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Regio- and Stereospecific Synthesis of Cholesterol Derivatives and Their Hormonal Activity in *Caenorhabditis elegans*

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Cholesterol is essential for the survival of the nematode *Caenorhabditis elegans*. Recent studies have demonstrated that cholesterol derivatives regulate two processes in the life cycle of worms: controlling molting and inducing a specialized non-feeding larval stage. However, the chemical structure of the cholesterol-derived signalling molecules for these or any other functions has not yet been identified. Herein, we describe the regio- and stereospecific synthesis of a number of cholesterol derivatives. The lithium–ammonia reduction of 4-cholesten-3-one was utilized to develop a general method for the introduction of diverse functional groups at C-4α of 5α-cholestan-3β-ol. Stereoselective functionalization at C-7 was achieved starting from 7-ketocholesterol derivatives. 6-Keto-5α-cholestan-3β-ol was utilized for specific functionalizations at C-6 and C-7. The structure–activity relationships of the different cholesterol derivatives have been investigated by feeding worms of different genetic background with these compounds. Our study is the first step in assigning the relationships of hormonal activity in *C. elegans* on the substitution at different positions of cholesterol.

Introduction

Cholesterol, a major constituent of the plasma membrane in most eukaryotic cells, plays multiple roles in the organism and the alterations of its normal metabolism; transport and distribution often lead to pathologies and diseases. Cholesterol controls membrane fluidity and permeability.[1,2] It has been proposed that, together with sphingolipids, cholesterol forms membrane "lipid rafts" which are platforms for the regulation of signalling events.[2,3] Cholesterol is also found covalently attached to proteins of the Hedgehog family.[4,5] Moreover, cholesterol is a precursor for biologically active molecules such as steroid hormones, bile acids, insect ecdysons, oxysterols, and vitamin D.

Data accumulated in last years have shown that the nematode *Caenorhabditis elegans* could be used as an excellent model for studying all these facets of sterol function on the level of a whole organism. This organism is one of the well-established genetic models and many aspects of its development have been well characterized. The generation time of *C. elegans* is relatively short (about 50 hours at 25 °C) and large amounts of worms can be easily grown for biochemical studies. Vast methodological knowledge on genetic manipulation has been accumulated that, in principle, could allow disruption of all genes that might regulate steroid functions, either by double-stranded RNA interference (RNAi) or by selection of targeted deletion or point mutations. In addition, one of the main advantages to use *C. elegans* as a model system for studies on sterol function is that nematodes are auxotrophic for these compounds: worms rely on exogenous sterols for their development and cannot synthesize them de novo.[6,7] This allows the investigation of structure–activity relationships by applying chemically modified sterols and combining the phenotypic analysis with genetics.

The analysis of worm sterols by GC-mass spectrometry or by TLC analysis of worms fed with radioactive cholesterol demonstrated that the bulk of exogenously added sterol remains unchanged;[8–10] however, *C. elegans* is able to carry out some modifications on them.[6,8–15] Thus, several enzymatic transformations of cholesterol were identified and the major metabolic pathway in *C. elegans* was outlined.[14] In this context, two transformations should be emphasized: the dehydrogenation of cholesterol at position 7 (production of 7-dehydrocholestrol) and methylation at position 4 (production of lophenol) (Scheme 1).

The normal reproductive cycle of *C. elegans* includes four subsequent larval stages each separated by a molt. Under inhospitable conditions, such as starvation or overcrowding, *C. elegans* enters an alternative third larval stage, called dauer (enduring).[16] A possible hormonal regulation of the dauer larva formation was initially proposed based on genetic studies. A number of genes (*daf*, from dauer formation) can mutate to either cause constitutive formation

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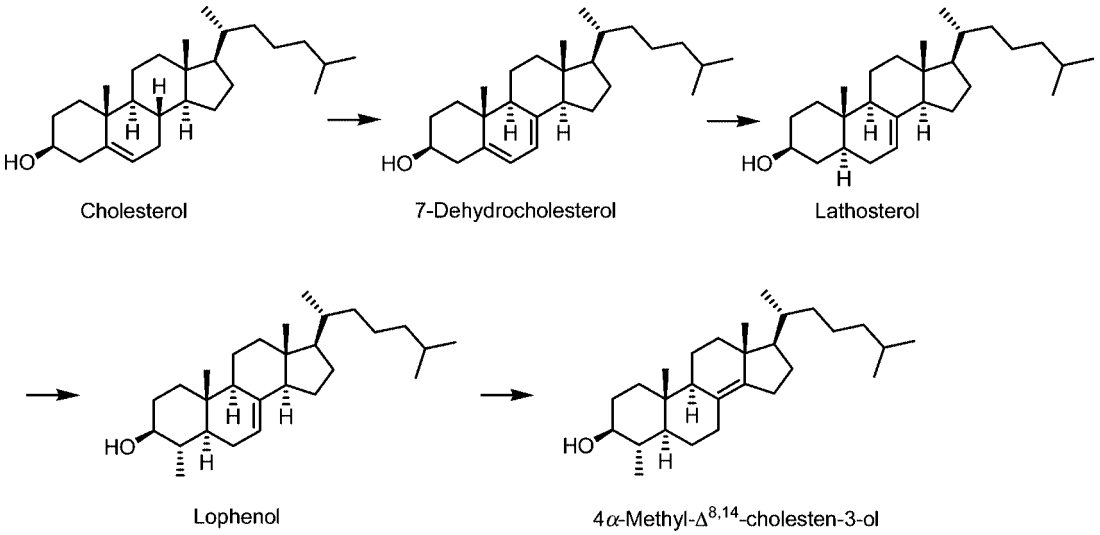


Scheme 1.

(DAF-c) of dauer larvae or prevent their formation (DAF-d).[16] Three signalling pathways (TGF-beta, cyclic GMP and insulin-like IGF-1) control the formation of dauer larvae.[16] The molecular identification of two genes, *daf-12* and *daf-9*, suggested the existence of a sterol related hormone that might integrate these pathways. DAF-12 is a nuclear hormone receptor required for execution of dauer formation, since *daf-12* null mutant fails to form dauer and undergoes reproductive development.[17,18] DAF-9 is a member of a cytochrome P450 family closely related to the mammalian CYP2 family of cytochrome P450 and might be involved in sterol metabolism.[19–22] DAF-9 is necessary for the reproductive development since *daf-9* mutants form constitutively dauers. The double mutant of *daf-9 daf-12* also cannot form dauer larvae indicating that *daf-9* acts upstream of *daf-12*. Taking this together, a scenario was proposed where DAF-9 is an enzyme that produces a steroid hormone that inhibits DAF-12. The absence of the hormone activated DAF-12 ultimately triggers the dauer larva formation.[19,21]

Direct evidence of the involvement of sterol-derived hormones in the process of the dauer larva formation is based on biochemical studies. As mentioned above, the strict cholesterol depletion induces worms to enter the dauer formation pathway.[15] Biochemical analysis has shown that in the second generation of sterol-depleted worms, the residual sterols were mostly in methylated form.[15] Furthermore, if worms were grown on lophenol, a 4α-methylsterol, they produced in the second generation regular dauer larvae despite sufficient food and low population density. This observation raises the question whether lophenol itself actively induces dauer larva formation and the methylation at position 4α is required for this process. The fact that 4α-fluorocholesterol, which cannot be methylated, also induces dauer larvae formation rules out this option. Thus, methylation per se is not mandatory for dauer larva formation but rather the accessibility of position 4 is required for another transformation in order to allow reproductive development.[15]

Many observations confirm that the molting process in *C. elegans* depends on sterols. One of the phenotypes described in cholesterol-depletion studies is an old cuticle with incomplete shedding.[23–25] As described above, larvae of the second generation grown without sterols have a double cuticle.[15] Furthermore, mutants that display defects in molting are sensitive to reduced cholesterol levels.[24] Mutations in LRP-1, the gp330/ megalin homologue in *C. elegans*, show arrest at the molt between the third and the fourth larval stage.[23] In mammals, megalin is an LDL receptor related protein and it has been suggested to be required for the uptake of vitamin D in kidney.[26] In *C. elegans*, *lrp-1* is expressed at the apical surface of *hyp-7*, a polarized epithelium that apically secretes cuticle, and it has been suggested that *lrp-1* is involved in the uptake of sterols/hormones in these cells.[23]

In *Drosophila*, ecdysones pulses are transduced through stage-specific regulatory cascades of nuclear hormone receptors.[27] In *C. elegans*, a number of nuclear hormone receptors have been identified as *Drosophila* orthologs.[28–32] Based on this observation, a conserved nuclear receptor "ecdysone cascade", controlling molting in *C. elegans*, has been proposed.[32] Only the isolation of the molting hormone from *C. elegans* can prove this hypothesis. However, the isolation and structural elucidation of the molting hormone remains a major challenge. Similar to gamravali, that regulates the dauer larva formation, this hormone should be present at depleting amounts in worms. A tempting speculation on the structure of the molting hormone(s) is that it derives from 4-methylated sterols. As mentioned above, *daf-12* can normally grow on lophenol for many generations without displaying defects in molting.

Results and Discussion

Synthesis of Cholesterol Derivatives

Cholestanol has a similar effect on the growth of worms as cholesterol.[15] Therefore, we decided to synthesize first

lophanol (4α-methyl-5α-cholestan-3β-ol) (**4b**) representing the saturated analogue of the 4α-methylated sterol lophenol. Methylation of 5α-cholestan-3-one (**1**) by a procedure which is known to suppress double alkylation[33] afforded an inseparable mixture of the 4α-methyl-regioisomer **2** (lophanone) and the 2α-methyl-regioisomer **3** in a 1:2 ratio (Scheme 2). Reduction at low temperature with lithium aluminum hydride led to the corresponding diastereoisomeric alcohols **4** and **5**. The more polar 3β-alcohols **4b** and **5b** could be separated from the 3α-alcohols **4a** and **5a** (ratio, 5.5:1). However, the 4α-methyl- and 2α-methyl regioisomers remained inseparable. Transformation of the 3β-alcohols **4b** and **5b** into the *p*-bromobenzoates **6** and **7** followed by crystallization of the major regioisomer confirmed the structural assignment unambiguously by an X-ray analysis of compound **7** (Figure 1). Further structural confirmation of the alkylation products was obtained from independent synthesis of the 2α-methyl regioisomer **3** following a literature procedure.[34]

Since pure lophanol (**4b**) proved to be inaccessible by alkylation of 5α-cholestan-3-one (**1**), we devised an alternative approach. Following a procedure developed by Stork,[35–37] reduction of 4-cholesten-3-one (**8**) with lithium in liquid ammonia and subsequent alkylation using iodomethane afforded lophanone (4α-methyl-5α-cholestan-3-one) (**2**) (Scheme 3).[38,39] Stereoselective reduction of lophanone (**2**) with lithium aluminum hydride provided as major product lophanol (**4b**),[38] previously isolated from different natural sources.[39–45] The structure of lophanol (**4b**) was proven by 2D-NMR experiments and an X-ray crystal structure determination of the *p*-bromobenzoate **6** (Figure 2). The corresponding 4α-ethyl derivatives **9**, **10b**, and **11** were obtained by a similar sequence.

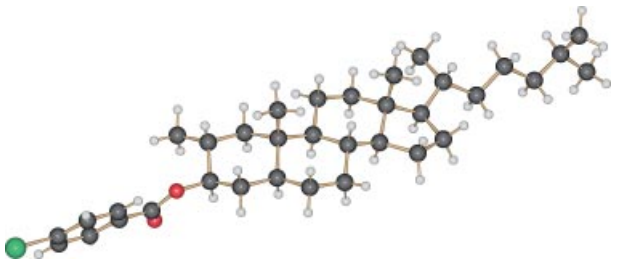
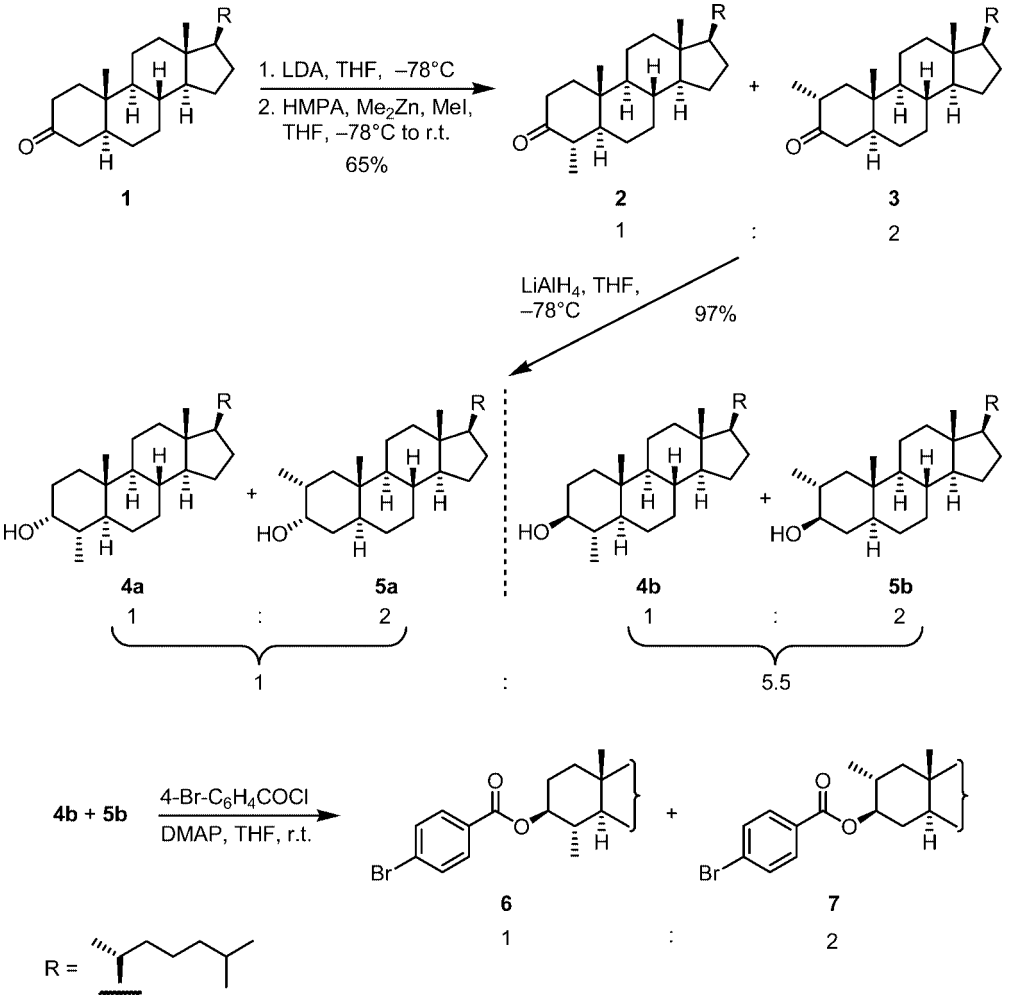
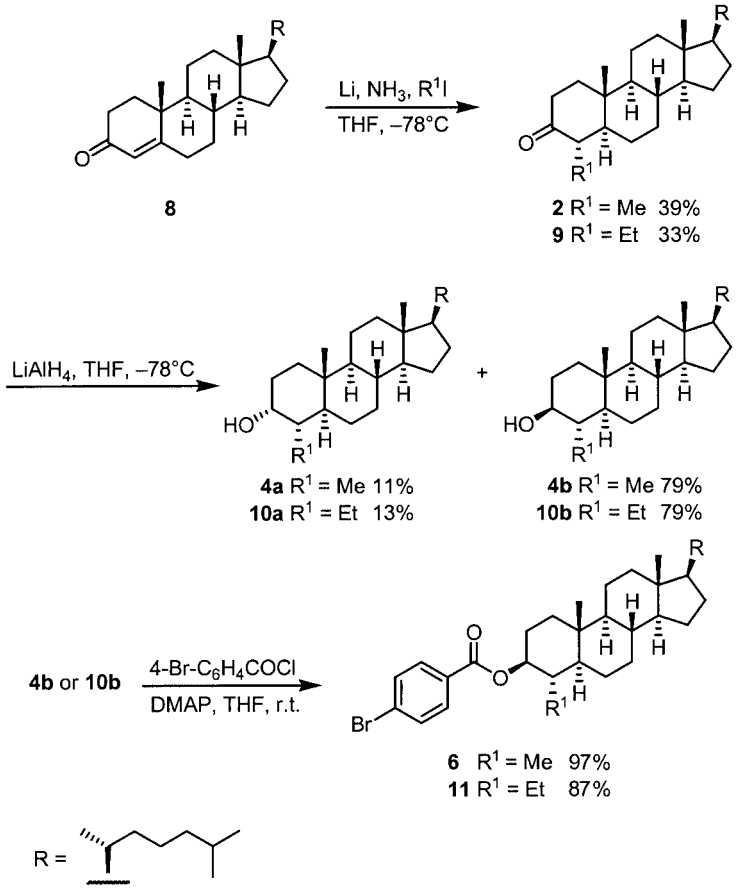


Figure 1. Molecular structure of the *p*-bromobenzoate **7** in the crystal.



Scheme 2.



Scheme 3.

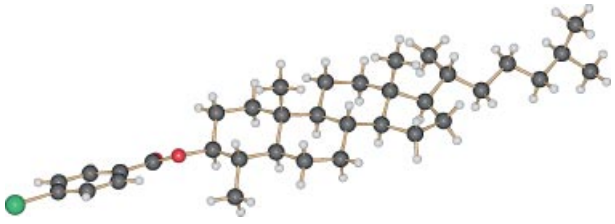
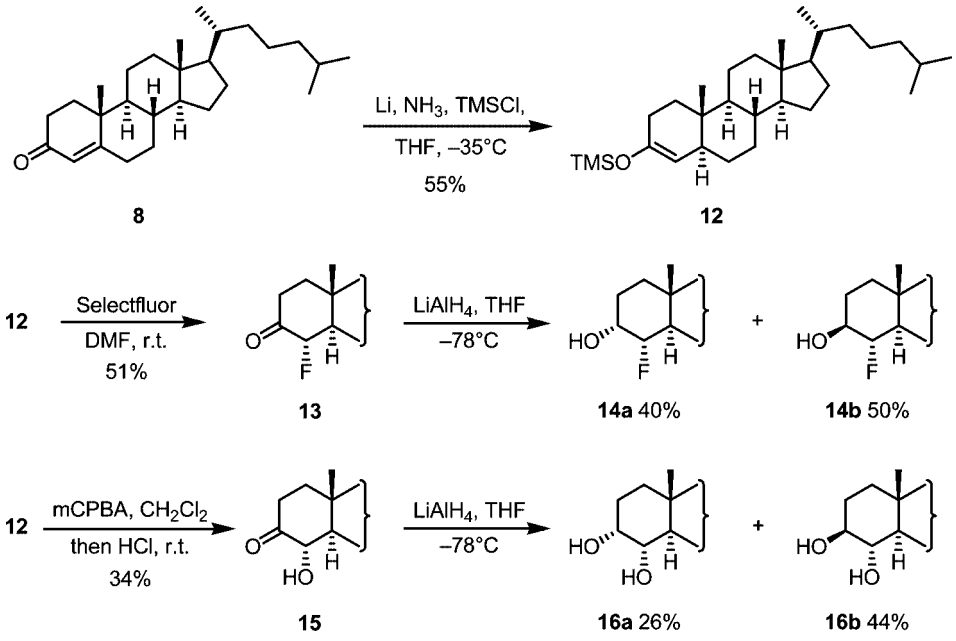


Figure 2. Molecular structure of the lophanol *p*-bromobenzoate **6** in the crystal.

We then turned our attention towards lophanol analogues (5α-cholestan-3β-ols) with different 4α-substituents. Using a protocol reported by Stork,[46] lithium–ammonia reduction of 4-cholesten-3-one (**8**) followed by treatment with chlorotrimethylsilane led to the trimethylsilyl enol ether **12** on a multi-gram scale (Scheme 4). The silyl enol ether **12**, as central intermediate of our transformations, can be stored for months and reacts with diverse electrophiles to provide different 4α-substituted 5α-cholestan-3β-ols. Moreover, silyl enol ethers can be converted regioselectively to the corresponding lithium enolates.[46] Thus, treatment of compound **12** with butyllithium provides the lithium 3,4-enolate, which cannot be prepared in a regioselective manner by deprotonation of 5α-cholestan-3-one (**1**) (cf. Scheme 2).

Nowadays a variety of electrophilic fluorinating agents with scalable fluorinating power is available.[47,48] Fluorination of the silyl enol ether **12** under mild conditions using Selectfluor in DMF[49,50] at room temperature afforded 4α-fluoro-5α-cholestan-3-one (**13**) (Scheme 4). 1-Fluoro-2,4,6-trimethylpyridinium triflate gave similar results (CH_2Cl_2, room temp., 2 d, 44%)[15] as Selectfluor, while the more powerful reagent 1,1′-difluoro-2,2′-bipyridinium bis(tetrafluoroborate) led to increased amounts of ether cleavage and decomposition.[51] Reduction of compound **13** with lithium aluminum hydride provided the desired 3β-alcohol **14b** which could easily be separated from the diastereoisomeric 3α-alcohol **14a** by flash chromatography. The decreased diastereoselectivity for the reduction of **13** as compared to the reduction of **2** or **9** presumably results from electrostatic repulsion between the hydride donor and the highly electronegative fluorine. The stereochemistry of 4α-fluoro-5α-cholestan-3β-ol (**14b**) was determined by NOESY experiments (Figure 3). Figure 3 shows a strong interaction between the hydrogen at C-4 and the angular methyl group (C-19), indicating that both are on the same face of the steroid A-ring. The other 1,3 interactions between the hydrogen at C-4 and the axial hydrogens at C-2 and C-6 confirm this assignment.

Rubottom oxidation[52] of compound **12** and subsequent reduction of the resulting hydroxy ketone **15** afforded the



Scheme 4.

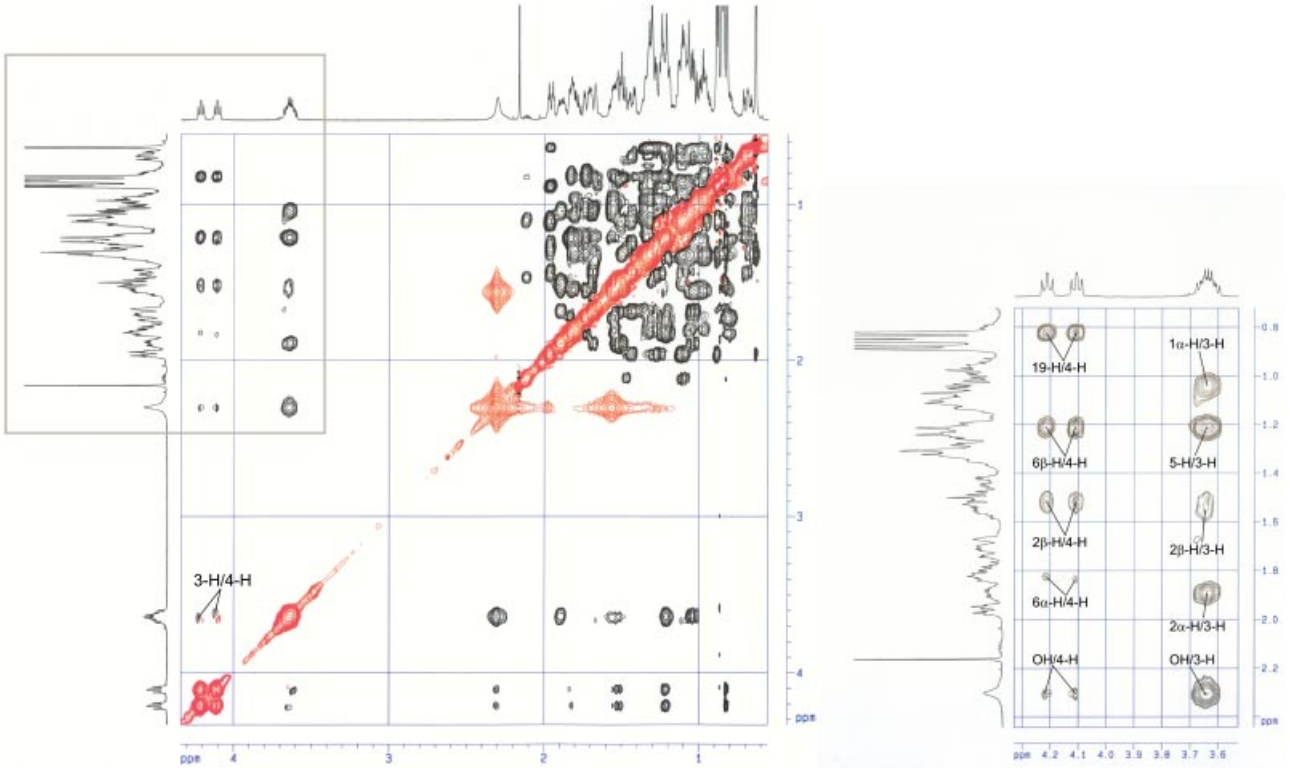
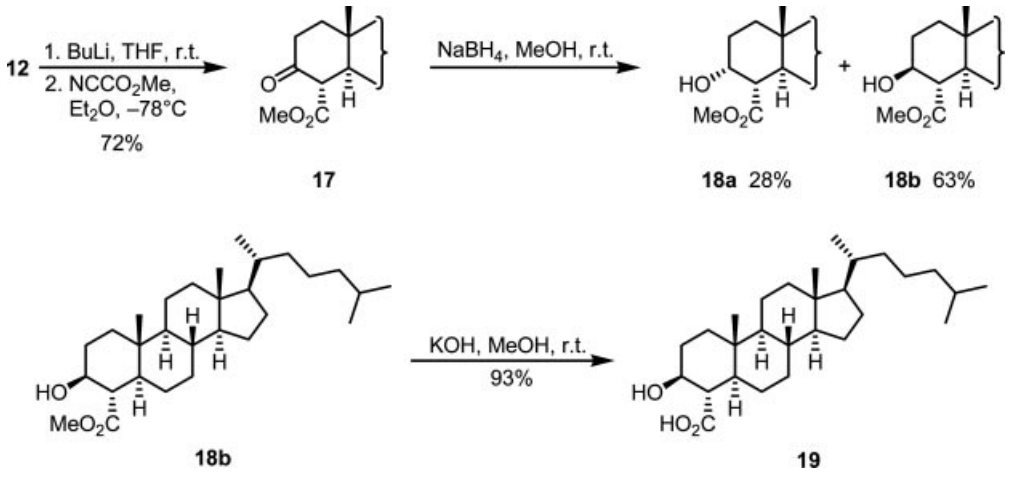


Figure 3. NOESY spectrum (500 MHz, $CDCl_3$) of 4α-fluoro-5α-cholestan-3β-ol (**14b**) and expansion of the region with characteristic signals.

3α-alcohol **16a** and the 3β-alcohol **16b** in a ratio of 1:1.7 (Scheme 4). Although crystalline **12** is stable, rapid decomposition occurs under acidic or neutral aqueous conditions, explaining the moderate yield of hydroxy ketone **15**. The stereochemistry was assigned based on comparison of the ^1H NMR spectra with the analogous compounds **4**, **10**, and **14**.

Synthesis of the β-hydroxy acid **19** requires a regio- and stereoselective methoxycarbonylation reaction at C-4. Reaction of lithium enolates with chloroformates often leads to *O*-acylation. β-Keto acids obtained from quenching of enolates with carbon dioxide are highly unstable.[53] To overcome these difficulties, Mander et al. introduced methyl cyanoformate.[54] Treatment of the silyl enol ether **12** with



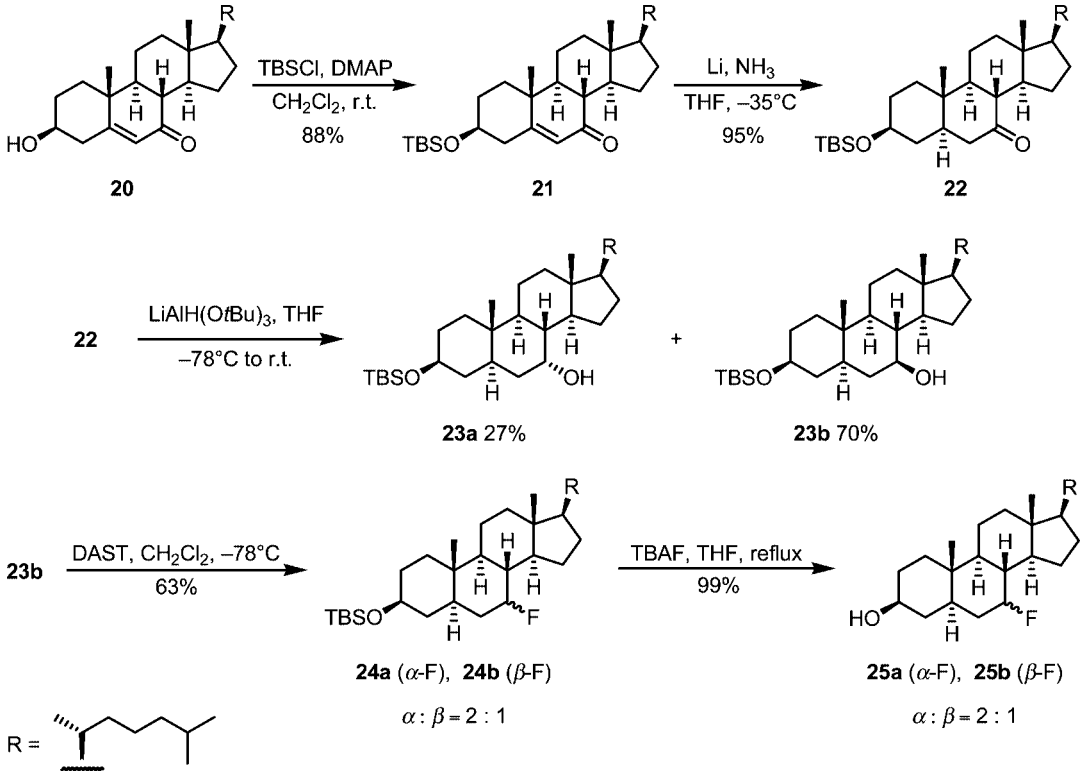
Scheme 5.

butyllithium and subsequent reaction of the resulting lithium enolate with methyl cyanoformate afforded the β-keto ester **17** (Scheme 5).[55] Reduction of **17** using sodium borohydride provided the 3α-alcohol **18a** and the 3β-alcohol **18b** in a ratio of 1:2.25. Saponification of the major diastereoisomer **18b** led to β-hydroxy acid **19**.

For the synthesis of 7-hydroxylated and 7-fluorinated sterols we started from commercially available 7-ketocholesterol (**20**). Transformation of **20** to the corresponding *tert*-butyldimethylsilyl ether **21** followed by reduction with lithium in ammonia provided the ketone **22** (Scheme 6). The diastereoselectivity of the reduction to the carbinols **23** was investigated using different reducing agents (Table 1). Depending on the steric demand of the reagent either the 7α-alcohol **23a** or the 7β-alcohol **23b** was obtained as major

Table 1. Results of the reduction of ketone **22**.

Reagent	Reaction conditions	Yields [%]	**23a/23b**
$NaBH_4$	MeOH, room temp., 2 h	100	2.6:1.0
$LiAlH_4$	THF, –78 °C to room temp., 24 h	92	2.4:1.0
DIBAL	CH_2Cl_2, –78 °C to room temp., 24 h	99	1.1:1.0
$LiAlH(OtBu)_3$	THF, –78 °C to room temp., 24 h	97	1.0:2.6



Scheme 6.

product. The diastereoisomeric alcohols **23a** and **23b** were easily separated by flash chromatography on silica gel. The stereochemistry at C-7 was assigned based on NOESY experiments (Figure 4). For the 7β-alcohol **23b** strong interactions of the hydrogen at C-7 and the hydrogens at C-5, C-9, and C-14 confirm the stereochemistry at C-7.

The most common reagent for transformation of carbinols to the corresponding fluoroalkanes is diethylaminosulfur trifluoride (DAST).[47,48,56] DAST is known to react mainly under inversion of configuration. However, neighbouring group effects can lead to retention of configuration, elimination to olefins, and various rearrangement products. While reaction of the 7α-carbinol **23a** with DAST resulted mostly in decomposition, fluorination of the diastereoisomeric 7β-carbinol **23b** provided an inseparable mixture of the 7α-fluoro derivative **24a** and the 7β-fluoro derivative **24b** in a 2:1 ratio (Scheme 6). The stereochemistry was assigned by comparison of the ^{1}H NMR spectra with those of analogous compounds. Cleavage of the silyl ether led to the 7-fluorinated 5α-cholestan-3β-ols **25a** and **25b**.

The diastereoisomeric diols **26a** and **26b** can be obtained individually by desilylation of the compounds **23a** and **23b** (Scheme 7). Alternatively these diols can be obtained from the much cheaper cholesteryl acetate. Allylic oxidation of cholesteryl acetate using Chandrasekaran's procedure provided 7-ketocholesteryl acetate (**27**).[57] Catalytic hydrogenation of **27** to the saturated ketone **28** and subsequent reduction with lithium aluminum hydride led directly to the 7α-alcohol **26a** and the 7β-alcohol **26b** which were separated by flash chromatography. Ester cleavage of compound **28** afforded 7-keto-5α-cholestan-3β-ol (**29**).

Analogous to the transformation of cholesteryl acetate into the diol **26a** (cf. Scheme 7), commercial 25-hydroxycholesterol (**30**) was converted into the corresponding triol. Acetylation of **30** followed by allylic oxidation of the resulting acetate **31** provided 25-hydroxy-7-ketocholesteryl acetate (**32**) (Scheme 8). Catalytic hydrogenation of compound **32** led to the saturated ketone **33**. Direct reduction of **33** gave the free C-7 diastereoisomeric triols **34**, which were inseparable by flash chromatography. Thus, the 25-hydroxy group was protected as trimethylsilyl ether followed by reduction with lithium aluminum hydride, chromatographic separation of the 25-silylated triols, and desilylation to afford 5α-cholestane-3β,7α,25-triol (**34a**) and 5α-cholestane-3β,7β,25-triol (**34b**).

In order to achieve specific functionalizations at C-6 and C-7 of cholesterol we started from commercial 6-keto-5α-cholestan-3β-ol (**35**). Protection of **35** as trimethylsilyl ether **36**, regioselective formation of the lithium enolate, and subsequent treatment with chlorotrimethylsilane afforded the silyl enol ether **37** (Scheme 9). Fluorination of **37** using Selectfluor led to the α-fluoro ketone **38**, which on reduction with sodium borohydride in methanol provided quantitatively 7α-fluoro-5α-cholestane-3β,6β-diol (**39**). NOESY experiments confirmed the stereochemistry of **39** (Figure 5). The absence of a diaxial interaction between the C-19 methyl group and the hydrogen at C-6 indicates that the 6-

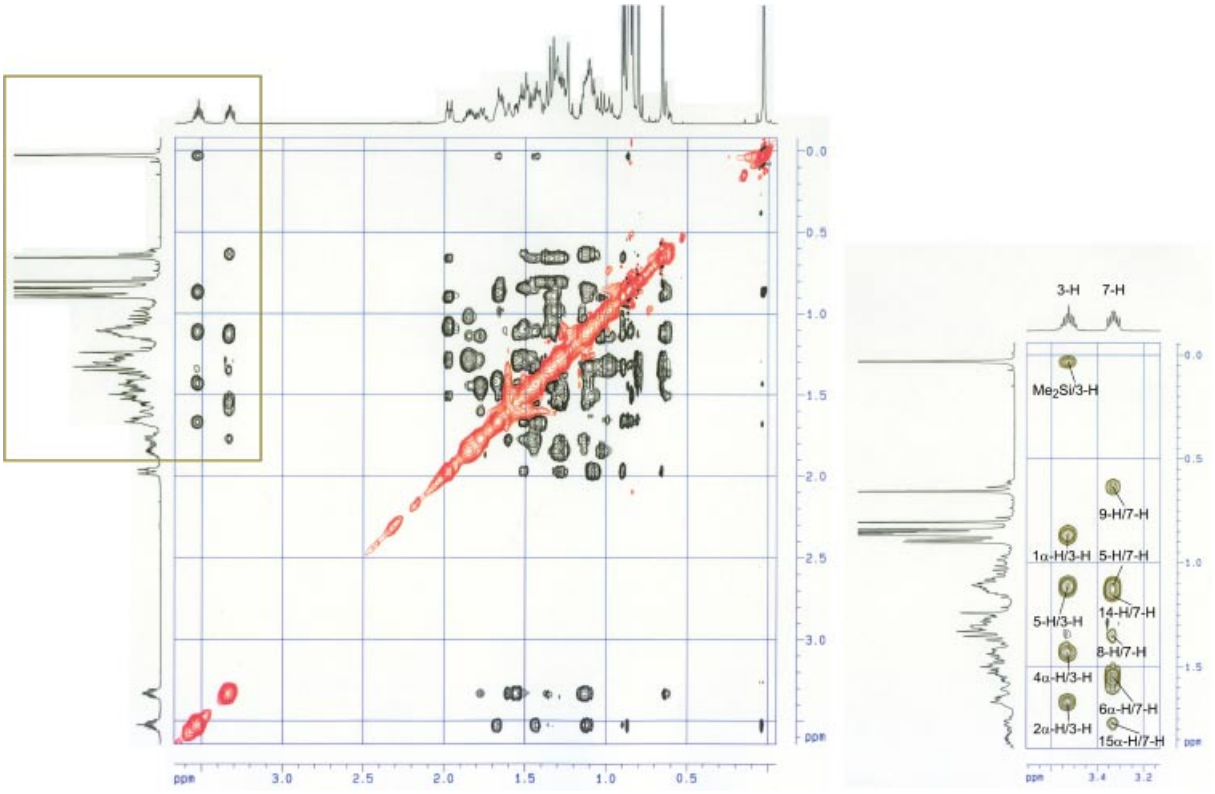
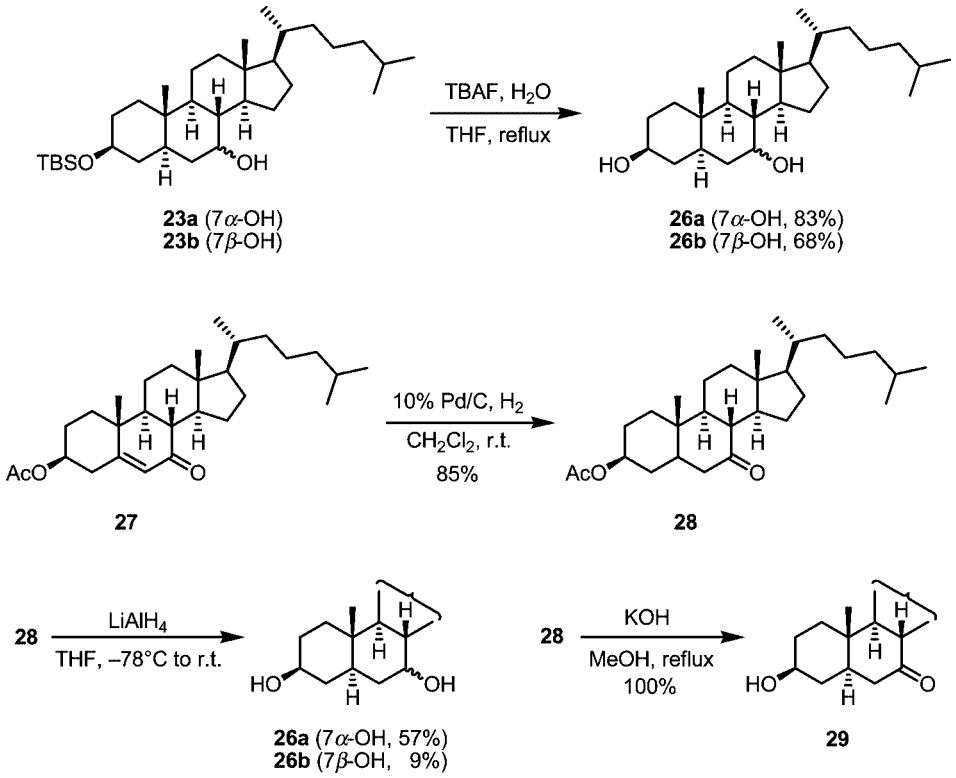
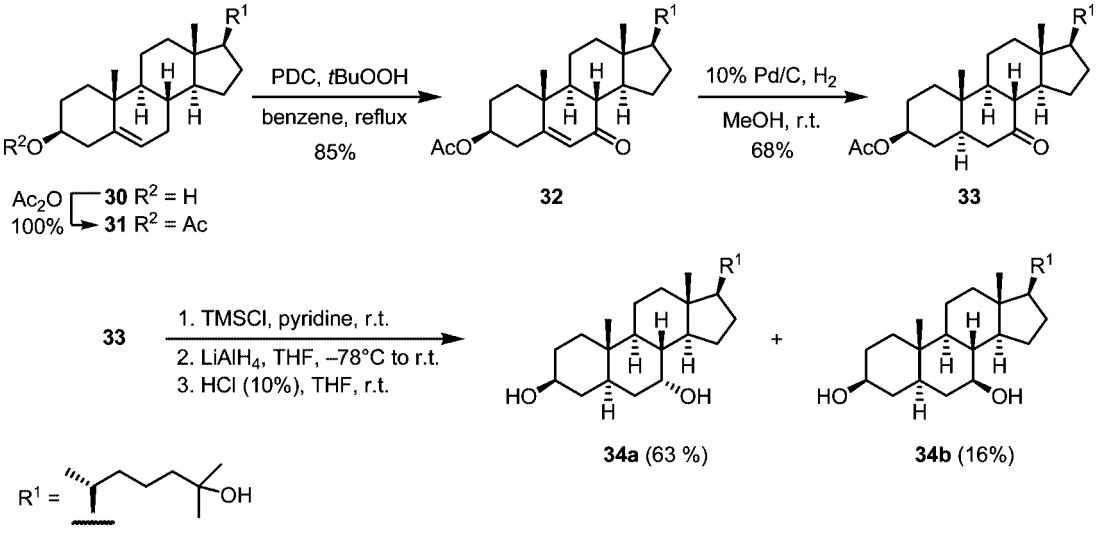


Figure 4. NOESY spectrum (500 MHz, $CDCl_3$) of 3β-(*tert*-butyldimethylsilyloxy)-5α-cholestan-7β-ol (**23b**) and expansion of the region with characteristic signals.



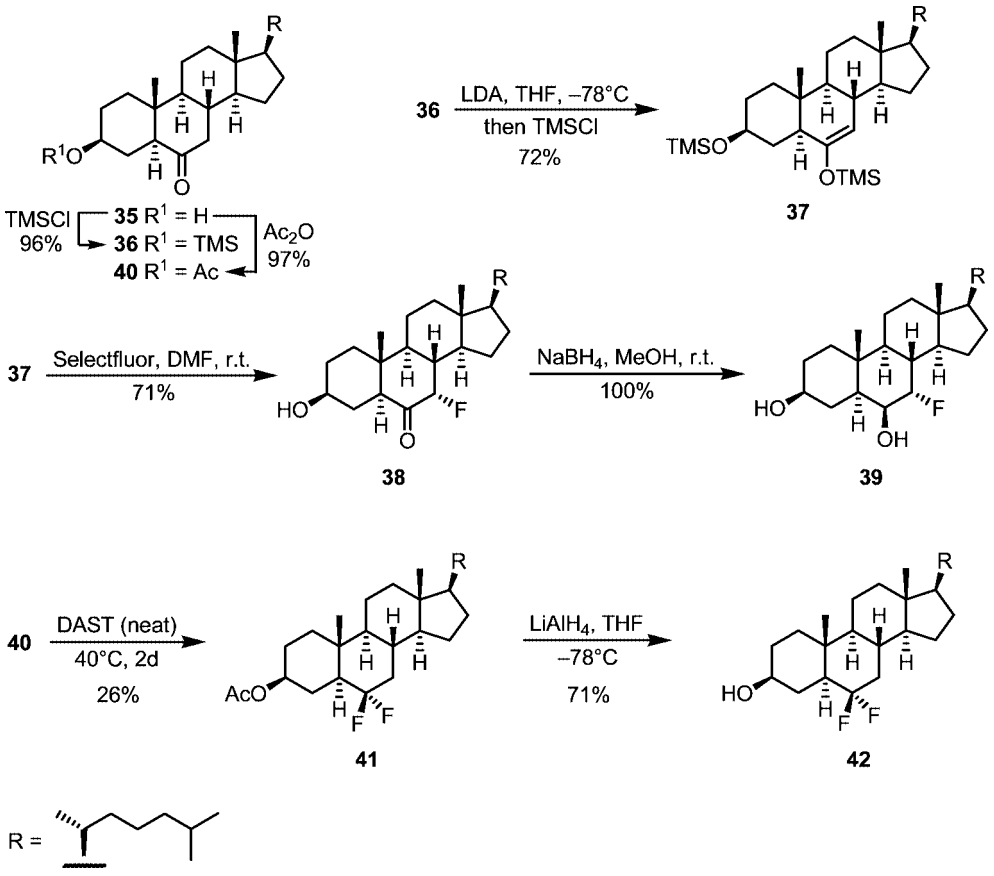
Scheme 7.



Scheme 8.

hydroxy group is on the β-face of the steroid skeleton. This assignment is confirmed by the interaction of the hydrogens at C-5 and C-6. The strong interaction between the hydrogen atoms at C-7 and C-8 indicates an α-stereochemistry of the fluorine atom at C-7.

Conversion of a ketone to the corresponding *gem*-difluoro compound can be achieved using DAST under drastic reaction conditions.[47,48,56] Acetylation of **35** followed by reaction of the resulting acetate **40** with neat DAST afforded the 6,6-difluoro derivative **41** in moderate yield. A milder procedure using Deoxofluor as fluorine source[58] led to an even lower yield (Deoxofluor, cat. HF, CH_2Cl_2, room temp., 3 d, 11%). Reductive cleavage of the ester provided 6,6-difluoro-5α-cholestan-3β-ol (**42**).



Scheme 9.

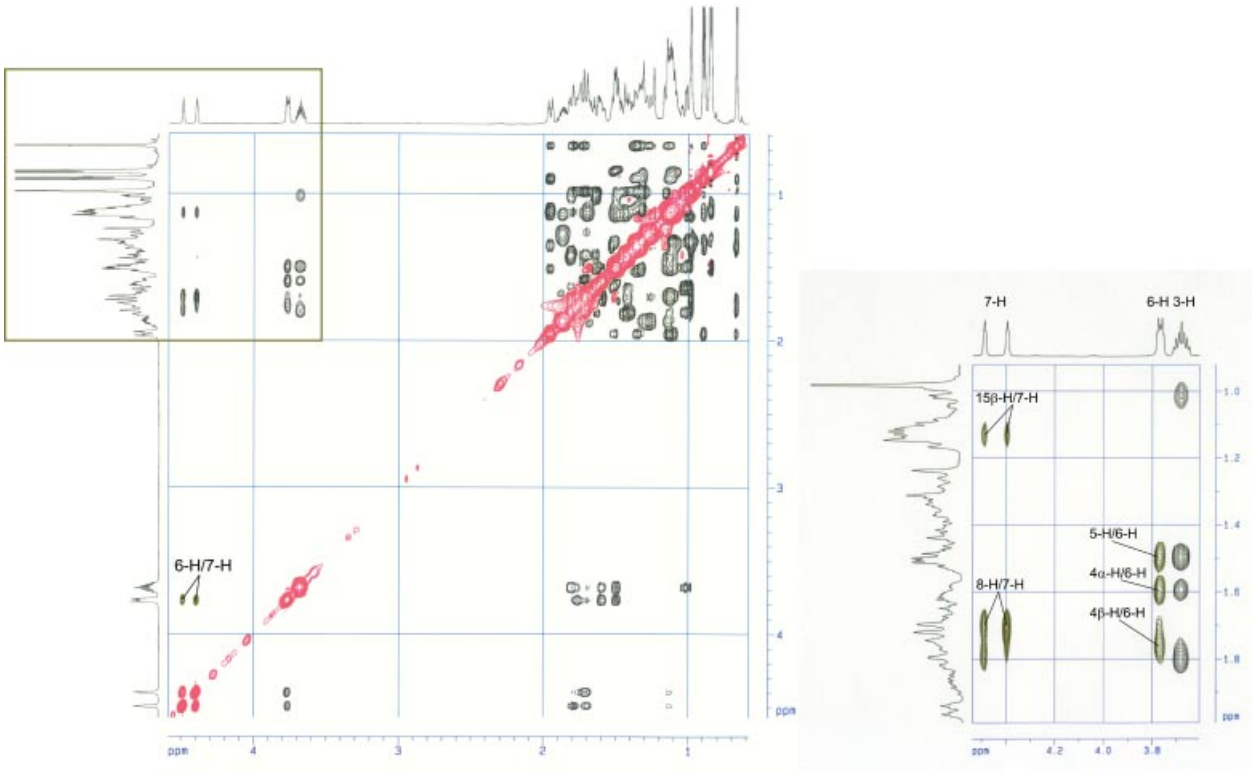


Figure 5. NOESY spectrum (500 MHz, $CDCl_3$) of 7α-fluoro-5α-cholestane-3β,6β-diol (**39**) and expansion of the region with characteristic signals.

Hormonal Activity of Cholesterol Derivatives

Wild-type N2 Bristol and *daf-12* mutant strains were routinely propagated on NGM-agar plates as described by Brenner.[7] The cholesterol-free conditions were achieved by replacement of agar with agarose that was extracted twice with chloroform. *E. coli* NA22 strain was grown in overnight culture in sterol-free media.

In order to test the effect of cholesterol derivatives on the life cycle, worms were grown on plates with all cholesterol replaced by a synthetic derivative. The synthetic compound was dissolved in a methanol/chloroform mixture (1:1) at a concentration of 1 mM. For feeding of worms, this solution was mixed with cholesterol-free bacteria to a final concentration of 13 μM. Subsequently, various volumes (e.g. 100–200 μL) of the bacterial suspension were plated on 6 cm cholesterol-free agarose dishes.

The first generation of wild-type N2 Bristol strain as well as mutant *daf-12* strain grown on cholesterol derivatives did not show any signs of abnormal development compared to controls. In order to obtain the second worm generation, eggs from gravid adults were isolated by treatment for 5 min with bleaching solution (4% NaOH in Klorix). Released eggs were washed twice with M9 medium before transfer onto a fresh plate.[7] Finally, worms were grown at 20 °C and after 3 days of egg transfer the second generation was analyzed in terms of reproduction, formation of dauer larvae or eventual molting defects. These stages can be well distinguished (Figure 6).

Figure 6. The different stages of development of *C. elegans*.

The results of feeding experiments are summarized in Table 2. It must be noted that none of the compounds tested could substitute cholesterol/cholestanol. All substances fall into two classes: one having the same effect as lophanol and the other mimicking the absence of sterols.

The following general conclusions can be drawn from our studies for the structure–activity relationship of cholesterol derivatives:

Table 2. Effect of cholesterol derivatives on the life cycle and molting process in the second generation of wild type and mutant *daf-12* line.

Compound	Wild type	daf-12
Cholestanol	R	R
Lophanol (**4b**), **10b**, **14b**, **16b**, **25a/25b**, **29**, **39**, **42**	D	R
No sterols, **4a**, **5a**, **5b**, **18b**, **19**, **26a**, **26b**, **34a**, **34b**	md	md

R: normal reproductive growth; D: dauer larva formation; md: molting defect

1. The activity in dauer formation as well as in molting processes require a β-orientation of the hydroxy group at C-3 (compare **4a** and **4b**).
2. Methylation at C-2 (**5b**) corresponds to loss of the activity of cholestanol.
3. A few modifications, e.g. alkylation, fluorination, and hydroxylation, at C-4 are possible (**4b**, **10b**, **14b**, **16b**), but not the introduction of methoxycarbonyl or carboxy groups (**18b**, **19**).
4. Modifications carried out at C-6 (**39**, **42**) lead to a similar activity as for lophanol (**4b**).
5. Introduction of a hydroxy group at C-7 (**26**, **34**) destroys the activity of cholestanol.

Experimental Section

General: All reactions were carried out in dry solvents under an inert gas atmosphere (argon or nitrogen). THF and diethyl ether were dried using a solvent purification system (MBraun-SPS). Chemicals were used as received from commercial sources. Flash chromatography: Merck silica gel (0.040–0.063 mm). Melting points: Electrothermal IA9100. IR spectra: Thermo Nicolet Avatar 360 FT-IR; $\tilde{\nu}$ in cm^{-1}. NMR spectra: Bruker DRX 500; δ in ppm, J in Hz; complete assignment of the ^1H NMR and ^{13}C NMR signals was routinely achieved by measuring the following set of 2D NMR spectra: COSY, HSQC, HMBC, and NOESY. Mass spectra: Finnigan MAT-95, ionization potential: 70 eV. Elemental analyses: EuroVector EuroEA3000. X-ray analyses: Bruker-Nonius Kappa CCD with Oxford Cryosystems and STOE IPDS 2 image plate. Software: Collect (Nonius BV, 1997-2000), Dirax/lsq (Duisenberg & Schreurs, 1989-2000), SHELXS-97 (G. M. Sheldrick, 1990), EvalCCD (Duisenberg & Schreurs 1990-2000), SADABS version 2.03. (G. M. Sheldrick, Bruker AXS Inc., 2002), SHELXL-97 (G. M. Sheldrick, 1997), Schakal-99 (E. Keller, 1999), X-Area (STOE, 2003), X-Red (STOE, 2003).

4α-Methyl-5α-cholestan-3-one (Lophanone) (2): Lithium (50 mg, 7.2 mmol) was added to a solution of 4-cholesten-3-one (**8**) (1.00 g, 2.60 mmol) in anhydrous THF (20 mL) and ammonia (25 mL) at –78 °C. After warming to –35 °C and stirring for 4 h under nitrogen, the solution was cooled to –78 °C and iodomethane (5.17 g, 2.27 mL, 36.4 mmol) was added. Ammonia was allowed to evaporate overnight, water was added, and the aqueous layer was acidified by addition of 10% HCl. The aqueous layer was extracted with diethyl ether three times and the combined organic layers were dried with sodium sulfate. Evaporation of the solvent and flash chromatography (pentane/diethyl ether, 10:1) of the residue on silica gel afforded **2** as colorless crystals, yield: 402 mg (39%), m.p. 103–105 °C. IR (ATR): $\tilde{\nu}$ = 2931, 2866, 2848, 1709, 1467, 1441, 1383, 1376, 959 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 0.66 (s, 3 H), 0.68 (m, 1 H), 0.848 (d, J = 6.6 Hz, 3 H), 0.853 (d, J = 6.6 Hz,

3 H), 0.89 (d, J = 6.5 Hz, 3 H), 0.93–1.01 (m, 2 H), 0.96 (d, J = 6.5 Hz, 3 H), 1.03–1.20 (m, 8 H), 1.05 (s, 3 H), 1.22–1.27 (m, 1 H), 1.31–1.39 (m, 6 H), 1.48–1.59 (m, 4 H), 1.64–1.66 (m, 1 H), 1.71–1.75 (m 1 H), 1.77–1.84 (m, 1 H), 1.95–2.04 (m, 2 H), 2.27–2.32 (m, 2 H), 2.43 (m, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 11.50 (CH_3), 12.06 (CH_3), 12.70 (CH_3), 18.65 (CH_3), 21.38 (CH_2), 22.56 (CH_3), 22.82 (CH_3), 23.82 (CH_2), 24.19 (CH_2), 25.65 (CH_2), 28.01 (CH), 28.27 (CH_2), 31.94 (CH_2), 34.87 (CH), 35.78 (CH), 36.14 (CH_2), 36.34 (C), 38.06 (CH_2), 39.28 (CH_2), 39.50 (CH_2), 39.93 (CH_2), 42.53 (C), 45.06 (CH), 53.58 (CH), 54.08 (CH), 56.24 (CH), 56.32 (CH), 213.80 (C=O) ppm. MS (80 °C): m/z (%) = 400 (60) [M^+], 385 (24), 260 (12), 246 (52), 245 (100), 231 (24). HRMS: m/z [M^+] calcd. for $C_{28}H_{48}O$: 400.3705; found 400.3709. $C_{28}H_{48}O$ (400.68): calcd. C 83.93, H 12.07; found C 83.87, H 12.07.

4α-Methyl-5α-cholestan-3α-ol (4a) and 4α-Methyl-5α-cholestan-3β-ol (Lophanol) (4b): A 1 M solution of lithium aluminum hydride in THF (0.75 mL, 0.75 mmol) was added to a solution of 4α-methyl-5α-cholestan-3-one (**2**) (300 mg, 0.75 mmol) in anhydrous THF (10 mL) at 0 °C. After stirring for 4 h at 0 °C under an argon atmosphere, water and then 10% HCl were added. The aqueous layer was extracted with diethyl ether three times. The combined organic layers were washed with a saturated solution of sodium hydrogencarbonate and dried with sodium sulfate. Removal of the solvent and purification of the residue by flash chromatography (pentane/diethyl ether, 5:1) on silica gel provided **4a** as colorless crystals, yield: 34 mg (11%), m.p. 97 °C. IR (ATR): $\tilde{\nu}$ = 3629, 3416, 2928, 2866, 1465, 1379, 1227, 979, 946 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.63 (s, 3 H), 0.71 (m, 1 H), 0.79 (s, 3 H), 0.81 (m, 1 H), 0.846 (d, J = 6.6 Hz, 3 H), 0.851 (d, J = 6.6 Hz, 3 H), 0.88 (d, J = 6.9 Hz, 3 H), 0.90 (d, J = 7.2 Hz, 3 H), 0.92–1.13 (m, 11 H), 1.15–1.32 (m, 7 H), 1.36–1.57 (m, 4 H), 1.63–1.82 (m, 5 H), 1.95 (dt, J = 12.4, 3.2 Hz, 1 H), 3.73 (m, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 12.06 (CH_3), 12.33 (CH_3), 16.42 (CH_3), 18.65 (CH_3), 20.92 (CH_2), 22.56 (CH_3), 22.82 (CH_3), 23.81 (CH_2), 24.05 (CH_2), 24.13 (CH_2), 28.01 (CH), 28.26 (CH_2), 29.21 (CH_2), 32.14 (CH_2), 32.24 (CH_2), 35.01 (CH), 35.21 (CH), 35.80 (CH), 36.16 (CH_2), 36.31 (C), 39.51 (CH_2), 40.08 (CH_2), 42.43 (C), 44.79 (CH), 54.39 (CH), 56.19 (CH), 56.60 (CH), 71.97 (CH) ppm. MS (20 °C): m/z (%) = 402 (65) [M^+], 387 (28), 369 (24), 248 (38), 247 (51), 229 (46), 121 (29), 95 (42), 93 (30), 81 (41), 79 (22), 71 (22), 69 (30), 67 (25), 57 (51), 55 (52), 43 (100). HRMS: m/z [M^+] calcd. for $C_{28}H_{50}O$: 402.3862; found 402.3864.

4b was obtained from the more polar fraction as colorless crystals, yield: 239 mg (79%), m.p. 145 °C. IR (ATR): $\tilde{\nu}$ = 3322, 2926, 2864, 2850, 1444, 1380, 1037, 1012, 957 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.59 (m, 1 H), 0.63 (s, 3 H), 0.70 (m, 1 H), 0.79 (m, 1 H), 0.81 (s, 3 H), 0.847 (d, J = 6.6 Hz, 3 H), 0.852 (d, J = 6.6 Hz, 3 H), 0.88 (d, J = 6.5 Hz, 3 H), 0.91–1.15 (m, 10 H), 0.93 (d, J = 6.3 Hz, 3 H), 1.18–1.37 (m, 7 H), 1.43–1.57 (m, 4 H), 1.63–1.73 (m, 3 H), 1.77–1.82 (m, 2 H), 1.95 (dt, J = 12.6, 3.4 Hz, 1 H), 3.07 (ddd, J = 11.0, 10.0, 4.9 Hz, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 12.06 (CH_3), 13.35 (CH_3), 15.13 (CH_3), 18.65 (CH_3), 21.13 (CH_2), 22.55 (CH_3), 22.81 (CH_3), 23.82 (CH_2), 24.17 (CH_2), 24.19 (CH_2), 28.00 (CH), 28.28 (CH_2), 31.06 (CH_2), 32.23 (CH_2), 34.84 (CH), 35.79 (CH), 35.99 (C), 36.16 (CH_2), 36.82 (CH_2), 39.22 (CH), 39.51 (CH_2), 40.07 (CH_2), 42.51 (C), 50.92 (CH), 54.55 (CH), 56.26 (CH), 56.53 (CH), 76.62 (CH) ppm. MS (150 °C): m/z (%) = 402 (100) [M^+], 400 (53), 387 (52), 385 (25), 369 (26), 262 (38), 248 (57), 247 (80), 246 (53), 245 (85), 231 (38), 229 (90). HRMS: m/z [M^+] calcd. for $C_{28}H_{50}O$: 402.3862; found 402.3849. $C_{28}H_{50}O$ (402.70): calcd. C 83.51, H 12.51; found C 83.69, H 12.45.

4α-Methyl-5α-cholestan-3β-yl 4-Bromobenzoate (6): 4α-Methyl-5α-cholestan-3β-ol (**4b**) (204 mg, 507 μmol) was added to a solution of *p*-bromobenzoyl chloride (151 mg, 690 μmol) and triethylamine (700 mg, 957 μL, 690 μmol) in THF (15 mL) at room temperature. The solution was stirred for 24 h and filtered through a pad of silica gel with diethyl ether. Evaporation of the solvent gave **6** as colorless crystals, yield: 287 mg (97%), m.p. 159 °C. IR (ATR): $\tilde{\nu}$ = 2927, 2867, 2843, 1714, 1590, 1269, 1171, 1112, 1099, 1069, 1012, 958, 846, 756, 683 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.63 (m, 1 H), 0.65 (s, 3 H), 0.82–0.90 (m, 2 H), 0.849 (d, J = 6.3 Hz, 3 H), 0.852 (d, J = 6.6 Hz, 3 H), 0.86 (d, J = 6.6 Hz, 3 H), 0.88 (s, 3 H), 0.89 (d, J = 6.5 Hz, 3 H), 0.93–1.14 (m, 10 H), 1.20–1.36 (m, 7 H), 1.48–1.61 (m, 4 H), 1.66–1.81 (m, 4 H), 1.96 (m, 2 H), 4.60 (dt, J = 5.0, 10.9 Hz, 1 H), 7.56 (d, J = 8.5 Hz, 2 H), 7.90 (d, J = 8.5 Hz, 2 H) ppm. ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 12.03 (CH_3), 13.28 (CH_3), 15.24 (CH_3), 18.63 (CH_3), 21.13 (CH_2), 22.53 (CH_3), 22.79 (CH_3), 23.80 (CH_2), 24.14 (CH_2), 24.18 (CH_2), 27.16 (CH_2), 27.98 (CH), 28.24 (CH_2), 32.08 (CH_2), 34.83 (CH), 35.77 (CH), 35.91 (C), 36.13 (CH_2), 36.23 (CH), 36.47 (CH_2), 39.48 (CH_2), 39.97 (CH_2), 42.47 (C), 50.97 (CH), 54.32 (CH), 56.22 (CH), 56.42 (CH), 79.96 (CH), 127.71 (C), 129.76 (C), 131.04 (2 CH), 131.57 (2 CH), 165.60 (C=O) ppm. MS (150 °C): m/z (%) = 584 (9) [M^+], 384 (100), 369 (58), 355 (18), 343 (11), 244 (22), 231 (15), 230 (45), 229 (74), 215 (16), 185 (55), 183 (68), 161 (16), 149 (11), 122 (12), 121 (18), 109 (11), 107 (15), 95 (18), 81 (12). HRMS: m/z [M^+] calcd. for $C_{35}H_{53}BrO_2$: 584.3229; found 384.3218. $C_{35}H_{53}BrO_2$ (585.70): calcd. C 71.77, H 9.12; found C 71.87, H 9.17.

4α-Ethyl-5α-cholestan-3-one (9): Lithium (50 mg, 7.2 mmol) was added to a solution of 4-cholesten-3-one (**8**) (1.00 g, 2.60 mmol) in anhydrous THF (20 mL) and ammonia (25 mL) at –78 °C. After warming to –35 °C and stirring for 4 h under a nitrogen atmosphere, the solution was cooled to –78 °C and iodoethane (5.68 g, 2.91 mL, 36.4 mmol) was added. Ammonia was allowed to evaporate overnight, water was added, and the aqueous layer was acidified by addition of 10% HCl. The aqueous layer was extracted with diethyl ether three times and the combined organic layers were dried with sodium sulfate. Evaporation of the solvent and flash chromatography (pentane/diethyl ether, 10:1) of the residue on silica gel afforded **9** as colorless crystals, yield: 353 mg (33%), m.p. 112–114 °C. IR (ATR): $\tilde{\nu}$ = 2941, 2868, 2852, 1705, 1465, 1443, 1374, 1177, 878, 595 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.66 (s, 3 H), 0.68–0.73 (m, 1 H), 0.80–0.86 (m, 1 H), 0.81 (t, J = 7.3 Hz, 3 H), 0.848 (d, J = 6.6 Hz, 3 H), 0.852 (d, J = 6.6 Hz, 3 H), 0.89 (d, J = 6.5 Hz, 3 H), 0.93–1.00 (m, 2 H), 1.02–1.24 (m, 8 H), 1.03 (s, 3 H), 1.27–1.38 (m, 7 H), 1.43–1.59 (m, 4 H), 1.62–1.75 (m, 3 H), 1.80 (m, 1 H), 1.98 (m, 2 H), 2.16 (ddd, J = 12.1, 6.6, 2.7 Hz, 1 H), 2.28 (ddd, J = 14.7, 5.2, 2.5 Hz, 1 H), 2.39 (dt, J = 6.5, 14.2 Hz, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 10.71 (CH_3), 12.05 (CH_3), 12.75 (CH_3), 18.11 (CH_2), 18.64 (CH_3), 21.39 (CH_2), 22.55 (CH_3), 22.82 (CH_3), 23.82 (CH_2), 24.18 (CH_2), 25.53 (CH_2), 28.00 (CH), 28.27 (CH_2), 31.92 (CH_2), 34.92 (CH), 35.78 (CH), 36.14 (CH_2), 36.18 (C), 38.32 (CH_2), 38.89 (CH_2), 39.49 (CH_2), 39.95 (CH_2), 42.53 (C), 49.77 (CH), 50.89 (CH), 54.22 (CH), 56.24 (CH), 56.32 (CH), 213.33 (C=O) ppm. MS (100 °C): m/z (%) = 414 (72) [M^+], 399 (34), 386 (34), 274 (14), 260 (51), 259 (100), 246 (13), 245 (19), 191 (14). HRMS: m/z [M^+] calcd. for $C_{29}H_{50}O$: 414.3862; found 414.3870. $C_{29}H_{50}O$ (414.71): calcd. C 83.99, H 12.15; found C 84.25, H 12.31.

4α-Ethyl-5α-cholestan-3α-ol (10a) and 4α-Ethyl-5α-cholestan-3β-ol (10b): A 1 M solution of lithium aluminum hydride in THF (806 mL, 806 μmol) was added to a solution of 4α-ethyl-5α-cholestan-3-one (**9**) (334 mg, 806 μmol) in anhydrous THF (10 mL) at 0 °C. After stirring for 4 h at 0 °C under an argon atmosphere,

water and then 10% HCl were added. The aqueous layer was extracted with diethyl ether three times. The combined organic layers were washed with a saturated solution of sodium hydrogencarbonate and dried with sodium sulfate. Removal of the solvent and purification of the residue by flash chromatography (pentane/diethyl ether, 5:1) on silica gel provided **10a** as colorless crystals, yield: 43 mg (13%), m.p. 136 °C. IR (ATR): $\tilde{\nu}$ = 3604, 3439, 2928, 2868, 1464, 1379, 1123, 1034, 993, 844 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 0.63 (s, 3 H), 0.71 (m, 1 H), 0.79 (s, 3 H), 0.848 (d, J = 6.6 Hz, 3 H), 0.852 (d, J = 6.6 Hz, 3 H), 0.85 (m, 1 H), 0.88 (d, J = 6.5 Hz, 3 H), 0.90 (t, J = 7.3 Hz, 3 H), 0.90 (m, 1 H), 0.93–1.19 (m, 10 H), 1.20–1.36 (m, 9 H), 1.44–1.60 (m, 5 H), 1.65–1.71 (m, 3 H), 1.79 (m, 1 H), 1.95 (dt, J = 12.5, 3.3 Hz, 1 H), 3.96 (s, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 11.85 (CH_3), 12.05 (CH_3), 12.35 (CH_3), 18.65 (CH_3), 20.97 (CH_2), 21.59 (CH_2), 22.55 (CH_3), 22.82 (CH_3), 23.78 (CH_2), 23.81 (CH_2), 24.12 (CH_2), 28.01 (CH), 28.27 (CH_2), 29.21 (CH_2), 32.19 (2 CH_2), 34.84 (CH), 35.79 (CH), 36.16 (CH_2), 36.42 (C), 39.51 (CH_2), 40.10 (CH_2), 41.46 (CH), 42.44 (C), 44.17 (CH), 54.49 (CH), 56.20 (CH), 56.59 (CH), 66.80 (CH) ppm. MS (20 °C): m/z (%) = 416 (74) [M^+], 401 (26), 383 (31), 262 (49), 261 (43), 243 (40), 135 (25), 121 (21), 109 (25), 107 (26), 95 (44), 81 (42), 57 (52), 55 (50), 43 (100). HRMS: m/z [M^+] calcd. for $C_{29}H_{52}O$: 416.4018; found 416.4005.

10b was obtained from the more polar fraction as colorless crystals, yield: 261 mg (79%), m.p. 141 °C. IR (ATR): $\tilde{\nu}$ = 3296, 2931, 2865, 2848, 1465, 1383, 1037, 1027, 874 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 0.61 (m, 1 H), 0.63 (s, 3 H), 0.77 (t, J = 7.5 Hz, 3 H), 0.78 (m, 1 H), 0.81 (s, 3 H), 0.847 (d, J = 6.6 Hz, 3 H), 0.851 (d, J = 6.6 Hz, 3 H), 0.88 (d, J = 6.5 Hz, 3 H), 0.89 (m, 1 H), 0.91–1.15 (m, 10 H), 1.18–1.36 (m, 9 H), 1.41–1.59 (m, 4 H), 1.64–1.71 (m, 3 H), 1.77–1.83 (m, 2 H), 1.95 (dt, J = 12.5, 3.3 Hz, 1 H), 3.36 (dt, J = 4.9, 10.7 Hz, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 7.81 (CH_3), 12.06 (CH_3), 13.35 (CH_3), 18.65 (CH_3), 18.66 (CH_2), 21.18 (CH_2), 22.55 (CH_3), 22.81 (CH_3), 23.84 (CH_2), 23.90 (CH_2), 24.17 (CH_2), 28.00 (CH), 28.28 (CH_2), 31.25 (CH_2), 32.22 (CH_2), 34.90 (CH), 35.80 (CH), 35.95 (C), 36.17 (CH_2), 36.82 (CH_2), 39.50 (CH_2), 40.09 (CH_2), 42.52 (C), 43.28 (CH), 46.15 (CH), 54.76 (CH), 56.28 (CH), 56.54 (CH), 71.81 (CH) ppm. MS (80 °C): m/z (%) = 416 (100) [M^+], 401 (44), 383 (33), 276 (22), 262 (73), 261 (52), 245 (23), 244 (33), 243 (90), 193 (44). HRMS: m/z [M^+] calcd. for $C_{29}H_{52}O$: 416.4018; found 416.4009. $C_{29}H_{52}O$ (416.72): calcd. C 83.58, H 12.58; found C 83.77, H 12.72.

4α-Ethyl-5α-cholestan-3β-yl 4-Bromobenzoate (11): 4α-Ethyl-5α-cholestan-3β-ol (**10b**) (242 mg, 580 μmol) was added to a solution of *p*-bromobenzoyl chloride (160 mg, 730 μmol), triethylamine (80 mg, 109 μL, 790 μmol) and a catalytic amount of DMAP in THF (15 mL) at room temperature. The solution was stirred for 24 h and filtered through a pad of silica gel with diethyl ether. Evaporation of the solvent gave **11** as colorless crystals, yield: 304 mg (87%), m.p. 156–158 °C. IR (ATR): $\tilde{\nu}$ = 2958, 2927, 2866, 2843, 1712, 1591, 1463, 1384, 1271, 1115, 1104, 1012, 847, 756, 683 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 0.65 (s, 3 H), 0.67 (m, 1 H), 0.74 (t, J = 7.5 Hz, 3 H), 0.82 (m, 2 H), 0.85 (d, J = 6.6 Hz, 3 H), 0.86 (d, J = 6.6 Hz, 3 H), 0.88 (s, 3 H), 0.89 (d, J = 6.8 Hz, 3 H), 0.92–1.15 (m, 12 H), 1.22–1.36 (m, 7 H), 1.40–1.63 (m, 4 H), 1.69–1.83 (m, 4 H), 1.96 (m, 2 H), 4.86 (dt, J = 5.0, 11.1 Hz, 1 H), 7.56 (d, J = 8.6 Hz, 2 H), 7.89 (d, J = 8.6 Hz, 2 H) ppm. ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 7.86 (CH_3), 12.06 (CH_3), 13.32 (CH_3), 18.65 (CH_3), 19.12 (CH_2), 21.21 (CH_2), 22.56 (CH_3), 22.82 (CH_3), 23.86 (CH_2), 24.17 (2 CH_2), 27.32 (CH_2), 28.01 (CH), 28.28 (CH_2), 32.10 (CH_2), 34.94 (CH), 35.80 (CH), 35.88 (C), 36.16 (CH_2), 36.45 (CH_2), 39.51 (CH_2), 40.03 (CH_2), 40.32 (CH), 42.51 (C), 46.29 (CH), 54.55 (CH), 56.26 (CH), 56.46 (CH), 75.61 (CH), 127.73 (C), 129.79 (C), 131.08 (2 CH), 131.60 (2 CH), 165.45 (C=O) ppm. MS (150 °C): m/z (%) = 600 (5) [M^+], 398 (100), 384 (29), 383 (61), 369 (39), 357 (24), 355 (36), 258 (17), 244 (35), 243 (57). HRMS: m/z [M^+] calcd. for $C_{36}H_{55}BrO_2$: 598.3385; found 598.3395. $C_{36}H_{55}BrO_2$ (599.72): calcd. C 72.10, H 9.24; found C 72.15, H 9.28.

3-Trimethylsilyloxy-5α-cholest-3-ene (12): Lithium (40 mg, 5.7 mmol) was added to a solution of 4-cholesten-3-one (**8**) (1.00 g, 2.60 mmol) in anhydrous THF (20 mL) and ammonia (25 mL) at –78 °C. The solution was warmed to –35 °C, stirred for 2 h under a nitrogen atmosphere, and ammonia was evaporated by warming to room temperature. After addition of THF (10 mL), the reaction mixture was cooled to –10 °C, and triethylamine (1.05 g, 1.46 mL, 10.4 mmol) and chlorotrimethylsilane (1.13 g, 1.30 mL, 10.4 mmol) were added. The reaction mixture was stirred for 30 min, diluted by addition of ether (30 mL), washed with a saturated solution of sodium hydrogencarbonate, and then with brine. The organic layer was dried with sodium sulfate and the solvent was evaporated. Flash chromatography (hexane with 1% triethylamine) of the residue on neutral alumina provided the trimethylsilyl enol ether (**12**) as colorless crystals, yield: 653 mg (55%), m.p. 97–103 °C. IR (ATR): $\tilde{\nu}$ = 2928, 2868, 1660, 1466, 1443, 1375, 1250, 1203, 923, 888, 841, 759 cm^{-1}. ^1H NMR (500 MHz, [D_6]benzene): δ = 0.34 (s, 9 H), 0.77 (m, 1 H), 0.79 (s, 3 H), 0.97 (s, 3 H), 1.01–1.09 (m, 2 H), 1.040 (d, J = 6.6 Hz, 3 H), 1.043 (d, J = 6.6 Hz, 3 H), 1.13 (d, J = 6.5 Hz, 3 H), 1.15–1.62 (m, 17 H), 1.64–1.69 (m, 2 H), 1.77–1.81 (m, 2 H), 1.95–1.98 (m, 1 H), 2.08–2.13 (m, 2 H), 2.24–2.30 (m, 2 H), 4.81 (s, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, [D_6]benzene): δ = 1.00 (3 CH_3), 12.60 (CH_3), 12.93 (CH_3), 19.49 (CH_3), 22.32 (CH_2), 23.26 (CH_3), 23.51 (CH_3), 24.84 (CH_2), 25.00 (CH_2), 28.85 (CH_2), 28.89 (CH), 29.06 (CH_2), 29.16 (CH_2), 32.89 (CH_2), 35.59 (CH_2), 35.87 (C), 36.37 (CH), 36.72 (CH), 37.15 (CH_2), 40.42 (CH_2), 40.96 (CH_2), 43.51 (C), 46.00 (CH), 53.81 (CH), 57.16 (CH), 57.18 (CH), 108.58 (CH), 150.21 (C) ppm. MS (20 °C): m/z (%) = 458 (100) [M^+], 443 (16), 429 (16), 316 (10), 195 (10), 143 (68), 142 (41), 73 (14). HRMS: m/z [M^+] calcd. for $C_{30}H_{54}OSi$: 458.3944; found 458.3930. $C_{30}H_{54}OSi$ (458.83): calcd. C 78.53, H 11.86; found C 78.59, H 11.91.

4α-Fluoro-5α-cholestan-3-one (13): Selectfluor (155 mg, 437 μmol) was added to a suspension of the silyl enol ether **12** (200 mg, 437 μmol) in DMF and stirred for 15 min. A 1 M solution of TBAF in THF (437 μL, 437 μmol) was added, stirring was continued for 5 min and water was added. After 2 h the mixture was extracted three times with ether, the combined organic layers were dried with sodium sulfate and the solvent was evaporated. Purification of the residue by flash chromatography (petroleum ether/diethyl ether, 10:1) on silica gel afforded **13** as colorless crystals, yield: 90.8 mg (51%), m.p. 164–165 °C. IR (ATR): $\tilde{\nu}$ = 2933, 2866, 2852, 1735, 1467, 1444, 1382, 1101, 1065, 1040, 890, 592 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 0.66 (s, 3 H), 0.77 (m, 1 H), 0.849 (d, J = 6.6 Hz, 3 H), 0.853 (d, J = 6.6 Hz, 3 H), 0.89 (d, J = 6.5 Hz, 3 H), 0.95–1.17 (m, 8 H), 1.08 (s, 3 H), 1.20–1.43 (m, 9 H), 1.45–1.66 (m, 4 H), 1.75–1.86 (m, 2 H), 1.88–1.92 (m, 1 H), 1.96–2.05 (m, 2 H), 2.45 (m, 2 H), 4.72 (dd, J = 49.2, 12.3 Hz, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 12.04 (CH_3), 12.91 (CH_3), 18.64 (CH_3), 21.12 (CH_2), 22.54 (CH_3), 22.80 (CH_3), 23.65 (CH_2), 23.80 (CH_2), 24.17 (CH_2), 28.00 (CH), 28.21 (CH_2), 30.88 (CH_2), 34.97 (CH), 35.76 (CH), 36.10 (CH_2), 36.74 (CH_2), 37.56 (d, $^3J_{C,F}$ = 7.3 Hz, C), 38.74 (CH_2), 39.48 (CH_2), 39.71 (CH_2), 42.50 (C), 52.96 (d, $^2J_{C,F}$ = 15.9 Hz, CH), 53.89 (CH), 56.08 (CH), 56.19 (CH), 93.49 (d, $^1J_{C,F}$ = 189.3 Hz, CH), 205.70 (d, $^2J_{C,F}$ = 14.3 Hz, C=O) ppm. MS (20 °C): m/z (%) = 404 (69) [M^+], 389 (8), 250 (68), 249 (100), 235 (27). HRMS: m/z [M^+] calcd. for $C_{27}H_{45}FO$: 404.3454;

found 404.3475. $C_{27}H_{45}FO$ (404.64): calcd. C 80.14, H 11.21; found C 80.11, H 11.34.

4α-Fluoro-5α-cholestan-3α-ol (14a) and 4α-Fluoro-5α-cholestan-3β-ol (14b): A 1 M solution of lithium aluminum hydride in THF (134 μL, 134 μmol) was added to a solution of 4α-fluoro-5α-cholestan-3-one (**13**) (45.2 mg, 112 μmol) in anhydrous THF (10 mL) at room temperature. After stirring for 4 d at room temperature under an argon atmosphere, water and then 10% HCl were added. The aqueous layer was extracted with diethyl ether three times. The combined organic layers were washed with a saturated solution of sodium hydrogencarbonate and dried with sodium sulfate. Evaporation of the solvent and purification of the residue by flash chromatography (petroleum ether/*tert*-butyl methyl ether, 5:1) on silica gel provided **14a** as colorless crystals, yield: 18.4 mg (40%), m.p. 128 °C. IR (ATR): $\tilde{\nu}$ = 3600, 3587, 2928, 2867, 2849, 1467, 1378, 1234, 1063, 1021, 972, 949, 857 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 0.64 (s, 3 H), 0.78 (m, 1 H), 0.79 (s, 3 H), 0.849 (d, J = 6.6 Hz, 3 H), 0.854 (d, J = 6.6 Hz, 3 H), 0.89 (d, J = 6.6 Hz, 3 H), 0.95–1.15 (m, 9 H), 1.18–1.39 (m, 9 H), 1.44–1.63 (m, 6 H), 1.71–1.84 (m, 2 H), 1.93–1.97 (m, 2 H), 4.14 (m, 1 H), 4.34 (ddd, J = 47.5, 11.2, 3.1 Hz, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 12.05 (CH_3), 12.51 (CH_3), 18.65 (CH_3), 20.77 (CH_2), 22.16 (d, $^3J_{C,F}$ = 3.5 Hz, CH_2), 22.55 (CH_3), 22.81 (CH_3), 23.81 (CH_2), 24.13 (CH_2), 26.15 (d, $^3J_{C,F}$ = 6.1 Hz, CH_2), 28.00 (CH), 28.21 (CH_2), 31.04 (CH_2), 31.09 (CH_2), 35.05 (CH), 35.78 (CH), 36.14 (CH_2), 37.70 (d, $^3J_{C,F}$ = 8.4 Hz, C), 39.50 (CH_2), 39.89 (CH_2), 42.46 (C), 43.49 (d, $^2J_{C,F}$ = 15.7 Hz, CH), 54.08 (CH), 56.17 (CH), 56.36 (CH), 67.48 (d, $^2J_{C,F}$ = 18.0 Hz, CH), 94.78 (d, $J_{C,F}$ = 172.0 Hz, CH) ppm. MS (20 °C): m/z (%) = 406 (76) [M^+], 252 (63), 251 (100), 233 (20), 231 (23), 95 (35), 93 (21). HRMS: m/z [M^+] calcd. for $C_{27}H_{47}FO$: 406.3611; found 406.3624.

14b was obtained from the more polar fraction as colorless crystals, yield: 21.4 mg (52%), m.p. 99–105 °C. IR (ATR): $\tilde{\nu}$ = 3566, 3337, 2932, 2866, 2849, 1467, 1382, 1163, 1145, 1081, 1059, 1024, 977, 929, 890, 613, 568 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 0.64 (s, 3 H), 0.70 (m, 1 H), 0.80 (m, 1 H), 0.82 (s, 3 H), 0.847 (d, J = 6.6 Hz, 3 H), 0.852 (d, J = 6.6 Hz, 3 H), 0.88 (d, J = 6.5 Hz, 3 H), 0.93–1.15 (m, 9 H), 1.18–1.37 (m, 8 H), 1.42–1.59 (m, 4 H), 1.67–1.77 (m, 2 H), 1.78–1.84 (m, 2 H), 1.86–1.91 (m, 1 H), 1.96 (dt, J = 12.6, 3.3 Hz, 1 H), 2.31 (br. s, 1 H), 3.64 (m, 1 H), 4.16 (ddd, J = 52.6, 10.3, 8.6 Hz, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 12.05 (CH_3), 13.37 (CH_3), 18.65 (CH_3), 20.89 (CH_2), 22.34 (d, $^3J_{C,F}$ = 3.6 Hz, CH_2), 22.55 (CH_3), 22.80 (CH_3), 23.81 (CH_2), 24.16 (CH_2), 27.48 (d, $^3J_{C,F}$ = 7.8 Hz, CH_2), 28.00 (CH), 28.22 (CH_2), 31.10 (CH_2), 35.01 (CH), 35.77 (CH), 35.83 (CH_2), 36.13 (CH_2), 37.76 (d, $^3J_{C,F}$ = 7.8 Hz, C), 39.49 (CH_2), 39.86 (CH_2), 42.50 (C), 49.09 (d, $^2J_{C,F}$ = 15.0 Hz, CH), 54.27 (CH), 56.23 (CH), 56.31 (CH), 74.23 (d, $^2J_{C,F}$ = 18.6 Hz, CH), 97.99 (d, $^1J_{C,F}$ = 170.7 Hz, CH) ppm. MS (100 °C): m/z (%) = 406 (48) [M^+], 391 (17), 252 (50), 251 (100). HRMS: m/z [M^+] calcd. for $C_{27}H_{47}FO$: 406.3611; found 406.3643. $C_{27}H_{47}FO$ (406.66): calcd. C 79.74, H 11.65; found C 79.89, H 11.47.

3-Keto-5α-cholestan-4α-ol (15): MCPBA (152 mg, 873 μmol) was added to a solution of the trimethylsilyl enol ether **12** (200 mg, 437 μmol) in dichloromethane (10 mL). After stirring of the reaction mixture for 24 h at room temperature under an argon atmosphere, aqueous HCl (10%, 7 mL) was added. The mixture was stirred for 1 h and then the layers were separated and the aqueous layer was washed with dichloromethane two times. The combined organic layers were dried with potassium carbonate and the solvent was evaporated. Purification of the residue by flash chromatography (petroleum ether/diethyl ether, 1:1) on silica gel afforded **15** as colorless crystals, yield: 60.7 mg (34%), m.p. 149–152 °C. IR (ATR): $\tilde{\nu}$ = 3333, 2932, 2865, 1718, 1447, 1296, 1262, 1261, 1191, 1175, 1118, 1066, 985, 970, 798, 739, 710 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 0.65 (s, 3 H), 0.71 (m, 1 H), 0.82 (m, 1 H), 0.836 (d, J = 6.6 Hz, 3 H), 0.841 (d, J = 6.6 Hz, 3 H), 0.88 (d, J = 6.5 Hz, 3 H), 0.93–1.16 (m, 9 H), 1.08 (s, 3 H), 1.19–1.39 (m, 8 H), 1.43–1.57 (m, 3 H), 1.73–1.82 (m, 2 H), 1.96 (m, 2 H), 2.05 (ddd, J = 13.2, 6.1, 2.5 Hz, 1 H), 2.48 (m, 2 H), 3.46 (br. s, 1 H), 3.93 (d, J = 11.7 Hz, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 12.01 (CH_3), 12.94 (CH_3), 18.62 (CH_3), 21.10 (CH_2), 22.52 (CH_3), 22.78 (CH_3), 23.77 (CH_2), 24.16 (CH_2), 24.34 (CH_2), 27.96 (CH), 28.20 (CH_2), 31.35 (CH_2), 35.01 (CH), 35.73 (CH), 35.73 (CH_2), 36.08 (CH_2), 36.90 (C), 39.36 (CH_2), 39.45 (CH_2), 39.77 (CH_2), 42.47 (C), 53.89 (CH), 55.35 (CH), 56.18 (2 CH), 75.28 (CH), 211.73 (C=O) ppm. MS (150 °C): m/z (%) = 402 (94) [M^+], 400 (6), 387 (27), 249 (20), 248 (75), 247 (100), 233 (26), 195 (21), 95 (26). HRMS: m/z [M^+] calcd. for $C_{27}H_{46}O_2$: 402.3498; found 402.3505.

5α-Cholestane-3α,4α-diol (16a) and 5α-Cholestane-3β,4α-diol (16b): Sodium borohydride (12 mg, 316 μmol) was added to a solution of 3-keto-5α-cholestan-4α-ol (**15**) (68 mg, 169 mmol) in methanol (10 mL) at 0 °C and the mixture was stirred for 12 h. Water (10 mL) was added and the mixture was extracted with dichloromethane three times. The combined organic layers were washed with brine, dried with sodium sulfate and the solvent was evaporated. Purification of the residue by flash chromatography (petroleum ether/diethyl ether, 1:1) on silica gel afforded **16a** as colorless crystals, yield: 18 mg (26%), m.p. 211–214 °C. IR (ATR): $\tilde{\nu}$ = 3323, 2930, 2865, 1467, 1455, 1376, 1067, 1035, 1006, 997, 951, 906, 850 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 0.63 (s, 3 H), 0.74 (m, 1 H), 0.79 (s, 3 H), 0.846 (d, J = 6.6 Hz, 3 H), 0.850 (d, J = 6.6 Hz, 3 H), 0.88 (d, J = 6.5 Hz, 3 H), 0.93–1.15 (m, 9 H), 1.16–1.43 (m, 9 H), 1.44–1.60 (m, 4 H), 1.64–1.84 (m, 5 H), 1.95 (dt, J = 12.5, 3.3 Hz, 1 H), 2.09 (br. s, 1 H), 3.45 (m, 1 H), 4.11 (m, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 12.05 (CH_3), 12.59 (CH_3), 18.64 (CH_3), 20.80 (CH_2), 22.55 (CH_3), 22.71 (CH_2), 22.81 (CH_3), 23.81 (CH_2), 24.13 (CH_2), 26.93 (CH_2), 28.00 (CH), 28.23 (CH_2), 31.36 (CH_2), 31.54 (CH_2), 35.08 (CH), 35.78 (CH), 36.14 (CH_2), 37.09 (C), 39.49 (CH_2), 39.95 (CH_2), 42.45 (C), 45.62 (CH), 54.21 (CH), 56.18 (CH), 56.45 (CH), 69.36 (CH), 71.83 (CH) ppm. MS (150 °C): m/z (%) = 404 (100) [M^+], 389 (12), 371 (25), 353 (6), 264 (14), 250 (51), 249 (59), 231 (41), 215 (20). HRMS: m/z [M^+] calcd. for $C_{27}H_{48}O_2$: 404.3654; found 404.3645.

16b was obtained from the more polar fraction as colorless crystals, yield: 30 mg (44%), m.p. 233 °C. IR (ATR): $\tilde{\nu}$ = 3309, 2928, 2866, 1455, 1374, 1260, 1138, 1064, 1041, 1005, 932, 893 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 0.63 (s, 3 H), 0.66 (m, 1 H), 0.80 (m, 1 H), 0.82 (s, 3 H), 0.846 (d, J = 6.6 Hz, 3 H), 0.851 (d, J = 6.6 Hz, 3 H), 0.88 (d, J = 6.5 Hz, 3 H), 0.91–1.17 (m, 9 H), 1.19–1.40 (m, 8 H), 1.42–1.60 (m, 4 H), 1.68–1.85 (m, 5 H), 1.95 (dt, J = 12.7, 3.2 Hz, 1 H), 2.00 (br. s, 1 H), 2.27 (br. s, 1 H), 3.27 (m, 1 H), 3.34 (m, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 12.05 (CH_3), 13.59 (CH_3), 18.65 (CH_3), 20.93 (CH_2), 22.55 (CH_3), 22.63 (CH_2), 22.81 (CH_3), 23.81 (CH_2), 24.18 (CH_2), 28.00 (CH), 28.25 (CH_2), 28.34 (CH_2), 31.49 (CH_2), 34.98 (CH), 35.78 (CH), 36.14 (CH_2), 36.20 (CH_2), 37.27 (C), 39.49 (CH_2), 39.92 (CH_2), 42.51 (C), 50.74 (CH), 54.40 (CH), 56.23 (CH), 56.37 (CH), 75.62 (CH), 76.49 (CH) ppm. MS (150 °C): m/z (%) = 404 (94) [M^+], 389 (28), 371 (5), 353 (3), 264 (21), 250 (56), 249 (100), 232 (26). HRMS: m/z [M^+] calcd. for $C_{27}H_{48}O_2$: 404.3654; found 404.3640.

4α-Methoxycarbonyl-5α-cholestan-3-one (17): A 1.47 M solution of butyllithium in hexane (755 μL, 1.11 mmol) was added to a solu-

tion of the trimethylsilyl enol ether (**12**) (500 mg, 1.09 mmol) in diethyl ether (20 mL). After stirring of the reaction mixture for 30 min at room temperature under an argon atmosphere and cooling to –78 °C, methyl cyanoformate (104 μL, 11 mg, 1.31 mmol) was added. The mixture was warmed to room temperature and stirred for 24 h. Water (10 mL) and diethyl ether (5 mL) were added and stirring was continued for further 10 min. After addition of water (15 mL) the phases were separated and the aqueous phase was extracted three times with ether. The combined organic layers were washed with brine, dried with sodium sulfate, and the solvent was evaporated. Purification of the residue by flash chromatography (petroleum ether/diethyl ether, 10:1) on silica gel afforded **17** as colorless crystals, yield: 350 mg (72%), m.p. 159–164 °C. IR (ATR): $\tilde{\nu}$ = 2932, 2861, 1741, 1711, 1464, 1440, 1373, 1266, 1175, 1025, 737 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.66 (s, 3 H), 0.78 (m, 1 H), 0.84 (d, J = 6.6 Hz, 3 H), 0.85 (d, J = 6.6 Hz, 3 H), 0.89 (d, J = 6.5 Hz, 3 H), 0.91–1.18 (m, 10 H), 1.03 (s, 3 H), 1.19–1.45 (m, 7 H), 1.47–1.57 (m, 4 H), 1.67 (dq, J = 13.2, 3.4 Hz, 1 H), 1.81 (m, 1 H), 1.92 (m, 1 H), 1.99 (m, 2 H), 2.40 (m, 2 H), 3.25 (d, J = 12.9 Hz, 1 H), 3.73 (s, 3 H) ppm. ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 12.05 (CH_3), 12.40 (CH_3), 18.64 (CH_3), 21.32 (CH_2), 22.55 (CH_3), 22.81 (CH_3), 23.80 (CH_2), 24.14 (CH_2), 26.90 (CH_2), 28.00 (CH), 28.21 (CH_2), 31.34 (CH_2), 35.11 (CH), 35.49 (C), 35.76 (CH), 36.11 (CH_2), 37.69 (CH_2), 37.85 (CH_2), 39.48 (CH_2), 39.79 (CH_2), 42.54 (C), 48.71 (CH), 51.92 (CH_3), 53.69 (CH), 56.13 (CH), 56.17 (CH), 60.04 (CH), 170.60 (C=O), 206.27 (C=O) ppm. MS (100 °C): m/z (%) = 444 (87) [M$^+$], 426 (34), 413 (25), 412 (35), 369 (27), 316 (26), 315 (46), 314 (27), 290 (31), 289 (78), 258 (20), 257 (34), 231 (43), 229 (62), 149 (53), 129 (100). HRMS: m/z [M$^+$] calcd. for $C_{29}H_{48}O_3$: 444.3603; found 444.3621.

4α-Methoxycarbonyl-5α-cholestan-3α-ol (18a) and 4α-Methoxycarbonyl-5α-cholestan-3β-ol (18b): Sodium borohydride (27 mg, 720 μmol) was added to a solution of the β-keto ester (**17**) (320 mg, 720 μmol) in methanol (50 mL)/dichloromethane (15 mL) and the mixture was stirred for 6 h. Water was added and the precipitate was dissolved by addition of hydrochloric acid. The phases were separated and the aqueous phase was extracted three times with ether. After washing with brine, the combined organic layers were dried with magnesium sulfate and the solvent was evaporated. Purification of the residue by flash chromatography (petroleum ether/diethyl ether, 1:1) on silica gel afforded **18a** as colorless crystals, yield: 90 mg (28%), m.p. 78 °C. IR (ATR): $\tilde{\nu}$ = 3514, 2929, 2866, 1718, 1442, 1382, 1197, 1170, 1112, 1060, 1005, 734, 590 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.63 (s, 3 H), 0.75–0.91 (m, 2 H), 0.81 (s, 3 H), 0.84 (d, J = 6.6 Hz, 3 H), 0.85 (d, J = 6.6 Hz, 3 H), 0.88 (d, J = 6.6 Hz, 3 H), 0.96–1.03 (m, 3 H), 1.05–1.13 (m, 6 H), 1.15–1.44 (m, 7 H), 1.46–1.58 (m, 6 H), 1.64 (dq, J = 13.1, 3.1 Hz, 1 H), 1.73–1.79 (m, 2 H), 1.86 (dt, J = 3.1, 12.3 Hz, 1 H), 1.95 (dt, J = 12.5, 3.2 Hz, 1 H), 2.46 (dd, J = 12.3, 2.0 Hz, 1 H), 3.54 (br. s, 1 H), 3.69 (s, 3 H), 4.03 (m, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 12.05 (CH_3), 12.06 (CH_3), 18.63 (CH_3), 20.80 (CH_2), 22.55 (CH_3), 22.82 (CH_3), 23.80 (CH_2), 24.10 (CH_2), 25.65 (CH_2), 27.50 (CH_2), 28.01 (CH), 28.20 (CH_2), 31.50 (CH_2), 31.62 (CH_2), 35.10 (CH), 35.78 (CH), 36.11 (C), 36.14 (CH_2), 39.50 (CH_2), 39.91 (CH_2), 41.24 (CH), 42.46 (C), 48.20 (CH), 51.54 (CH_3), 54.06 (CH), 56.13 (CH), 56.35 (CH), 66.27 (CH), 177.39 (C=O) ppm. MS (180 °C): m/z (%) = 446 (100) [M$^+$], 431 (13), 428 (16), 414 (16), 413 (45), 292 (45), 291 (42), 275 (19), 274 (28), 273 (80). HRMS: m/z [M$^+$] calcd. for $C_{29}H_{50}O_3$: 446.3760; found 446.3769.

18b was obtained from the more polar fraction as colorless crystals, yield: 202 mg (63%), m.p. 171 °C. IR (ATR): $\tilde{\nu}$ = 3485, 2924, 2862, 2849, 1717, 1439, 1282, 1253, 1073, 1027, 734, 721, 569 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.63 (s, 3 H), 0.65 (m, 1 H), 0.80–0.88 (m, 1 H), 0.82 (s, 3 H), 0.84 (d, J = 6.6 Hz, 3 H), 0.85 (d, J = 6.6 Hz, 3 H), 0.88 (d, J = 6.5 Hz, 3 H), 0.90–1.18 (m, 10 H), 1.19–1.36 (m, 7 H), 1.44–1.53 (m, 4 H), 1.63 (dq, J = 13.1, 3.1 Hz, 1 H), 1.71–1.85 (m, 4 H), 1.95 (dt, J = 12.6, 3.3 Hz, 1 H), 2.32 (t, J = 10.8 Hz, 1 H), 3.69 (s, 3 H), 3.78 (dt, J = 4.6, 10.7 Hz, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 12.03 (CH_3), 12.87 (CH_3), 18.83 (CH_3), 21.19 (CH_2), 22.54 (CH_3), 22.80 (CH_3), 23.79 (CH_2), 24.12 (CH_2), 25.73 (CH_2), 27.99 (CH), 28.20 (CH_2), 30.30 (CH_2), 31.59 (CH_2), 35.02 (CH), 35.60 (C), 35.75 (CH), 36.12 (CH_2), 36.41 (CH_2), 39.48 (CH_2), 39.90 (CH_2), 42.49 (C), 47.25 (CH), 51.47 (CH_3), 53.65 (CH), 54.12 (CH), 56.17 (CH), 56.28 (CH), 72.84 (CH), 175.85 (C=O) ppm. MS (180 °C): m/z (%) = 446 (100) [M$^+$], 431 (19), 428 (24), 414 (11), 413 (21), 292 (40), 291 (58), 275 (24), 274 (37), 273 (61). HRMS: m/z [M$^+$] calcd. for $C_{29}H_{50}O_3$: 446.3760; found 446.3774.

4α-Carboxy-5α-cholestan-3β-ol (19): The ester **18b** (50 mg, 112 μmol) was added to a solution of potassium hydroxide in methanol (20%, 12 mL), refluxed for 20 h, and cooled to room temperature. Water (70 mL) was added and the solution was acidified by addition of hydrochloric acid. The mixture was extracted three times with ethyl acetate, the combined organic layers were washed with water and dried with magnesium sulfate. After evaporation of the solvent **19** was isolated as colorless crystals, yield 45 mg (93%), m.p. 276 °C. IR (ATR): $\tilde{\nu}$ = 3315, 2930, 2868, 2849, 1699, 1682, 1466, 1438, 1376, 1365, 1271, 1234, 1134, 1068, 700 cm^{-1}. ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ = 0.62 (s, 3 H), 0.63 (m, 1 H), 0.74 (m, 1 H), 0.76 (s, 3 H), 0.836 (d, J = 6.5 Hz, 3 H), 0.840 (d, J = 6.5 Hz, 3 H), 0.87 (d, J = 6.4 Hz, 3 H), 0.90–1.01 (m, 4 H), 1.02–1.38 (m, 15 H), 1.45–1.55 (m, 3 H), 1.61–1.66 (m, 3 H), 1.76 (m, 1 H), 1.91 (d, J = 12.3 Hz, 1 H), 2.04 (t, J = 10.0 Hz, 1 H), 3.45 (m, 1 H), 4.67 (br. s, 1 H), 11.87 (br. s, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, [D$_6$]DMSO): δ = 11.86 (CH_3), 12.66 (CH_3), 18.50 (CH_3), 20.77 (CH_2), 22.40 (CH_3), 22.67 (CH_3), 23.17 (CH_2), 23.75 (CH_2), 25.30 (CH_2), 27.39 (CH), 27.80 (CH_2), 30.46 (CH_2), 31.39 (CH_2), 34.62 (CH), 34.98 (C), 35.18 (CH), 35.62 (CH_2), 38.18 (CH_2), 38.93 (CH_2), 39.45 (CH_2), 42.07 (C), 46.73 (CH), 53.39 (CH), 53.63 (CH), 55.66 (CH), 55.82 (CH), 71.40 (CH), 176.08 (C=O) ppm. MS (200 °C): m/z (%) = 432 (100) [M$^+$], 417 (20), 414 (12), 399 (13), 278 (43), 277 (65), 260 (32), 259 (50). HRMS: m/z [M$^+$] calcd. for $C_{28}H_{48}O_3$: 432.3603; found 432.3621.

3β-(*tert*-Butyldimethylsilyloxy)cholest-5-en-7-one (21): TBSCl (471 mg, 3.12 mmol) and DMAP (381 mg, 3.12 mmol) were added to a solution of 7-ketocholesterol (**20**) (1.00 g, 2.50 mmol) in dichloromethane (10 mL). The mixture was stirred for 24 h at room temperature and subjected directly to flash chromatography (petroleum ether/diethyl ether, 10:1) on silica gel to afford **21** as colorless crystals, yield: 1.13 g (88%), m.p. 212 °C. IR (ATR): $\tilde{\nu}$ = 2952, 2935, 2859, 1665, 1626, 1471, 1375, 1253, 1191, 1093, 834, 805, 773 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.05 (s, 6 H), 0.66 (s, 3 H), 0.847 (d, J = 6.6 Hz, 3 H), 0.852 (d, J = 6.6 Hz, 3 H), 0.88 (s, 9 H), 0.91 (d, J = 6.5 Hz, 3 H), 0.99–1.37 (m, 13 H), 1.17 (s, 3 H), 1.45–1.64 (m, 5 H), 1.81 (m, 1 H), 1.89 (m, 2 H), 2.01 (dt, J = 12.7, 3.3 Hz, 1 H), 2.22 (dd, J = 12.2, 10.9 Hz, 1 H), 2.34–2.43 (m, 3 H), 3.59 (m, 1 H), 5.65 (d, J = 1.3 Hz, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = –4.70 (CH_3), –4.67 (CH_3), 11.94 (CH_3), 17.28 (CH_3), 18.14 (C), 18.86 (CH_3), 21.18 (CH_2), 22.54 (CH_3), 22.79 (CH_3), 23.79 (CH_2), 25.82 (3 CH_3), 26.30 (CH_2), 27.98 (CH), 28.54 (CH_2), 31.72 (CH_2), 35.69 (CH), 36.16 (CH_2), 36.39 (CH_2), 38.34 (C), 38.70 (CH_2), 39.45 (CH_2), 42.52 (CH_2), 43.05 (C), 45.39 (CH), 49.91 (CH), 49.97 (CH), 54.75 (CH), 71.31 (CH), 125.79 (CH), 165.85 (C), 202.47 (C=O) ppm. MS (150 °C): m/z (%)

= 514 (0.5) [M^+], 499 (3), 457 (100), 365 (2), 75 (12). HRMS: *m/z* [$(M-tBu)^+$] calcd. for $C_{29}H_{49}O_2Si^+$: 457.3496; found 457.3503. $C_{33}H_{58}O_2Si$ (514.90): calcd. C 76.98, H 11.35; found C 76.91, H 11.36.

3β-(*tert*-Butyldimethylsilyloxy)-5α-cholestan-7-one (22): Lithium (15 mg, 2.13 mmol) was added to a solution of the enone **21** (500 mg, 969 μmol) in anhydrous THF (20 mL) and ammonia (25 mL) at –78 °C. The solution was warmed to –35 °C and stirred for 3 h under a nitrogen atmosphere. Methanol (20 mL) and water (5 mL) were added and the ammonia was allowed to evaporate. Diethyl ether (100 mL) was added, the mixture was washed with sodium hydrogencarbonate solution and brine, dried with sodium sulfate and the solvent was evaporated. Purification of the residue by flash chromatography (petroleum ether/diethyl ether, 40:1) on silica gel afforded **22** as colorless crystals, yield: 476 mg (95%), m.p. 183 °C. IR (ATR): $\tilde{\nu}$ = 2929, 2858, 1708, 1470, 1375, 1251, 1097, 1051, 1005, 943, 871, 834, 774 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 0.03 (s, 6 H), 0.64 (s, 3 H), 0.85 (d, *J* = 6.6 Hz, 3 H), 0.86 (d, *J* = 6.7 Hz, 3 H), 0.87 (s, 9 H), 0.90 (d, *J* = 6.5 Hz, 3 H), 0.93–1.15 (m, 9 H), 1.07 (s, 3 H), 1.19–1.57 (m, 12 H), 1.72 (m, 2 H), 1.89 (m, 1 H), 1.98 (m, 2 H), 2.17 (m, 1 H), 2.34 (t, *J* = 11.4 Hz, 2 H), 3.54 (m, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = –4.66 (2 CH_3), 11.86 (CH_3), 12.03 (CH_3), 18.20 (C), 18.77 (CH_3), 21.84 (CH_2), 22.54 (CH_3), 22.79 (CH_3), 23.72 (CH_2), 24.94 (CH_2), 25.87 (3 CH_3), 27.97 (CH), 28.39 (CH_2), 31.52 (CH_2), 35.62 (CH), 36.01 (C), 36.12 (CH_2), 36.21 (CH_2), 38.44 (CH_2), 38.76 (CH_2), 39.45 (CH_2), 42.46 (C), 46.21 (CH_2), 47.13 (CH), 48.84 (CH), 50.01 (CH), 54.99 (CH), 55.46 (CH), 71.51 (CH), 212.45 (C=O) ppm. MS (100 °C): *m/z* (%) = 501 (2), 459 (100) [$(M-tBu)^+$], 457 (11), 75 (13), 57 (4). HRMS: *m/z* [$(M-tBu)^+$] calcd. for $C_{29}H_{51}O_2Si^+$: 459.3653; found 459.3685. $C_{33}H_{60}O_2Si$ (516.91): calcd. C 76.68, H 11.70; found C 76.77, H 11.74.

3β-(*tert*-Butyldimethylsilyloxy)-5α-cholestan-7α-ol (23a) and 3β-(*tert*-Butyldimethylsilyloxy)-5α-cholestan-7β-ol (23b): Lithium (tri-*tert*-butoxy)aluminum hydride (51 mg, 200 μmol) was added to a solution of 3β-(*tert*-butyldimethylsilyloxy)-5α-cholestan-7-one (**22**) (100 mg, 194 μmol) in THF (20 mL) at –78 °C. The mixture was stirred for 24 h and warmed to room temperature. After addition of diethyl ether (50 mL) and water (10 mL) the aqueous phase was acidified with aqueous HCl (10%), the organic layer was separated, washed with sodium hydrogen carbonate solution and brine, and the solvent was evaporated. Purification of the residue by flash chromatography (petroleum ether/diethyl ether, 10:1) on silica gel afforded **23a** as colorless crystals, yield: 27 mg (27%), m.p. 174–176 °C. IR (ATR): $\tilde{\nu}$ = 3467, 2929, 2857, 1463, 1375, 1251, 1100, 1075, 947, 869, 834, 772 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 0.03 (s, 6 H), 0.64 (s, 3 H), 0.78 (s, 3 H), 0.846 (d, *J* = 6.7 Hz, 3 H), 0.851 (d, *J* = 6.7 Hz, 3 H), 0.86 (s, 9 H), 0.89 (d, *J* = 6.5 Hz, 3 H), 0.99 (m, 2 H), 1.06–1.17 (m, 7 H), 1.21–1.68 (m, 18 H), 1.85 (m, 1 H), 1.93 (dt, *J* = 12.6, 3.2 Hz, 1 H), 3.57 (m, 1 H), 3.81 (m, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = –4.58 (2 CH_3), 11.27 (CH_3), 11.81 (CH_3), 18.25 (C), 18.63 (CH_3), 20.96 (CH_2), 22.55 (CH_3), 22.80 (CH_3), 23.65 (CH_2), 23.71 (CH_2), 25.94 (3 CH_3), 27.99 (CH), 28.19 (CH_2), 31.86 (CH_2), 35.58 (C), 35.75 (CH), 36.12 (CH_2), 36.29 (CH_2), 36.91 (CH_2), 37.21 (CH), 38.18 (CH_2), 39.49 (CH_2), 39.52 (CH_2), 39.54 (CH), 42.65 (C), 45.93 (CH), 50.58 (CH), 56.08 (CH), 68.12 (CH), 71.96 (CH) ppm. MS (150 °C): *m/z* (%) = 461 (100) [$(M-tBu)^+$], 443 (2), 299 (23), 271 (24), 269 (39), 163 (44), 75 (9). HRMS: *m/z* [$(M-tBu)^+$] calcd. for $C_{29}H_{53}O_2Si^+$: 461.3809; found 461.3825. $C_{33}H_{62}O_2Si$ (518.93): calcd. C 76.38, H 12.04; found C 76.42, H 12.32.

23b was obtained from the more polar fraction as colorless crystals, yield: 70 mg (70%), m.p. 120–121 °C. IR (ATR): $\tilde{\nu}$ = 3404, 2929, 2855, 1464, 1383, 1250, 1100, 1072, 943, 869, 835, 774 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 0.03 (s, 6 H), 0.64 (m, 1 H), 0.66 (s, 3 H), 0.81 (s, 3 H), 0.846 (d, *J* = 6.6 Hz, 3 H), 0.851 (d, *J* = 6.6 Hz, 3 H), 0.87 (s, 9 H), 0.90 (d, *J* = 6.5 Hz, 3 H), 0.90 (m, 1 H), 0.97–1.17 (m, 8 H), 1.21–1.57 (m, 14 H), 1.61 (br. s, 1 H), 1.67 (m, 2 H), 1.76–1.86 (m, 2 H), 1.97 (dt, *J* = 12.7, 3.4 Hz, 1 H), 3.33 (dt, *J* = 5.3, 9.5 Hz, 1 H), 3.53 (m, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = –4.57 (2 CH_3), 12.15 (CH_3), 12.48 (CH_3), 18.25 (C), 18.78 (CH_3), 21.42 (CH_2), 22.55 (CH_3), 22.81 (CH_3), 23.82 (CH_2), 25.93 (3 CH_3), 26.91 (CH_2), 28.01 (CH), 28.73 (CH_2), 31.87 (CH_2), 34.95 (C), 35.67 (CH), 36.19 (CH_2), 37.06 (CH_2), 38.11 (CH_2), 38.19 (CH), 39.49 (CH_2), 40.01 (CH_2), 42.18 (CH_2), 43.44 (CH), 43.60 (C), 52.57 (CH), 55.21 (CH), 55.74 (CH), 71.92 (CH), 75.25 (CH) ppm. MS (150 °C): *m/z* (%) = 518 (0.1) [M^+], 461 (100) [$(M-tBu)^+$], 443 (2), 386 (14), 368 (6), 353 (5), 75 (11). HRMS: *m/z* [$(M-tBu)^+$] calcd. for $C_{29}H_{53}O_2Si^+$: 461.3809; found 461.3808. $C_{33}H_{62}O_2Si$ (518.93): calcd. C 76.38, H 12.04; found C 76.07, H 12.27.

3β-(*tert*-Butyldimethylsilyloxy)-7α-fluoro-5α-cholestane (24a) and 3β-(*tert*-Butyldimethylsilyloxy)-7β-fluoro-5α-cholestane (24b): A solution of the alcohol **23b** (186 mg, 359 μmol) in dichloromethane (3 mL) was added dropwise to a solution of DAST (58 mg, 47 μL, 359 μmol) in dichloromethane at –78 °C. The mixture was stirred for 40 min and water was added (5 mL). After warming to room temperature dichloromethane (20 mL) and water (10 mL) were added and the phases were separated. The aqueous phase was extracted with dichloromethane and the combined organic layers were washed with water and dried with magnesium sulfate. After evaporation of the solvent the residue was purified by flash chromatography (petroleum ether/diethyl ether, 40:1) on silica gel. **24a** and **24b** were isolated as a crystalline, colorless mixture of diastereoisomers (**24a**/**24b**, 2:1), yield: 118 mg (63%). IR (ATR): $\tilde{\nu}$ = 2951, 2928, 2857, 1471, 1376, 1251, 1098, 1075, 1006, 946, 871, 834, 772 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 0.03 (s, 6 H), 0.63 (s) and 0.66 (s, Σ 3 H), 0.78 (s) and 0.83 (s, Σ 3 H), 0.848 (d, *J* = 6.6 Hz, 3 H), 0.853 (d, *J* = 6.6 Hz, 3 H), 0.87 (s, 9 H), 0.89 (d, *J* = 6.5 Hz, 3 H), 0.91–1.17 (m, 9 H), 1.21–1.59 (m, 14 H), 1.60–1.73 (m, 4 H), 1.85 (m, 1 H), 1.93 (dt, *J* = 12.6, 3.3 Hz) and 1.98 (dt, *J* = 12.8, 3.4 Hz, Σ 1 H), 3.55 (m, 1 H), 4.16 (ddt, *J* = 49.3, 5.5, 9.7 Hz) and 4.61 (br. d, *J* = 49.2 Hz, Σ 1 H) ppm. MS (100 °C): *m/z* (%) = 463 (100) [$(M-tBu)^+$], 443 (5), 367 (1), 85 (3), 75 (14), 57 (7). HRMS: *m/z* [$(M-tBu)^+$] calcd. for $C_{29}H_{52}FOSi^+$: 463.3766; found 463.3752.

7α-Fluoro-5α-cholestan-3β-ol (25a) and 7β-Fluoro-5α-cholestan-3β-ol (25b): A mixture of 3β-(*tert*-butyldimethylsilyloxy)-7α-fluoro-5α-cholestane (**24a**) and 3β-(*tert*-butyldimethylsilyloxy)-7β-fluoro-5α-cholestane (**24b**) (86 mg, 165 μmol), water (6 μL, 333 μmmol), THF (6 mL) and a 1 M solution of TBAF in THF (248 μL, 248 μmol) was refluxed for 6 h. After cooling to room temperature, a saturated solution of ammonium chloride in water was added and the mixture was extracted three times with diethyl ether. The combined organic layers were washed with brine, dried with sodium sulfate and the solvent was evaporated. Purification of the residue by flash chromatography (petroleum ether/diethyl ether, 1:1) on silica gel afforded **25a** and **25b** as a crystalline, colorless mixture of diastereoisomers (**25a**/**25b**, 2:1), yield: 66 mg (99%). IR (ATR): $\tilde{\nu}$ = 3336, 2929, 2866, 1467, 1375, 1261, 1168, 1130, 1093, 1007, 989, 941, 885, 811, 740 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 0.63 (s) and 0.66 (s, Σ 3 H), 0.78 (s) and 0.84 (s, Σ 3 H), 0.847 (d, *J* = 6.6 Hz, 3 H), 0.851 (d, *J* = 6.6 Hz, 3 H), 0.89 (d, *J* = 6.5 Hz, 3 H), 0.94–1.19 (m, 9 H), 1.21–1.65 (m, 14 H), 1.66–1.72 (m, 3 H), 1.78–1.90 (m, 2 H), 1.94 (dt, *J* = 12.7, 3.3 Hz) and 1.98 (dt, *J* = 12.8, 3.4 Hz, Σ 1 H), 3.61 (m, 1 H), 4.17 (ddt, *J* = 49.2, 5.5, 9.7 Hz) and

4.61 (br. d, J = 49.2 Hz, Σ 1 H) ppm. MS (100 °C): m/z (%) = 406 (100) [M$^+$], 386 (21), 273 (11), 252 (29), 233 (26), 232 (29). HRMS: m/z [M$^+$] calcd. for $C_{27}H_{47}FO$: 406.3611; found 406.3623.

5α-Cholestane-3β,7α-diol (26a): A mixture of 3β-(*tert*-butyldimethylsilyloxy)-5α-cholestan-7α-ol (**23a**) (44 mg, 85 μmol), THF (12 mL) and a 1 M solution of TBAF in THF (130 μL, 130 μmol) was refluxed for 24 h. After cooling to room temperature, a saturated solution of ammonium chloride in water was added and the mixture was extracted with diethyl ether three times. The combined organic layers were washed with brine, dried with magnesium sulfate and the solvent was evaporated. Purification of the residue by flash chromatography (petroleum ether/diethyl ether, 1:10) on silica gel afforded **26a** as colorless crystals, yield: 28.6 mg (83%), m.p. 156 °C. IR (ATR): $\tilde{\nu}$ = 3348, 2928, 2866, 1467, 1375, 1030, 942, 732 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.64 (s, 3 H), 0.79 (s, 3 H), 0.84 (d, J = 6.6 Hz, 3 H), 0.85 (d, J = 6.6 Hz, 3 H), 0.89 (d, J = 6.5 Hz, 3 H), 0.97–1.15 (m, 9 H), 1.22–1.54 (m, 14 H), 1.59–1.66 (m, 2 H), 1.69 (dt, J = 13.2, 3.5 Hz, 1 H), 1.78–1.87 (m, 2 H), 1.94 (dt, J = 12.6, 3.4 Hz, 1 H), 3.62 (m, 1 H), 3.82 (q, J = 2.7 Hz, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 11.23 (CH_3), 11.82 (CH_3), 18.63 (CH_3), 20.98 (CH_2), 22.55 (CH_3), 22.79 (CH_3), 23.64 (CH_2), 23.73 (CH_2), 27.99 (CH), 28.18 (CH_2), 31.38 (CH_2), 35.54 (C), 35.76 (CH), 36.11 (CH_2), 36.29 (CH_2), 36.72 (CH_2), 37.05 (CH), 37.70 (CH_2), 39.48 (2 CH_2), 39.54 (CH), 42.64 (C), 45.86 (CH), 50.56 (CH), 56.08 (CH), 68.01 (CH), 71.16 (CH) ppm. MS (150 °C): m/z (%) = 404 (30) [M$^+$], 386 (100), 371 (18), 273 (10), 260 (16), 250 (20), 249 (50), 247 (12), 246 (35). HRMS: m/z [M$^+$] calcd. for $C_{27}H_{48}O_2$: 404.3654; found 404.3647. $C_{27}H_{48}O_2$ (404.67): calcd. C 80.14, H 11.96; found C 79.52, H 12.12.

5α-Cholestane-3β,7β-diol (26b): A mixture of 3β-(*tert*-butyldimethylsilyloxy)-5α-cholestan-7β-ol (**23b**) (45 mg, 87 μmol), water (6 μL, 333 μmol), THF (12 mL) and a 1 M solution of TBAF in THF (130 μL, 130 μmol) was refluxed for 24 h. After cooling to room temperature, a saturated solution of ammonium chloride in water was added and the mixture was extracted with diethyl ether three times. The combined organic layers were washed with brine, dried with magnesium sulfate and the solvent was evaporated. Purification of the residue by flash chromatography (petroleum ether/diethyl ether, 1:10) on silica gel afforded **26b** as colorless crystals, yield: 23.8 mg (68%). m.p. 165 °C. IR (ATR): $\tilde{\nu}$ = 3328, 2928, 2858, 1465, 1376, 1124, 1096, 1040, 736 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.64 (m, 1 H), 0.66 (s, 3 H), 0.82 (s, 3 H), 0.84 (d, J = 6.6 Hz, 3 H), 0.85 (d, J = 6.6 Hz, 3 H), 0.90 (d, J = 6.6 Hz, 3 H), 0.90 (m, 1 H), 0.94–1.21 (m, 8 H), 1.24–1.65 (m, 15 H), 1.70 (dt, J = 13.3, 3.5 Hz, 1 H), 1.76–1.88 (m, 2 H), 1.98 (dt, J = 12.6, 3.4 Hz, 1 H), 3.35 (ddd, J = 10.8, 9.4, 5.3 Hz, 1 H), 3.57 (m, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 12.14 (CH_3), 12.42 (CH_3), 18.76 (CH_3), 21.42 (CH_2), 22.54 (CH_3), 22.80 (CH_3), 23.82 (CH_2), 26.89 (CH_2), 27.99 (CH), 28.71 (CH_2), 31.42 (CH_2), 34.91 (C), 35.66 (CH), 36.17 (CH_2), 36.86 (CH_2), 37.70 (CH_2), 37.99 (CH_2), 39.47 (CH_2), 39.95 (CH_2), 42.00 (CH), 43.40 (CH), 43.58 (C), 52.44 (CH), 55.20 (CH), 55.69 (CH), 71.09 (CH), 75.14 (CH) ppm. MS (150 °C): m/z (%) = 404 (12) [M$^+$], 386 (100), 371 (23), 273 (22), 260 (20), 259 (10), 255 (14), 250 (36), 249 (20), 246 (12), 215 (12). HRMS: m/z [M$^+$] calcd. for $C_{27}H_{48}O_2$: 404.3654; found 404.3651.

3β-Acetoxy-5α-cholestan-7-one (28): 7-Ketocholesteryl acetate (**27**) (246 mg, 575 μmol) was added to a suspension of 10% palladium on activated charcoal (25 mg) in dichloromethane (30 mL) and stirred under a hydrogen atmosphere (1 atm) for 24 h. The mixture was filtered through a short pad of Celite (dichloromethane) and after evaporation of the solvent the residue was purified by flash chromatography (petroleum ether/diethyl ether, 40:1 then 10:1) on silica gel. **28** was isolated as colorless crystals, yield: 209 mg (85%), m.p. 143–144 °C. IR (ATR): $\tilde{\nu}$ = 2946, 2869, 1728, 1706, 1469, 1447, 1369, 1261, 1175, 1067, 1031 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.63 (s, 3 H), 0.840 (d, J = 6.6 Hz, 3 H), 0.845 (d, J = 6.6 Hz, 3 H), 0.89 (d, J = 6.5 Hz, 3 H), 0.93 (dd, J = 12.0, 6.4 Hz, 1 H), 1.00 (m, 1 H), 1.04–1.14 (m, 7 H), 1.08 (s, 3 H), 1.21 (m, 1 H), 1.29–1.59 (m, 10 H), 1.63 (m, 1 H), 1.77 (dt, J = 13.4, 3.6 Hz, 1 H), 1.87 (m, 2 H), 1.97 (dt, J = 12.9, 3.4 Hz, 1 H), 2.01 (s, 3 H), 2.02 (m, 1 H), 2.17 (m, 1 H), 2.32 (m, 2 H), 4.66 (m, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 11.70 (CH_3), 12.04 (CH_3), 18.76 (CH_3), 21.34 (CH_3), 21.76 (CH_2), 22.54 (CH_3), 22.79 (CH_3), 23.75 (CH_2), 24.97 (CH_2), 27.08 (CH_2), 27.97 (CH), 28.39 (CH_2), 33.81 (CH_2), 35.63 (CH), 35.80 (CH_2), 35.93 (C), 36.11 (CH_2), 38.66 (CH_2), 39.44 (CH_2), 42.48 (C), 45.86 (CH_2), 46.48 (CH), 48.83 (CH), 49.95 (CH), 54.97 (2 CH), 72.76 (CH), 170.49 (C=O), 211.63 (C=O) ppm. MS (220 °C): m/z (%) = 444 (100) [M$^+$], 426 (21), 384 (6), 313 (17), 299 (12), 291 (21), 290 (51), 289 (26), 253 (12), 249 (15), 236 (51). HRMS: m/z [M$^+$] calcd. for $C_{29}H_{48}O_3$: 444.3603; found 444.3612. $C_{29}H_{48}O_3$ (444.69): calcd. C 78.33, H 10.88; found C 78.36, H 10.88.

5α-Cholestane-3β,7α-diol (26a) and 5α-Cholestane-3β,7β-diol (26b): A 1 M solution of lithium aluminum hydride in THF (676 μL, 676 μmol) was added to a solution of 3β-acetoxy-5α-cholestan-7-one (**28**) (150 mg, 338 μmol) in anhydrous THF (8 mL) at –78 °C. After stirring for 24 h and warming to room temperature, water and then 10% HCl were added. The aqueous layer was extracted with dichloromethane three times and the combined organic layers were dried with sodium sulfate. Evaporation of the solvent and purification of the residue by flash chromatography (petroleum ether/diethyl ether, 1:10) on silica gel provided **26a** as colorless crystals, yield: 77 mg (57%) and the more polar **26b** as colorless crystals, yield: 13 mg (9%); spectroscopic data for **26a** and **26b**, see above.

7-Keto-5α-cholestan-3β-ol (29): 3β-Acetoxy-5α-cholestan-7-one (**28**) (200 mg, 450 μmol) was added to a solution of KOH in methanol (20%, 15 mL) and stirred under reflux for 48 h. Water was added and the mixture was extracted with dichloromethane three times. The combined organic layers were dried with sodium sulfate and the solvent was evaporated. Purification of the residue by flash chromatography (petroleum ether/diethyl ether, 1:5) on silica gel provided **29** as colorless crystals, yield: 163 mg (100%), m.p. 143–144 °C. IR (ATR): $\tilde{\nu}$ = 3449, 2930, 2851, 1694, 1465, 1446, 1384, 1333, 1291, 1174, 1077, 1035 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.64 (s, 3 H), 0.84 (d, J = 6.6 Hz, 3 H), 0.85 (d, J = 6.6 Hz, 3 H), 0.89 (d, J = 6.5 Hz, 3 H), 0.93 (dd, J = 12.1, 6.4 Hz, 1 H), 0.96–1.11 (m, 7 H), 1.07 (s, 3 H), 1.13–1.58 (m, 12 H), 1.61 (m, 1 H), 1.75 (dt, J = 13.4, 3.5 Hz, 1 H), 1.86 (m, 2 H), 1.97 (dt, J = 13.0, 3.5 Hz, 1 H), 2.01 (dd, J = 12.5, 3.2 Hz, 1 H), 2.17 (m, 1 H), 2.34 (m, 2 H), 3.60 (m, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 11.81 (CH_3), 12.04 (CH_3), 18.76 (CH_3), 21.83 (CH_2), 22.54 (CH_3), 22.74 (CH_3), 23.78 (CH_2), 24.95 (CH_2), 27.97 (CH), 28.39 (CH_2), 31.04 (CH_2), 35.63 (CH), 35.96 (C), 36.06 (CH_2), 36.12 (CH_2), 37.88 (CH_2), 38.72 (CH_2), 39.45 (CH_2), 42.48 (C), 46.09 (CH_2), 46.83 (CH), 48.85 (CH), 49.98 (CH), 54.99 (CH), 55.22 (CH), 70.71 (CH), 212.12 (C=O) ppm. MS (200 °C): m/z (%) = 402 (100) [M$^+$], 384 (19), 290 (12), 271 (18), 249 (16), 248 (33), 247 (24), 207 (12), 194 (43). HRMS: m/z [M$^+$] calcd. for $C_{27}H_{46}O_2$: 402.3498; found 402.3506. $C_{27}H_{46}O_2$ (402.65): calcd. C 80.54, H 11.51; found C 80.52, H 11.46.

25-Hydroxycholesteryl Acetate (31): A catalytic amount of DMAP was added to a solution of 25-hydroxycholesterol (**30**) (700 mg,

1.74 mmol), acetic anhydride (197 μL, 213 mg, 2.09 mmol), and triethylamine (586 μL, 422 mg, 4.18 mmol) in dry THF (20 mL) and the solution was stirred for 20 h at room temperature. Aqueous ammonium chloride was added and the mixture was extracted with dichloromethane three times. The combined organic layers were dried with sodium sulfate and the solvent was evaporated. Purification of the residue by flash chromatography (petroleum ether/diethyl ether, 1:1) on silica gel afforded **31** as colorless crystals, yield: 770 mg (100%), m.p. 142 °C. IR (ATR): $\tilde{\nu}$ = 3286, 2938, 2864, 1732, 1468, 1440, 1374, 1236, 1158, 1036 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 0.66 (s, 3 H), 0.91 (d, J = 6.5 Hz, 3 H), 0.93–1.27 (m, 8 H), 1.00 (s, 3 H), 1.19 (s, 6 H), 1.32–1.58 (m, 12 H), 1.83 (m, 3 H), 1.93–2.03 (m, 2 H), 2.01 (s, 3 H), 2.30 (m, 2 H), 4.59 (m, 1 H), 5.35 (d, J = 4.6 Hz, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 11.83 (CH_3), 18.65 (CH_3), 19.28 (CH_3), 20.75 (CH_2), 20.98 (CH_2), 21.43 (CH_3), 24.24 (CH_2), 27.73 (CH_2), 28.22 (CH_2), 29.18 (CH_3), 29.31 (CH_3), 31.81 (CH), 31.85 (CH_2), 35.73 (CH), 36.40 (CH_2), 36.54 (C), 36.95 (CH_2), 38.08 (CH_2), 39.68 (CH_2), 42.28 (C), 44.38 (CH_2), 49.96 (CH), 56.02 (CH), 56.63 (CH), 71.07 (C), 73.95 (CH), 122.60 (CH), 139.61 (C), 170.54 (C=O) ppm. MS (160 °C): m/z (%) = 384 (100) [$(M-AcOH)^+$], 369 (12), 366 (58), 351 (20), 258 (10), 255 (17), 253 (16), 245 (21), 213 (14). HRMS: m/z [$(M-AcOH)^+$] calcd. for $C_{27}H_{44}O$: 384.3392; found 384.3414. $C_{29}H_{48}O_3$ (444.69): calcd. C 78.33, H 10.88; found C 78.18, H 10.86.

25-Hydroxy-7-ketocholesteryl Acetate (32): A 5.5 M solution of *tert*-butyl hydroperoxide in decane (670 μL, 3.35 mmol) was added to a suspension of 25-hydroxycholesteryl acetate (**31**) (372 mg, 839 μmol), pyridinium dichromate (1.26 g, 3.35 mmol) and Celite (976 mg) in dry benzene at 0 °C. After warming to room temperature and stirring for 48 h the suspension was filtered through a pad of silica gel (ether). After evaporation of the solvent and purification of the residue by flash chromatography (petroleum ether/diethyl ether, 1:2) on silica gel **32** was obtained as colorless crystals, yield: 301 mg (85%), m.p. 150 °C. IR (ATR): $\tilde{\nu}$ = 3321, 2944, 2863, 1723, 1666, 1466, 1375, 1248, 1183, 1041, 937, 908 cm^{-1}. ^1H NMR (500 MHz, [D_6]benzene): δ = 0.71 (s, 3 H), 0.83 (m, 1 H), 0.84 (s, 3 H), 1.10 (m, 1 H), 1.12 (d, J = 6.5 Hz, 3 H), 1.17–1.25 (m, 2 H), 1.21 (s, 6 H), 1.29–1.35 (m, 3 H), 1.37–1.57 (m, 11 H), 1.83 (s, 3 H), 1.89 (m, 1 H), 2.04 (m, 1 H), 2.07–2.16 (m, 2 H), 2.26 (m, 1 H), 2.40 (ddd, J = 13.8, 4.9, 2.2 Hz, 1 H), 3.08 (m, 1 H), 4.80 (m, 1 H), 5.83 (d, J = 1.7 Hz, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, [D_6]benzene): δ = 12.60 (CH_3), 17.41 (CH_3), 19.63 (CH_3), 21.32 (CH_3), 21.66 (CH_2), 21.76 (CH_2), 27.32 (CH_2), 28.14 (CH_2), 29.51 (CH_2), 29.97 (CH_3), 30.11 (CH_3), 36.43 (CH_2), 36.64 (CH), 37.47 (CH_2), 38.26 (CH_2), 38.58 (C), 39.54 (CH_2), 43.74 (C), 45.18 (CH_2), 46.00 (CH), 50.15 (CH), 50.90 (CH), 55.74 (CH), 70.63 (C), 72.69 (CH), 127.68 (CH), 162.66 (C), 169.83 (C=O), 200.50 (C=O) ppm. MS (200 °C): m/z (%) = 440 (3) [$(M-H_2O)^+$], 416 (10), 398 (30) [$(M-AcOH)^+$], 383 (24), 381 (31), 380 (100), 365 (11), 269 (21), 267 (14), 229 (11), 227 (11), 187 (48), 174 (80), 161 (30). HRMS: m/z [$(M-AcOH)^+$] calcd. for $C_{27}H_{42}O_2$: 398.3185; found 398.3166.

3β-Acetoxy-7-keto-5α-cholestan-25-ol (33): 25-Hydroxy-7-ketocholesteryl acetate (**32**) (84 mg, 183 μmol) was added to a suspension of 10% palladium on activated charcoal (8 mg) in dichloromethane (20 mL) and stirred under a hydrogen atmosphere (1 atm) for 3 d. The mixture was filtered through a short pad of Celite (dichloromethane) and after evaporation of the solvent the residue was purified by flash chromatography (petroleum ether/diethyl ether, 1:2) on silica gel. **33** was isolated as colorless crystals, yield: 58 mg (68%), m.p. 141 °C. IR (ATR): $\tilde{\nu}$ = 3371, 2941, 2869, 1726, 1706, 1471, 1447, 1371, 1262, 1177, 1149, 1031, 911 cm^{-1}. ^1H NMR (500 MHz, [D_6]benzene): δ = 0.66 (m, 1 H), 0.69 (s, 3 H), 0.75 (s, 3 H), 0.88 (dt, J = 5.3, 11.8 Hz, 1 H), 1.07 (m, 1 H), 1.12 (d, J = 6.5 Hz, 3 H), 1.15–1.26 (m, 4 H), 1.22 (s, 6 H), 1.28–1.36 (m, 3 H), 1.38–1.47 (m, 4 H), 1.48–1.56 (m, 5 H), 1.59–1.65 (m, 2 H), 1.85 (s, 3 H), 1.87–2.02 (m, 4 H), 2.05–2.19 (m, 2 H), 2.82 (m, 1 H), 4.76 (m, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, [D_6]benzene): δ = 11.35 (CH_3), 12.27 (CH_3), 19.06 (CH_3), 20.94 (CH_3), 21.16 (CH_2), 21.88 (CH_2), 25.48 (CH_2), 27.46 (CH_2), 28.85 (CH_2), 29.48 (CH_3), 29.61 (CH_3), 34.06 (CH_2), 35.71 (C), 35.78 (CH_2), 36.10 (CH), 36.95 (CH_2), 39.14 (CH_2), 42.77 (C), 44.69 (CH_2), 45.72 (CH_2), 45.76 (CH), 49.51 (CH), 49.79 (CH), 54.57 (CH), 55.52 (CH), 70.15 (C), 72.61 (CH), 169.51 (C=O), 208.88 (C=O) ppm. MS (180 °C): m/z (%) = 445 (8) [$(M-CH_3)^+$], 442 (59) [$(M-H_2O)^+$], 427 (46), 424 (25), 358 (42), 357 (30), 331 (27), 330 (50), 329 (100), 316 (39), 290 (35), 289 (25), 249 (26), 236 (85). HRMS: m/z [$(M-H_2O)^+$] calcd. for $C_{29}H_{46}O_3$: 442.3447; found 442.3444.

5α-Cholestane-3β,7α,25-triol (34a) and 5α-Cholestane-3β,7β,25-triol (34b): TMSCl (41 mg, 49 μL, 381 μmol) was added to a solution of 3β-acetoxy-7-keto-5α-cholestan-25-ol (**33**) (117 mg, 254 μmol) in pyridine (10 mL) and the mixture was stirred for 1 h at room temperature. Water was added, the aqueous phase was extracted with diethyl ether three times, the combined organic layers were dried with sodium sulfate and the solvent was evaporated. The crude product was dissolved in anhydrous THF (8 mL), cooled to –78 °C, a 1 M solution of lithium aluminum hydride in THF (508 μL, 508 μmol) was added and the mixture was stirred for 16 h at –78 °C. After warming to room temperature water was added and the suspension was extracted with diethyl ether three times. The combined organic layers were washed with water and brine, dried with sodium sulfate, and the solvent was evaporated. Purification of the residue by flash chromatography (petroleum ether/diethyl ether, 1:10) on silica gel afforded two fractions. The separated products were dissolved in THF, aqueous HCl (10%) was added, and the mixtures were stirred for 30 min each. Aqueous sodium hydrogencarbonate was added and the mixture was extracted with diethyl ether three times. The combined organic layers were dried with sodium sulfate and the solvent was evaporated to provide **34a** from the less polar fraction as colorless crystals, yield: 68 mg (63%), m.p. 217 °C. IR (ATR): $\tilde{\nu}$ = 3330, 2934, 2862, 1468, 1445, 1374, 1155, 1144, 1037, 1015, 945, 905 cm^{-1}. ^1H NMR (500 MHz, [D_5]pyridine): δ = 0.70 (s, 3 H), 0.89 (s, 3 H), 0.98 (d, J = 6.4 Hz, 3 H), 1.08–1.37 (m, 7 H), 1.41 (s, 6 H), 1.43–1.51 (m, 3 H), 1.53–1.62 (m, 5 H), 1.65–1.87 (m, 9 H), 1.96 (m, 2 H), 2.05 (m, 1 H), 2.15 (br. t, J = 12.8 Hz, 1 H), 3.89 (m, 1 H), 4.02 (m, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, [D_5]pyridine): δ = 11.56 (CH_3), 12.17 (CH_3), 18.93 (CH_3), 21.15 (CH_2), 21.46 (CH_2), 24.00 (CH_2), 28.63 (CH_2), 29.89 (CH_3), 30.12 (CH_3), 32.54 (CH_2), 36.05 (C), 36.14 (CH), 37.04 (CH_2), 37.54 (CH_2), 37.57 (CH), 37.94 (CH_2), 39.21 (CH_2), 40.13 (CH_2), 40.36 (CH), 43.72 (C), 45.24 (CH_2), 46.25 (CH), 51.03 (CH), 56.56 (CH), 67.03 (CH), 69.57 (C), 70.79 (CH) ppm. MS (180 °C): m/z (%) = 402 (74) [$(M-H_2O)^+$], 387 (17), 385 (35), 384 (100), 369 (66), 289 (35), 273 (41), 271 (42), 271 (63), 249 (38), 246 (49). HRMS: m/z [$(M-H_2O)^+$] calcd. for $C_{27}H_{46}O_2$: 402.3498; found 402.3499.

5α-Cholestane-3β,7β,25-triol (34b) was obtained from the more polar fraction as colorless crystals, yield: 17 mg (16%), m.p. 191 °C. IR (ATR): $\tilde{\nu}$ = 3300, 2926, 2853, 1466, 1376, 1124, 1097, 1041, 933 cm^{-1}. ^1H NMR (500 MHz, [D_5]pyridine): δ = 0.69 (m, 1 H), 0.72 (s, 3 H), 0.87 (s, 3 H), 0.94 (m, 1 H), 1.01 (d, J = 6.5 Hz, 3 H), 1.05–1.36 (m, 7 H), 1.42 (s, 6 H), 1.44–1.78 (m, 12 H), 1.79–1.93 (m, 4 H), 1.99 (m, 1 H), 2.06 (m, 1 H), 2.33 (m, 1 H), 3.55 (dt, J = 5.1, 9.9 Hz, 1 H), 3.86 (m, 1 H), 5.23 (br. s, 1 H), 5.44 (br. s, 1 H), 5.99 (br. s, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, [D_5]pyridine): δ = 12.49 (CH_3), 12.66 (CH_3), 19.11 (CH_3), 21.33 (CH_2),

21.89 (CH_2), 27.76 (CH_2), 29.19 (CH_2), 29.95 (CH_3), 30.15 (CH_3), 32.57 (CH_2), 35.33 (C), 36.18 (CH), 37.15 (CH_2), 37.53 (CH_2), 39.09 (CH_2), 40.36 (CH_2), 40.48 (CH_2), 42.76 (CH), 43.72 (C), 43.79 (CH), 45.27 (CH_2), 53.02 (CH), 55.81 (CH), 56.67 (CH), 69.58 (C), 70.52 (CH), 74.66 (CH) ppm. MS (180 °C): *m/z* (%) = 402 (36) [$(M-H_2O)^+$], 387 (60), 385 (23), 384 (59), 369 (40), 317 (27), 290 (43), 289 (100), 273 (49), 271 (41), 255 (20). HRMS: *m/z* [$(M-H_2O)^+$] calcd. for $C_{27}H_{46}O_2$: 402.3498; found 402.3495.

3β-Trimethylsilyloxy-5α-cholestan-6-one (36): TMSCl (353 mg, 4.15 μL, 3.25 mmol) and DMAP (397 mg, 3.25 mmol) were added to a solution of 6-keto-5α-cholestan-3β-ol (**35**) (1.09 g, 2.71 mmol) in THF (20 mL). The mixture was stirred for 1 h at room temperature. Filtration over silica gel (diethyl ether) and evaporation of the solvent gave **36** as colorless crystals, yield: 1.12 g (96%), m.p. 127 °C. IR (ATR): $\tilde{\nu}$ = 2936, 2866, 1716, 1707, 1467, 1382, 1249, 1092, 1081, 980, 900, 881, 838 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 0.09 (s, 9 H), 0.64 (s, 3 H), 0.73 (s, 3 H), 0.848 (d, J = 6.6 Hz, 3 H), 0.853 (d, J = 6.6 Hz, 3 H), 0.90 (d, J = 6.5 Hz, 3 H), 0.94–1.27 (m, 11 H), 1.28–1.40 (m, 4 H), 1.43–1.55 (m, 4 H), 1.59 (m 1 H), 1.67–1.85 (m, 5 H), 1.92 (t, J = 12.8 Hz, 1 H), 2.02 (dt, J = 12.6, 3.2 Hz, 1 H), 2.16 (dd, J = 12.6, 2.4 Hz, 1 H), 2.30 (dd, J = 13.2, 4.5 Hz, 1 H), 3.51 (m, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 0.19 (3 CH_3), 12.00 (CH_3), 13.11 (CH_3), 18.63 (CH_3), 21.48 (CH_2), 22.54 (CH_3), 22.79 (CH_3), 23.79 (CH_2), 23.97 (CH_2), 28.00 (CH), 28.04 (CH_2), 30.16 (CH_2), 31.21 (CH_2), 35.68 (CH), 36.08 (CH_2), 36.86 (CH_2), 37.86 (CH), 39.46 (CH_2), 39.54 (CH_2), 40.92 (C), 42.97(C), 46.77 (CH_2), 54.01 (CH), 56.12 (CH), 56.79 (CH), 56.97 (CH), 71.18 (CH), 211.02 (C=O) ppm. MS (180 °C): *m/z* (%) = 474 (27) [M^+], 459 (84), 445 (100), 402 (15), 384 (6). HRMS: *m/z* [M^+] calcd. for $C_{30}H_{54}O_2Si$: 474.3893; found 474.3892. $C_{30}H_{54}O_2Si$ (474.83): calcd. C 75.88, H 11.46; found C 75.95, H 11.57.

3β,6-Bis(trimethylsilyloxy)-5α-cholest-6-ene (37): A 1.6 M solution of butyllithium in hexane (4.4 mL, 7.04 mmol) was added at –5 °C to solution of diisopropylamine (704 mg, 980 μL, 6.9 mmol) in THF (20 mL). The mixture was stirred for 10 min, cooled to –78 °C and a solution of ketone **36** (1.50 g, 3.2 mmol) in THF (20 mL) was added dropwise. After stirring for 3 h at –78 °C, TMSCl (1.02 g, 1.21 mL, 9.50 mmol) was added and the mixture was warmed to room temperature. The mixture was quenched with sodium hydrogen carbonate solution, extracted with diethyl ether and the organic phase was dried with sodium sulfate. Evaporation of the solvent and purification of the residue by flash chromatography (petroleum ether with 1% of triethylamine) on neutral aluminum oxide provided **37** as colorless crystals, yield: 1.31 g (72%), m.p. 124–125 °C. IR (ATR): $\tilde{\nu}$ = 3470, 2936, 2866, 1705, 1692, 1467, 1381, 1365, 1249, 1172, 1065, 964, 898, 882, 839, 751 cm^{-1}. ^1H NMR (500 MHz, [D_6]benzene): δ = 0.32 (s, 9 H), 0.33 (s, 9 H), 0.78 (s, 3 H), 0.96 (s, 3 H), 0.96–1.07 (m, 2 H), 1.04 (d, J = 6.6 Hz, 6 H), 1.11 (d, J = 6.5 Hz, 3 H), 1.14–1.42 (m, 10 H), 1.52–1.69 (m, 7 H), 1.81–2.00 (m, 4 H), 2.14 (m, 3 H), 2.52 (m 1 H), 3.77 (m, 1 H), 4.96 (s, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, [D_6]benzene): δ = 0.33 (3 CH_3), 0.56 (3 CH_3), 12.05 (CH_3), 12.42 (CH_3), 18.94 (CH_3), 21.51 (CH_2), 22.75 (CH_3), 23.02 (CH_3), 24.35 (CH_2), 24.43 (CH_2), 28.41 (CH), 28.64 (CH_2), 32.04 (CH_2), 32.15 (CH_2), 35.06 (CH_2), 35.22 (C), 36.14 (CH), 36.24 (CH), 36.62 (CH_2), 39.90 (CH_2), 40.53 (CH_2), 43.59(C), 48.45 (CH), 53.10 (CH), 55.67 (CH), 56.62 (CH), 72.78 (CH), 105.00 (CH), 151.16 (C) ppm. MS (120 °C): *m/z* (%) = 546 (15), 531 (3), 475 (17), 474 (37), 460 (32), 459 (86), 445 (100), 403 (21), 402 (58), 149 (43). HRMS: *m/z* [M^+] calcd. for $C_{33}H_{62}O_2Si_2$: 546.4288; found 546.4286. $C_{33}H_{62}O_2Si_2$ (547.02): calcd. C 72.46, H 11.42; found C 72.67, H 11.69.

7α-Fluoro-6-keto-5α-cholestan-3β-ol (38): Selectfluor (435 mg, 1.23 mmol) was added to a suspension of the silyl enol ether **37** (672 mg, 1.23 mmol) in DMF and stirred for 15 min at room temperature. A 1 M solution of TBAF in THF (1.23 mL, 1.23 mmol) was added, stirring was continued for 5 min and water was added. After 2 h the mixture was extracted three times with diethyl ether, the combined organic layers were dried with sodium sulfate and the solvent was evaporated. Purification of the residue by flash chromatography (petroleum ether/diethyl ether, 10:1) on silica gel afforded **38** as colorless crystals, yield: 369 mg (71%), m.p. 124 °C. IR (ATR): $\tilde{\nu}$ = 3522, 3369, 2945, 2868, 1723, 1467, 1383, 1365, 1282, 1251, 1159, 1076, 1012, 962, 634 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 0.64 (s, 3 H), 0.72 (s, 3 H), 0.849 (d, J = 6.6 Hz, 3 H), 0.854 (d, J = 6.6 Hz, 3 H), 0.90 (d, J = 6.5 Hz, 3 H), 1.00 (m, 1 H), 1.06–1.20 (m, 6 H), 1.24–1.43 (m, 7 H), 1.48–1.73 (m, 7 H), 1.78–1.91 (m, 4 H), 1.99 (m, 1 H), 2.81 (ddd, J = 12.5, 6.2, 2.8 Hz, 1 H), 3.63 (m, 1 H), 4.44 (dd, J = 52.7, 1.6 Hz, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 11.59 (CH_3), 12.29 (CH_3), 18.60 (CH_3), 21.39 (CH_2), 22.53 (CH_3), 22.79 (CH_3), 23.15 (CH_2), 23.75 (CH_2), 27.97 (CH_2), 27.98 (CH), 29.25 (CH_2), 30.52 (CH_2), 35.73 (CH), 36.04 (CH_2), 36.81 (CH_2), 38.97 (CH_2), 39.43 (CH_2), 42.12 (C), 42.39 (d, $^2J_{C,F}$ = 21.6 Hz, CH), 42.94 (C), 46.45 (CH), 49.33 (CH), 52.26 (d, $^3J_{C,F}$ = 2.1 Hz, CH), 55.90 (CH), 70.31 (CH), 94.25 (d, $^1J_{C,F}$ = 178.8 Hz, CH), 206.87 (d, $^2J_{C,F}$ = 21.3 Hz, C=O) ppm. MS (200 °C): *m/z* (%) = 420 (61) [M^+], 400 (15), 385 (5), 266 (12), 139 (100), 111 (10), 95 (20). HRMS: *m/z* [M^+] calcd. for $C_{27}H_{45}FO_2$: 420.3404; found 420.3415.

7α-Fluoro-5α-cholestane-3β,6β-diol (39): Sodium borohydride (90 mg, 2.38 mmol) was added to a solution of 7α-fluoro-6-keto-5α-cholestan-3β-ol (**38**) (50 mg, 119 μmol) in methanol (5 mL) and the mixture was stirred at room temperature for 2 h. Water (20 mL) was added and the mixture was extracted with dichloromethane three times. The combined organic layers were washed with brine, dried with sodium sulfate and the solvent was evaporated. **39** was isolated as colorless crystals without further purification, yield: 54 mg (100%), m.p. 169–172 °C. IR (ATR): $\tilde{\nu}$ = 3409, 2932, 2866, 1467, 1366, 1323, 1299, 1173, 1127, 1099, 1041, 1022, 1007, 973, 949 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 0.67 (s, 3 H), 0.847 (d, J = 6.6 Hz, 3 H), 0.851 (d, J = 6.6 Hz, 3 H), 0.90 (d, J = 6.5 Hz, 3 H), 0.88–1.05 (m, 2 H), 0.98 (s, 3 H), 1.06–1.17 (m, 7 H), 1.24–1.53 (m, 10 H), 1.58–1.63 (m, 2 H), 1.64–1.89 (m, 5 H), 1.95 (dt, J = 12.7, 3.3 Hz, 1 H), 3.68 (m, 1 H), 3.77 (dt, J = 7.5, 3.0 Hz, 1 H), 4.44 (dt, J = 46.7, 2.5 Hz, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 11.65 (CH_3), 15.11 (CH_3), 18.63, (CH_3), 20.80 (CH_2), 22.54 (CH_3), 22.79 (CH_3), 23.47 (CH_2), 23.75 (CH_2), 27.98 (CH), 28.13 (CH_2), 31.33 (CH_2), 34.25 (CH_2), 34.61 (d, $^2J_{C,F}$ = 19.3 Hz, CH), 35.04 (C), 35.79 (CH), 36.10 (CH_2), 38.20 (CH_2), 39.36 (CH_2), 39.47 (CH_2), 41.82 (CH), 42.61 (C), 46.09 (CH), 49.43 (d, $^3J_{C,F}$ = 2.1 Hz, CH), 56.02 (CH), 71.50 (CH), 72.81 (d, $^2J_{C,F}$ = 28.9 Hz, CH), 92.26 (d, $^1J_{C,F}$ = 172.7 Hz, CH) ppm. MS (25 °C): *m/z* (%) = 422 (20) [M^+], 404 (15), 384 (3), 299 (8), 269 (13), 250 (20), 149 (100), 111 (25), 97 (38), 95 (33), 91 (28), 85 (34). HRMS: *m/z* [M^+] calcd. for $C_{27}H_{47}FO_2$: 422.3560; found 422.3546.

3β-Acetoxy-5α-cholestan-6-one (40): 6-Keto-5α-cholestan-3β-ol (**35**) (1.00 g, 2.49 mmol), acetic anhydride (382 mg, 354 μL, 3.74 mmol) and triethylamine (753 mg, 1.05 mL, 7.46 mmol) were dissolved in THF (20 mL) and stirred for 24 h. Addition of diethyl ether (20 mL) and filtration (petroleum ether/diethyl ether, 1:1) over a short pad of silica gel provided **40** as colorless crystals, yield: 1.07 g (97%), m.p. 125 °C. IR (ATR): $\tilde{\nu}$ = 2945, 2866, 2853, 1724, 1715, 1465, 1446, 1382, 1364, 1249, 1235, 1099, 1034, 996, 963, 924, 905 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 0.65 (s, 3 H), 0.75 (s, 3 H), 0.848 (d, J = 6.6 Hz, 3 H), 0.853 (d, J = 6.6 Hz, 3 H), 0.90

(d, J = 6.5 Hz, 3 H), 0.97–1.18 (m, 5 H), 1.20–1.38 (m, 10 H), 1.45–1.61 (m, 5 H), 1.75–1.85 (m 4 H), 1.88–1.97 (m, 2 H), 2.01 (s, 3 H), 2.04 (m, 1 H), 2.25 (dd, J = 12.7, 2.7 Hz, 1 H), 2.30 (dd, J = 13.2, 4.5 Hz, 1 H), 4.66 (tt, J = 11.6, 4.7 Hz, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 11.99 (CH_3), 13.01 (CH_3), 18.61 (CH_3), 21.33 (CH_3), 21.45 (CH_2), 22.53 (CH_3), 22.79 (CH_3), 23.78 (CH_2), 23.94 (CH_2), 26.10 (CH_2), 26.81 (CH_2), 27.98 (CH), 28.01 (CH_2), 35.68 (CH), 36.05 (CH_2), 36.38 (CH_2), 37.92 (CH), 39.42 (CH_2), 39.44 (CH_2), 40.93 (C), 42.96 (C), 46.65 (CH_2), 53.81 (CH), 56.08 (CH), 56.46 (CH), 56.65 (CH), 72.83 (CH), 170.61 (C=O), 210.46 (C=O) ppm. MS (150 °C): m/z (%) = 444 (7) [M^+], 384 (23), 163 (24), 149 (23), 125 (32), 123 (27), 111 (55), 109 (36), 97 (80), 95 (51), 85 (56), 83 (68), 71 (76), 69 (67), 57 (100). HRMS: m/z [M^+] calcd. for $C_{29}H_{48}O_3$: 444.3603; found 444.3620.

3β-Acetoxy-6,6-difluoro-5α-cholestane (41): A mixture of powdered 3β-acetoxy-5α-cholestan-6-one (**40**) and DAST (162 mg, 200 μL, 1.01 mmol) was heated at 40 °C under an argon atmosphere for 2 d. Water (10 mL) was added and the mixture was extracted with dichloromethane three times. The combined organic layers were dried with sodium sulfate and the solvent was evaporated. Purification of the residue by flash chromatography (petroleum ether/diethyl ether, 40:1) on silica gel afforded **41** as colorless crystals, yield: 54 mg (26%), m.p. 93 °C. IR (ATR): $\tilde{\nu}$ = 2954, 2928, 2869, 1736, 1468, 1380, 1364, 1237, 1207, 1197, 1032, 907, 892 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.66 (s, 3 H), 0.74 (m, 1 H), 0.84 (d, J = 6.6 Hz, 3 H), 0.85 (d, J = 6.6 Hz, 3 H), 0.89 (d, J = 6.5 Hz, 3 H), 0.91 (d, $^5J_{H,F}$ = 3.4 Hz, 3 H), 0.98 (m, 1 H), 1.04–1.16 (m, 8 H), 1.19–1.38 (m, 6 H), 1.42–1.63 (m, 7 H), 1.73 (br. d, J = 13.5 Hz, 1 H), 1.82 (m, 2 H), 1.99 (dt, J = 12.7, 3.4 Hz, 1 H), 2.02 (s, 3 H), 2.04–2.14 (m, 2 H), 4.68 (m, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 11.95 (CH_3), 13.78 (d, $^4J_{C,F}$ = 5.9 Hz, CH_3), 18.62 (CH_3), 20.91 (CH_2), 21.34 (CH_3), 22.53 (CH_3), 22.79 (CH_3), 23.79 (CH_2), 23.86 (CH_2), 24.02 (CH_2), 26.89 (CH_2), 27.98 (CH), 28.04 (CH_2), 32.77 (d, $^3J_{C,F}$ = 9.6 Hz, CH), 35.70 (CH), 36.07 (CH_2), 36.55 (d, $^3J_{C,F}$ = 6.7 Hz, C), 37.48 (CH_2), 39.46 (2 CH_2), 39.85 (dd, $^2J_{C,F}$ = 24.8, 21.8 Hz, CH_2), 42.58 (C), 49.13 (dd, $^2J_{C,F}$ = 22.8, 18.9 Hz, CH), 53.00 (CH), 55.61 (CH), 56.08 (CH), 72.82 (CH), 122.80 (dd, $^1J_{C,F}$ = 245.2, 242.8 Hz, CF_2), 170.53 (C=O) ppm. MS (150 °C): m/z (%) = 466 (47) [M^+], 406 (23), 391 (15), 386 (59), 312 (24), 252 (37), 251 (100). HRMS: m/z [M^+] calcd. for $C_{29}H_{48}F_2O_2$: 466.3622; found 466.3605.

6,6-Difluoro-5α-cholestan-3β-ol (42): A 1 M solution of lithium aluminum hydride in THF (104 μL, 104 μmol) was added to a solution of 3β-acetoxy-6,6-difluoro-5α-cholestane (**41**) (48.2 mg, 103 μmol) in anhydrous THF (10 mL) at 0 °C. After stirring for 3 h at 0 °C under an argon atmosphere, water and then 10% HCl were added. The aqueous layer was extracted with diethyl ether three times. The combined organic layers were washed with a saturated solution of sodium hydrogencarbonate and dried with sodium sulfate. Evaporation of the solvent and purification of the residue by flash chromatography (petroleum ether/diethyl ether, 5:1) on silica gel provided **42** as colorless crystals, yield: 31.2 mg (71%), m.p. 122 °C. IR (ATR): $\tilde{\nu}$ = 3443, 2931, 2867, 2848, 1467, 1443, 1379, 1307, 1278, 1173, 1061, 1019, 992, 966, 922, 878, 837 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.66 (s, 3 H), 0.73 (m, 1 H), 0.849 (d, J = 6.6 Hz, 3 H), 0.853 (d, J = 6.6 Hz, 3 H), 0.89 (d, J = 6.8 Hz, 3 H), 0.90 (d, $^5J_{H,F}$ = 4.1 Hz, 3 H), 0.95–1.15 (m, 9 H), 1.20–1.40 (m, 6 H), 1.42–1.67 (m, 7 H), 1.72 (br. d, J = 13.5 Hz, 1 H), 1.83 (m, 2 H), 1.99 (dt, J = 12.7, 3.3 Hz, 1 H), 2.11 (m, 2 H), 3.59 (m, 1 H) ppm. ^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 11.96 (CH_3), 13.86 (d, $^4J_{C,F}$ = 5.7 Hz, CH_3), 18.63 (CH_3), 20.97 (CH_2), 22.54 (CH_3), 22.80 (CH_3), 23.79 (CH_2), 24.05 (CH_2), 27.68 (CH_2), 27.99 (CH), 28.05 (CH_2), 30.76 (CH_2), 32.80 (d, $^3J_{C,F}$ = 9.7 Hz, CH) 35.70 (CH), 36.08 (CH_2), 36.56 (d, $^3J_{C,F}$ = 7.1 Hz, C), 37.75 (CH_2), 39.46 (CH_2), 39.53 (CH_2), 39.93 (dd, $^2J_{C,F}$ = 25.0, 22.0 Hz, CH_2), 42.59 (C), 49.29 (dd, $^2J_{C,F}$ = 23.0, 19.1 Hz, CH), 53.13 (CH), 55.70 (CH), 56.10 (CH), 70.90 (CH), 123.03 (dd, $^1J_{C,F}$ = 244.7, 242.5 Hz, CF_2) ppm. MS (120 °C): m/z (%) = 424 (100) [M^+], 406 (2), 404 (3), 391 (13), 389 (7), 270 (38), 269 (45), 252 (24), 251 (42), 249 (25). HRMS: m/z [M^+] calcd. for $C_{27}H_{46}F_2O$: 424.3517; found 424.3505. $C_{27}H_{46}F_2O$ (424.65): calcd. C 76.37, H 10.92; found C 76.46, H 10.93.

Table 3. Crystallographic data for the *p*-bromobenzoates **6** and **7**.

	6	**7**
Formula	$C_{35}H_{53}BrO_2$	$C_{35}H_{53}BrO_2$
Formula weight [g mol^{-1}]	585.68	585.68
Habit, color	irregular block, colorless	polyhedron, colorless
Crystal size [mm]	0.46 × 0.28 × 0.23	0.33 × 0.19 × 0.06
Crystal system	monoclinic	monoclinic
Space group	$P2_1$	$P2_1$
a [Å]	12.496(1)	10.898(2)
b [Å]	11.367(1)	11.025(2)
c [Å]	22.714(2)	13.491(3)
β [°]	100.39(1)	101.90(3)
V [Å^3]	3173.4(4)	1586.1(5)
Z	4	2
$\rho_{calcd.}$ [g cm^{-3}]	1.23	1.23
Absorption coefficient [mm^{-1}]	1.32	1.33
F(000)	1256	628.0
λ [Å]	0.71073	0.71073
T [K]	198	200
θ range for data collection [°]	3.58–25.00	2.19–23.03
Reflections collected	43003	10719
Independent reflections	10741	4329
Refinement method	full-matrix least-squares on F^2	full-matrix least-squares on F^2
Data-to-parameter ratio	15.7:1	12.4:1
Final R indices [$I > 2\sigma(I)$]	R_1 = 0.0431; wR_2 = 0.0666	R_1 = 0.0463; wR_2 = 0.1253
R indices (all data)	R_1 = 0.0848; wR_2 = 0.0741	R_1 = 0.0493; wR_2 = 0.1274
Largest diff. peak/hole [e·Å^{-3}]	0.22/–0.23	1.20/–0.43

X-ray Crystallography: CCDC-606597 (for **6**) and -606598 (for **7**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. For selected crystallographic data for the *p*-bromobenzoates **6** and **7** see Table 3.

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