sulfone **15a** (61 mg, 0.116 mmol) in THF (4 cm^3) was added $LiAlH_4$ (0.25 M in THF; 0.6 cm^3, 0.150 mmol). The mixture was heated under reflux for 20 min. After cooling, the reaction mixture was quenched with MeOH (0.5 cm^3) and poured into 10% aq. tartaric acid. The product was isolated with CH_2Cl_2 and chromatographed on SiO_2 (2 g; hexane–EtOAc 50 : 1, 10 : 1 and 5 : 1) to give sulfone **7a** (49 mg, 82%).

Catalytic hydrogenation of 2

A solution of **2** (60 mg, 0.11 mmol) in EtOH (4.5 cm^3), containing 10% palladium on carbon (10 mg), was stirred under hydrogen at the reflux temperature for 5 h. The mixture was cooled and diluted with CH_2Cl_2. The solid was filtered off and the solvent was evaporated. A mixture of compounds **11** and **12** in the ratio 6.5 : 1 (^1H NMR) was obtained.

In an analogous reaction, a solution of **2** (60 mg, 0.11 mmol) in EtOH (4.5 cm^3), containing 10% palladium on carbon (10 mg), was treated with CF_3COOH (0.5 mmol) and the mixture was stirred at room temp. for 5 days. A mixture of **11** and **12** in the ratio 5.5 : 1 (^1H NMR) was obtained.

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