Synthesis of Novel 5α,9α-Bridged Steroids by a Boron Trifluoride–Diethyl Ether Induced Rearrangement

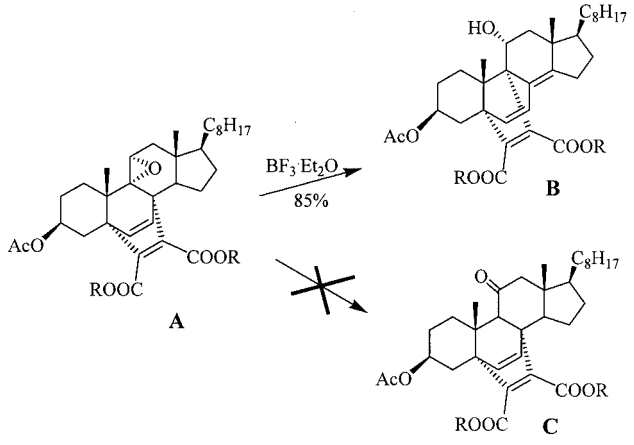
Lidija Bondarenko,*[a] Ljubinka Lorenc,[b] Dieter Bläser,[c] and Roland Boese[c]

Keywords: Steroids / Epoxides / Lewis acids / Rearrangements / Lactones

A stereoselective and synthetically useful rearrangement reaction of 5α,8α-bridged 9,11α-epoxy steroids induced by boron trifluoride–diethyl ether is presented, in the preparation of a new class of 5α,9α-bridged 11α-hydroxy steroid derivatives in high yields. Lactones were prepared from several of the rearranged 11α-hydroxy compounds.

Introduction

In our continuing studies of steroid transformations, we have been attempting to prepare an 11-oxo derivative of some 5,8-bridged steroids (**C**, Scheme 1). Opening of different steroidal epoxides to give ketones using boron trifluoride–diethyl ether is a well-investigated and high-yield reaction.[1] However, in the case of our bridged epoxide **A**, the bridge had migrated from position C-8 to C-9 to produce a 6,8(14)-dien-11α-ol as the only product, in high yield (**B**, Scheme 1).



Scheme 1. Reaction of epoxides with boron trifluoride–diethyl ether

This is not so surprising since it is known that treatment of epoxides with boron trifluoride–diethyl ether can give, in some cases, other rearrangement products besides ketones,[2] especially in natural product chemistry.[3] For some synthetic rearrangement reactions,[3a,4] various Lewis acids have been investigated, and it has been found that $BF_3{\cdot}Et_2O$ gives the best results. However, since there has been no comprehensive structure-dependency studies of these rearrangement reactions, we decided to prepare several easily accessible steroidal epoxy adducts to investigate the influence of the neighboring double bond on bridge migration.

The preparation of new steroid structures with useful biological activities is also of interest.[5] New derivatives are prepared by functional group transformations, functionalization of different nonactivated positions[6] and modification of the steroidal skeleton, as in seco-steroids,[6a,7] or homo- and aza-steroids.[6a,8] Different positions in steroids have been bridged by heteroatoms or other functions (lactones). Furthermore, in the past 20 years, steroids with small carbon bridges have been studied as potential therapeutic agents.[5] The most thoroughly investigated are: 6,19-bridged for antiherpes virus activity, anticonvulsant and other unusual activities,[9] 2,19-bridged as aromatase inhibitors,[10] 10,11-bridged as gestagens and antigestagens,[11] and 7α,15α-bridged steroids as antihypercholesterolemics.[12]

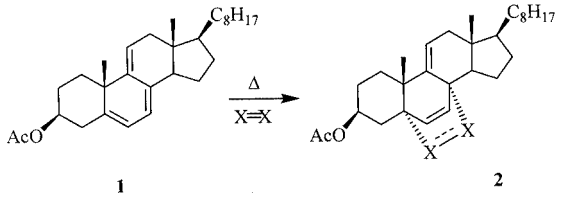
Substitution in the position C-9 in steroids is not very common. Halogen, hydroxy, methyl and cyano substituents at position C-9 are known in corticosteroids and in estrone derivatives, where this is a benzylic activated position.[6a] Only three carbon-bridged rings at the 8,9-position in steroids are known.[13] To the best of our knowledge, in steroid chemistry the presented work is the only known case where a carbocyclic ring is introduced between the two tertiary carbon atoms at the 5α,9α-positions.

[a] Institut für Organische Chemie, Technische Universität Braunschweig,
Hagenring 30, 38106 Braunschweig, Germany
Fax: (internat.) + 49-531-391-5388
E-mail: lidijabondarenko@netscape.net
[b] Faculty of Chemistry, University of Belgrade,
Studentski trg 12–16, P. O. Box 158, 11001 Belgrade, Serbia and Montenegro
[c] Fachbereich Chemie der Universität Duisburg-Essen, Campus Essen
Universitätstr. 3, 45117 Essen, Germany

  DOI: 10.1002/ejoc.200400117

Results and Discussion

The epoxy adducts were prepared using a method which is similar to those described previously.[14] The Diels–Alder reaction of 5,7,9(11)-cholestatriene[15] **1** with different dienophiles gave the corresponding adducts **2**[16] together with some unstable ene adducts in the case of acetylenedicarboxylate, as indicated by NMR spectroscopy (Scheme 2, Table 1).



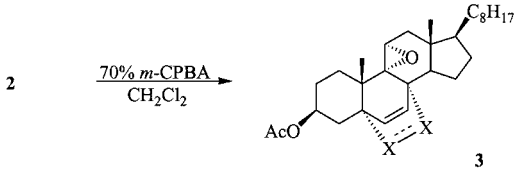
Scheme 2. The Diels–Alder reaction of 5,7,9(11)-cholestatriene acetate (**1**)

Table 1. Products and yields in the synthesis of 5α,8α-adducts **2**

Entry	X=X		Conditions	Product / Yield[a] [%]	
1.	$MeO_2C{-}{\equiv}{-}CO_2Me$	**a**	140 °C / 24 h	**2a**	50[b]
2.	$EtO_2C{-}{\equiv}{-}CO_2Et$	**b**	140 °C / 24 h	**2b**	30[c]
3.		**c**	80 °C / 6 h	**2c**	76
4.		**d**	–10 °C / 0.25 h	**2d**	75

[a] All yields refer to isolated, purified products. [b] 18% of an unstable 7-ene adduct was isolated. [c] 30% of an unstable 7-ene adduct was isolated.

Treatment of adducts **2** with *m*-CPBA in dichloromethane solution at room temperature yielded the 9,11α-epoxides **3** (Scheme 3, Table 2).



Scheme 3. Epoxidation of adducts **2**

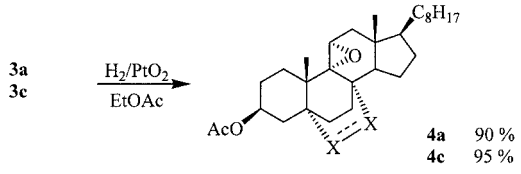
The epoxidation takes place selectively at the 9,11-double bond, since the other two double bonds are sterically more hindered.[17] Finally, the 6,7-double bond in adducts **3a**, **3c** were hydrogenated[16] in the presence of PtO_2 in ethyl acetate at atmospheric pressure (Scheme 4).

All epoxides **3a–d**, **4a**, **4c** were then allowed to react with $BF_3{\cdot}Et_2O$ under different reaction conditions (Scheme 5), and the results are presented in Table 3.

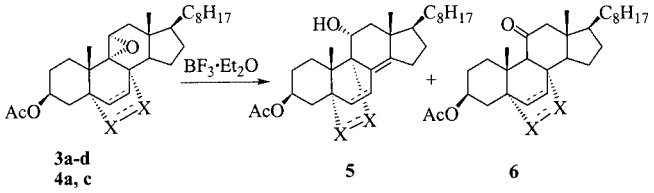
Table 2. Products and yields in the synthesis of epoxides **3**

Entry	2 X=X		Conditions	Product / Yield[a] [%]	
1.	$MeO_2C{-}{\equiv}{-}CO_2Me$	**a**	20 °C / 24 h	**3a**	85
2.	$EtO_2C{-}{\equiv}{-}CO_2Et$	**b**	20 °C / 24 h	**3b**	70
3.		**c**	20 °C / 24 h	**3c**	90
4.		**d**	20 °C / 72 h	**3d**	50[b]

[a] All yields refer to isolated, purified products. [b] 90% consumption.



Scheme 4. Hydrogenation of epoxy adducts **3a** and **3c**



Scheme 5. Rearrangement of 5α,8α-bridged 9,11α-epoxy steroids

Table 3. Products and yields of the rearrangement of 5α,9α-bridged 11α-epoxysteroids

Entry	Adduct	Solvent	Conditions	Products/Yields [%][a]
1	**2a**	Et_2O	20 °C/72 h	**2a**/95
2	**3a**	benzene	20 °C/0.1 h	**5a**/90
3	**3a**	Et_2O	20 °C/200 h	**5a**/80
4	**3b**	benzene	20 °C/0.1 h	**5b**/86
6	**3b**	Et_2O	20 °C/200 h	**5b**/85
7	**4a**	benzene	20 °C/0.2 h	**5a′**/80
8	**3c**	Et_2O	20 °C/100 h	**3c**/98
9	**3c**	benzene	20 °C/6 h	**5c**/88 + **6c**/2–5
10	**3c**	CH_2Cl_2	20 °C/12 h	**5c**/80 + **6c**/5
11	**4c**	benzene	20 °C/3 h	**5c′**/60 + **6c′**/32
12	**3d**	benzene	80 °C/4 h	**5d**/18[b]
13	**3d**	benzene	40 °C/36 h	**5d**/35[b]

[a] All yields refer to isolated, purified products. [b] The remaining complex mixture was not investigated.

The best solvents for the boron trifluoride–diethyl ether rearrangement reaction are benzene and dichloromethane because of the stabilization of the Lewis acid π-complex by

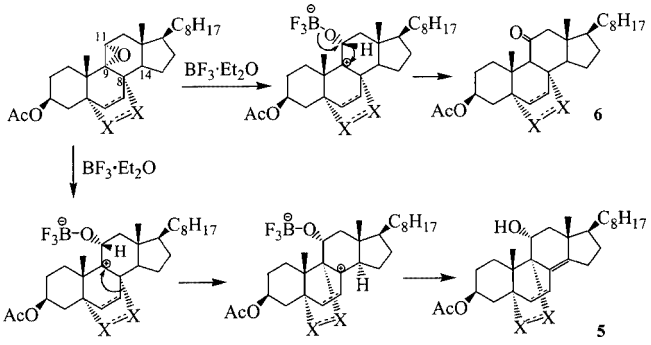
the solvent. Diethyl ether lowers the reaction rate (Entries 3, 6, 8, Table 3). The 6,7-double bond does not influence the reaction (Entry 7). However, while the double bond on the migrating bridge enhances the isomerisation reaction, its absence increases the rate of the competing epoxide-opening reaction, which forms a ketone (Entries 9, 10, Table 3), especially in the case of the completely saturated epoxide **4d** (Entry 11). The rearrangement of the triazoline epoxide **3d** can be explained by the participation of the electron pair on the nitrogen atom, while it is known from the literature that boron trifluoride−diethyl ether can cleave the triazoline, immediately regenerating the diene system.[18] The adduct **2a** does not react, thus proving that the Lewis acid opening of the epoxide is the initial reaction step.

A plausible mechanistic route, which is essentially based on the proposed mechanism for a similar acid-catalyzed rearrangement of epoxides,[3] is shown in Scheme 6. The coordination-activation of the Lewis acid to the epoxide oxygen atom leads to the C-9 carbocation intermediate, which can be stabilized in two ways. The usual 1,2-hydride shift from C-11 to C-9 with formation of the C-11 ketone **6** (Scheme 6) is not favored and the bridge at C-8 is migrating to C-9, with formation of an intermediate carbocation at C-8. This subsequently forms the 8,14-double bond by base abstraction of the proton at C-14. The bridge migrates to the α-side with retention of configuration at C-10. This rearrangement pathway is favored by an electron-rich double bond on the migrating bridge, and is stereocontrolled without further diene migration, resulting in a single product.

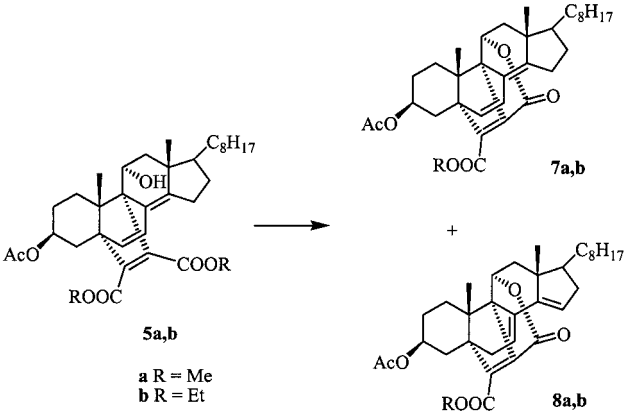
All compounds of type **5** have the same molecular formula as the starting epoxide. In the ^{1}H NMR spectra the observed change noted for 11-H in the epoxide was registered at δ = 2.8−3.5 ppm and in **5** at δ = 3.6−4.0 ppm (see Exp. Sect.) together with an IR signal at 3500 cm^{-1}, which indicates a hydroxy group at C-11. The angular methyl groups have a pattern typical for 8,14-unsaturated steroids with very similar chemical shifts.[19] The AB system of olefinic protons 6-H and 7-H were unchanged. In the ^{13}C NMR spectra signals of two new quaternary olefin carbon atoms appear, indicating a conjugated 6,8(14)-diene system, which was supported by an absorption maximum at ca. 312 nm in the UV spectra (pale yellow color). All compounds of type **5** are oils (resins), and only **5a** gave single crystals suitable for X-ray analysis. The structure presented in Figure 1, clearly shows the new five-membered ring containing the bridge at the α-side.

Compounds of type **6** were easily identified by disappearance of the 11-H signal in the ^{1}H NMR spectra and the appearance of a new signal for the C-11 oxo group in the ^{13}C NMR spectrum at δ = 212 ppm, the remainder of the molecule having resonances at about the same positions as the starting epoxide.

Furthermore, we prepared lactones **7a**,**b** and **8a**,**b** from alcohols **5a** and **5b** by acid-catalyzed[20] and thermal transesterification reactions (Scheme 7, Table 4). The bridge ester group reacts with the sterically close 11α-hydroxy group



Scheme 6. The proposed mechanism of the epoxide-opening rearrangement



Scheme 7. Lactonization of 5α,9α-bridged 11α-hydroxy steroid

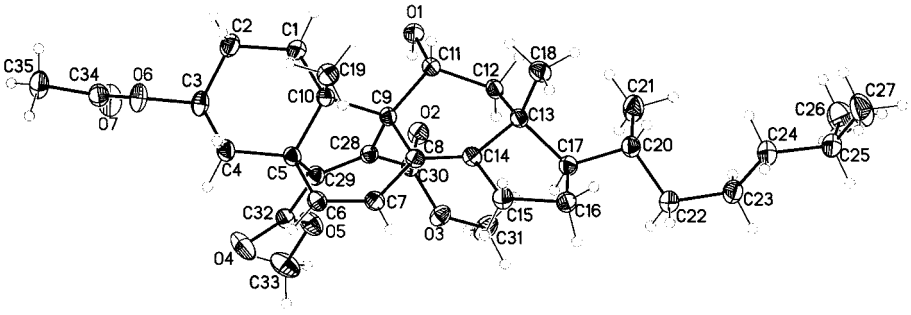


Figure 1. Structure and solid-state conformation of **5a**

Table 4. Yields of 5α,9α-bridged steroidal lactones

Entry	Alcohol	Catalyst	Conditions	Products/Yields [%][a]
1	**5a**	*p*TsOH	20 °C/24 h	**5a**/95
2	**5a**	*p*TsOH	80 °C/3 h	**7a**/64, **8a**/11
3	**5a**	none	80 °C/24 h	**7a**/42, **8a**/0, **5a**/33
4.	**5b**	*p*TsOH	80 °C/10 h	**7b**/65, **8b**/20
5	**5b**	none	140 °C/150 h	**7b**/95, **8b** 0
6	**3b**	*p*TsOH/BF_3·Et_2O	20 °C/36 h	**5b**/80

[a] All yields refer to isolated, purified products.

with elimination of methanol or ethanol. The acid catalysis increases the transesterification reaction rate (Entries 2 and 4), but it also causes the isomerisation of the 6,8(14)-diene to the 7,14-diene unit, indicated in the ^{1}H NMR spectra by signals of the two uncoupled olefinic protons instead of the AB system of the 6,8(14)-diene. The acid-catalyzed migration of steroid dienes has been investigated previously[19] and those results differ from ours, presumably because of the bridge position. The thermal lactonization only produced the lactone **7a**,**b**, but harsher conditions are needed. In both thermal and acid-catalyzed transesterification, the methyl ester is more reactive than its ethyl analogue. The one-pot rearrangement/lactonization of epoxide **3b** failed at room temperature.

In summary, we have developed a simple and efficient synthesis of a new class of 5α,9α-bridged steroid derivatives. The key step is a Lewis acid induced rearrangement, which was investigated and could be applied to other similar systems. Further cyclization/lactonization reactions produced several new steroidal lactones.

Experimental Section

General: ^{1}H and ^{13}C NMR spectra were recorded using a Bruker AC 200, ^{1}H NMR (200.1 MHz), ^{13}C NMR (50.3 MHz) and Bruker DRX-400, ^{1}H NMR (400.1 MHz), ^{13}C NMR (100.6 MHz) spectrometer. Chemical shifts (δ) are expressed in ppm downfield from tetramethylsilane using the residual nondeuterated solvent as internal standard ($CDCl_3$: ^{1}H: δ = 7.26 ppm; ^{13}C: δ = 77.00 ppm). Coupling constants are expressed in Hz. The degree of substitution of the carbon atoms was determined by employing the DEPT-135 technique. Other signal assignments were done by using H,H-COSY and C,H-correlation by HSQC/HMQC. IR spectra were recorded using a Nicolet 320 FT-IR spectrometer or Bruker Tensor 27. UV/Vis spectra were recorded using a Beckman UV 8452A Diode Array Spectrophotometer. Mass spectra were recorded using a Finnigan MAT 90 spectrometer (EI, 70 eV). Optical rotations were measured using a Propol-Digital Automatic Polarimeter, Dr. Kernchen. Melting points were determined using a Büchi 510 melting point apparatus and are uncorrected. Dry benzene, absolute puriss. over molecular sieves, was used as obtained, while dichloromethane and Et_2O were distilled from CaH_2 under nitrogen prior to use. Thin layer chromatography was performed using precoated plastic plates, polygram Sil G/ UV_{254} Macherey−Nagel & Co. (Düren), while column chromatography was performed on Silica gel 60 (70−230 mesh) from Merck. Preparative TLC was performed on PLC plates Silica gel 60 $F_{254+366}$, 2 mm from Merck. Elemental analysis: Faculty of Chemistry, University of Belgrade.

Cholesta-5,7,9(11)-trien-3β-yl Acetate (1): A solution of cholesta-5,7-dien-3β-yl acetate (4.6 g) in ethanol (270 mL), was heated to reflux, and then mercuric acetate (10 g), dissolved in a mixture of ethanol (160 mL) and acetic acid (5.5 mL), was added. The reaction mixture was refluxed for 30 min. The solvents were evaporated to dryness, and after addition of chloroform (80 mL), the solution was filtered through Celite, and the filtrate was concentrated. Crystallization from methanol gave cholesta-5,7,9(11)-trien-3β-yl acetate (**1**) [2.27 g (50%)] which was used without further purification. An analytical sample was dissolved in CH_2Cl_2, the solution filtered again through Celite, concentrated and the residue recrystallized from methanol and a little CH_2Cl_2 to give white crystals. M.p. 87−88 °C (ref.[15] 91−94 °C). ^{1}H NMR (400 MHz): δ = 0.61 (s, 3 H, 18-Me), 0.90 (d, *J* = 1.9 Hz, 3 H, 26-Me), 0.92 (d, *J* = 1.9 Hz, 3 H, 27-Me), 0.96 (d, *J* = 6.5 Hz, 3 H, 21-Me), 1.30 (s, 3 H, 19-Me), 2.08 (s, 3 H, AcO), 4.70 (m, 3 H, 3-H), 5.44 (dd, *J* = 2.6, 2.6 Hz, 1 H, 6-H), 5.55 (dd, *J* = 2.0, 4.4 Hz, 1 H, 7-H), 5.74 (dd, *J* = 1.7, 6.0 Hz, 1 H, 11-H) ppm. ^{13}C NMR (100 MHz): δ = 11.4 (q), 18.4 (q), 21.4 (q), 22.6 (q), 22.8 (2 × q), 23.9 (t), 28.0 (d), 28.3 (t), 28. 5 (t), 30.2 (d), 35.9 (d), 36.1 (t), 37.4 (t), 38.1 (t), 39.3 (s), 39.5 (t), 42.3 (s), 43.1 (t), 50.9 (d), 53.7 (s), 56.4 (d), 74.0 (d), 115.6 (d), 119.1 (d), 122.6 (d), 135.7 (s), 140.0 (s), 144.0 (s), 170.4 (s) ppm. MS (EI): *m*/*z* = 424(8) [M^+], 364 (100) [M^+ − AcOH], 349 (38) [M^+ − AcOH − Me], 209 (50). HRMS (EI) [M^+] ($C_{29}H_{44}O_2$): calcd. 424.3341; found 424.3333.

General Procedure for the Diels−Alder Addition: A solution of the diene [cholesta-5,7,9(11)-trien-3β-yl acetate] in dry xylene and a large excess of dienophile (6−10 equiv.) was refluxed under nitrogen for 24 h. In the case of maleic anhydride, the benzene solution was refluxed for 6 h. The solvent was evaporated to dryness, and the residue was chromatographed on silica gel.

5α,8α-[1′,2′-*cis*-Bis(methoxycarbonyl)etheno]cholesta-6,9(11)-dien-3β-yl Acetate (2a): Elution with CH_2Cl_2/Et_2O (96:4) afforded crude (**2a**) [2.7 g (50%)] which was crystallized from ethanol to give 1.43 g (26%) of pure product. M.p. 194−195 °C (ref.[16a] 192−194 °C). $[\alpha]_D^{20}$ = −40.00 (*c* = 1.00, $CHCl_3$). IR (Diamant-ATR): nu (tilde) = 1739 (s), 1725 (s), 1715 (s), 1267 (s), 1247 (s), 1217 (s), 1195 (m), 1023 (m) cm^{-1}. ^{1}H NMR (400 MHz): δ = 0.68 (s, 3 H, 18-Me), 0.86 (d, *J* = 1.09 Hz, 3 H 26-Me), 0.89 (d, *J* = 1.04 Hz, 3 H, 27-Me), 0.92 (d, *J* = 5.90 Hz, 3 H 21-Me), 1.14 (s, 3 H 19-Me), 2.04 (s, 3 H AcO), 2.62 (dd, *J* = 11.5, ca. 4.5 Hz, 1 H, 4-H), 2.88 (dd, *J* = 8.6, 4.8 Hz, 1 H, 12-H), 3.71 (s, 3 H, COOMe), 3.80 (s, 3 H, COOMe), 4.77 (m, 1 H, 3-H), 5.37 (d, *J* = 4.8 Hz, 1 H, 11-H), 6.13 (d, *J* = 7.3 Hz, 1 H, 7-H), 6.46 (d, *J* = 7.4 Hz, 1 H, 6-H) ppm.^{13}C NMR (100 MHz): δ = 12.5 (q, 18-Me), 18.4 (q, 21-Me), 21.3 (q, OAc), 22.4 (t), 22.6 (q, 26-Me), 22.8 (q, 27-Me), 23.8 (t), 26.5 (q, 19-Me), 26.7 (t), 27.9 (t), 28.0 (d), 29.8 (t), 35.4 (d), 35.7 (t), 36.0 (s), 39.5 (t), 41.2 (t), 41.7 (s), 45.1 (s), 46.0 (d), 51.8 (s), 52.1 (s), 52.2 (q, COOMe), 52.5 (q, COOMe), 55.8 (d, 17-C), 69.8 (d, 3-C), 118.2 (d, 11-C), 132.4 (d, 6-C), 139.3 (d, 7-C), 144.2 (s), 145.3 (s), 146.2 (s), 166.7 (s, COOMe), 167.0 (s, COOMe), 170.1 (s, AcO) ppm. MS (EI): *m*/*z* = 566 (10) [M^+], 534 (18) [M^+ − MeOH], 506 (100) [M^+ − AcOH]. $C_{35}H_{50}O_6$ (566.36): calcd. C 74.17, H 8.99; found C 74.41, H 8.19.

5α,8α-[1′,2′-*cis*-Bis(ethoxycarbonyl)etheno]cholesta-6,9(11)-dien-3β-yl Acetate (2b): Elution with CH_2Cl_2/Et_2O (97:3) afforded (**2b**) [666 mg (30%)], crystallization from methanol gave 385 mg (17%). M.p. 135 °C. $[\alpha]_D^{20}$ = −41.0 (*c* = 0.485, $CHCl_3$). IR (KBr): nu (tilde) = 1735 (s), 1720 (s), 1260−1240 (m) cm^{-1}. ^{1}H NMR

(200 MHz): δ = 0.69 (s, 3 H, 18-Me), 0.86 (d, *J* = 1.0 Hz, 3 H, 27-Me), 0.89 (s, *J* = 1.1 Hz, 3 H, 26-Me), 0.93 (d, *J* = 5.9 Hz, 3 H, 21-Me), 1.15 (s, 3 H, 19-Me), 1.26 (t, *J* = 7.14 Hz, 3 H, EtOCO), 1.29 (t, *J* = 7.08 Hz, 3 H, EtOCO), 2.02 (s, 3 H, AcO), 2.90 (dd, *J* = 4.7, 13.3 Hz, 1 H, 4-H), 2.60 [dd, *J* = 8.6, 11.7 Hz, 1 H, H−C(12)] 4.21 (m, 4 H, 2 × EtOCO), 4.81 (m, 1 H, 3-H), 5.36 (d, *J* = 4.8 Hz, 1 H, 11-H), 6.13 (d, *J* = 7.3 Hz, 1 H, 7-H), 6.46 (d, *J* = 7.4 Hz, 1 H 6-H) ppm. ^{13}C NMR (50 MHz): δ = 12.4(q, 18-Me), 13.9 (q, COOEt), 14.0 (q, COOEt), 18.4 (q, 21-Me), 21.2 (q, AcO), 22.4 (t), 22.5 (q), 22.8(q), 23.7 (t), 26.5 (q), 26.7 (t), 27.9 (t), 28.0(d), 29.8 (t), 35.3(d), 35.6 (t), 35.9 (t), 39.5 (t), 41.2(t), 41.6 (s), 45.1 (s), 45.8(d), 51.7(s), 52.1 (s), 55.8 (d), 61.0 (t, COOEt), 61.6 (t, COOEt), 69.8 (d, 3-C), 117.9 (d, 11-C), 132.3 (d, 6-C), 139.2(d, 7-C), 143.7 (s), 145.0(s), 146.3 (s), 166.2 (s, COOEt), 166.6 (s, COOEt), 170.0 (s, AcO) ppm. $C_{37}H_{54}O_6$ (594.83): calcd. C 74.71, H 10.15; found C 74.84, H 9.14.

5α,8α-(3,5-Dioxo-4-oxacyclopentane-1,2-diyl)cholesta-6,9(11)-dien-3β-yl Acetate (2c): M.p. 178−179 °C (ref.[16a] 181−182 °C). IR (Diamant-ATR): nu (tilde) = 1859 (s), 1771 (s), 1730 (s), 1252 (s), 1092 (m), 1078 (m), 1027 (s), 953 (m), 930 (s), 915 (s) cm^{-1}. ^{1}H NMR (400 MHz): δ = 0.61 (s, 3 H, 18-Me), 0.86 (d, *J* = 2.1 Hz, 3 H, 26-Me), 0.88 (d, *J* = 2.1 Hz, 3 H, 27-Me), 0.92 (d, *J* = 6.5 Hz, 3 H, 21-Me), 1.08 (s, 3 H, 19-Me), 2.07 (s, 3 H, AcO), 2.79 (d, *J* = 8.8 Hz, 1 H, 1′-H), 2.85 (m, 1 H, 4-Hα), 3.49 (d, *J* = 8.7 Hz, 1 H, 2′-H), 5.44 (dd, *J* = 7.2, 1.7 Hz, 1 H, 11-H), 5.94 (d, *J* = 8.6 Hz, 1 H, 7-H), 6.32 (d, *J* = 8.6 Hz, 1 H, 6-H) ppm. ^{13}C NMR (100 MHz): δ = 12.1 (q, 18-Me), 18.6 (q, 21-Me), 21.3 (q, AcO), 22.1 (t), 22.6 (q, 26-Me), 22.8 (q, 27-Me), 23.8 (t), 26.4 (q, 19-Me), 26.8 (t), 28.0 (d), 28.1 (t), 30.1 (t), 32.8 (t), 35.9 (t), 39.5 (t), 40.7 (t), 41.2 (s), 42.5 (s), 44.0 (d), 45.3 (s), 45.5 (s), 52.2 (d), 54.9 (d), 68.9 (d, 3-C), 119.5 (d, 11-C), 130.1 (d, 6-C), 136.5 (d, 7-C), 147.4 (s), 170.3 (s,), 170.5 (s), 171.3 (s,) ppm. MS (EI): *m*/*z* = 424 (5) [M$^+$ − maleic anhydride ($C_4H_2O_3$)], 364 (100) [M$^+$ − maleic anhydride ($C_4H_2O_3$) − AcOH].

5α,8α-(3,5-Dioxo-4-phenyl-1,2,4-triazolidine-1,2-diyl)cholesta-6,9(11)-dien-3β-yl Acetate (2d): A solution of 4-phenyl-1,2,4-triazoline-3,5-dione (ca. 300 mg) in dry acetone (10 mL) was added dropwise to a stirred and cooled (−10 °C) solution of cholesta-5,7,9(11)-trien-3β-yl acetate (758 mg, 1.34 mmol) in CH_2Cl_2 (10 mL, abs.) until the solution remained pink. The solution was filtered through neutral Al_2O_3, concentrated and chromatographed. Recrystallization from methanol gave the pure product. M.p. 134−135 °C. $[\alpha]_D^{20}$ = +16.0 (*c* = 1.00, $CHCl_3$). IR (Diamant-ATR): nu (tilde) = 1761 (m), 1731 (m), 1702 (s), 1399 (s), 1364 (s), 1240 (s), 1024 (s) cm^{-1}. ^{1}H NMR (400 MHz): δ = 0.69 (s, 3 H, 18-Me), 0.86 (d, *J* = 1.8 Hz, 3 H, 26-Me), 0.87 (d, *J* = 1.9 Hz, 3 H, 27-Me), 0.93 (d, *J* = 6.0 Hz, 3 H, 21-Me), 1.17 (s, 3 H, 19-Me), 2.02 (s, 3 H, AcO), 2.33−2.45(m, 2 H, 12-H), 2.75 (dd, *J* = 7.4, 12.0 Hz, 1 H, 4-H), 5.40 (m, 1 H, 3-H), 5.60 (dd, *J* = 1.7, 6.9 Hz, 1 H, 11-H), 6.22 (d, *J* = 8.3 Hz, 1 H, 7-H), 6.53 (d, *J* = 8.4 Hz, 1 H, 6-H), 7.27−7.34 (m, 1 H Ph), 7.37−7.47 (m, 4 H, Ph) ppm. ^{13}C NMR (100 MHz): δ = 12.5 (q, 18-Me), 18.6 (q, 21-Me), 21.3 (q, AcO), 22.5 (q, 26-Me), 22.8 (q, 27-Me), 22.9 (t), 23.7 (t), 25.2 (q, 19-Me), 26.7 (t), 27.6 (t), 28.0 (d), 30.7 (t), 32.3 (t), 35.3 (d), 35.8 (t), 39.5 (t), 40.5 (t), 41.4 (s), 43.3 (s), 47.5 (d), 54.9 (d), 64.3 (s), 65.8 (t), 66.0 (s), 70.4 (d, 3-C), 122.0 (d, 11-C), 126.0 (d, Ph), 127.8 (d, Ph), 128.8 (d, Ph), 129.3 [d, C(6)], 131.6 (s, Ph−N), 133.9 (d, 7-C), 141.7 (s, 9-C), 150.3 (s, CO), 151.4 (s, CO), 170.0 (s, AcO) ppm. MS (EI): *m*/*z* = 424 (10) [M$^+$ − $C_8H_5N_3O_2$ (PTAD)], 364 (100) [M$^+$ − $C_8H_5N_3O_2$ (PTAD) − AcOH]. $C_{37}H_{49}N_3O_4$ (599.75): calcd. C 74.08, H 8.25, N 7.00; found C 74.00, H 8.31, N 7.19.

General Procedure for the Epoxidation: A solution of the adduct in CH_2Cl_2 was added to an excess (for PTAD adduct a large excess) of 70% *m*-chloroperbenzoic acid, and was left at room temperature until full consumption of the starting material. The reaction was monitored by TLC in CH_2Cl_2/Et_2O (9:1).The organic solution was washed with solutions of $NaHSO_3$, $NaHCO_3$, NaCl, and dried with anhydrous $MgSO_4$ and the solvents were evaporated to dryness. The residue was chromatographed on silica gel when necessary.

5α,8α-[1′,2′-*cis*-Bis(methoxycarbonyl)etheno]-9α,11α-epoxycholest-6-en-3β-yl Acetate (3a): M.p. 158 °C (from ether). $[\alpha]_D^{20}$ = −94.3 (*c* = 1.00, $CHCl_3$). IR (KBr): nu (tilde) = 2955 (s), 2870 (m), 1731 (s), 1241 (s) cm^{-1}. ^{1}H NMR (400 MHz): δ = 0.81 (s, 3 H, 18-Me), 0.86 (d, *J* = 2.2 Hz, 3 H, 27-Me), 0.88 (d, *J* = 2.3 Hz, 3 H, 26-Me), 0.91 (d, *J* = 6.3 Hz, 3 H, 21-Me), 1.05 (s, 3 H, 19-Me), 2.03 (s, 3 H, AcO), 3.06 (d, *J* = 5.5 Hz, 1 H, 11-H), 3.71 (s, 3 H, COOMe), 3.82 (s, 3 H, COOMe), 4.75 (m, 1 H, 3-H), 6.29 (d, *J* = 7.5 Hz, 1 H, 6-H, 6.38 (d, *J* = 6.9 Hz, 1 H, 7-H) ppm. ^{13}C NMR (100 MHz): δ = 16.1 (q, 18-Me), 18.4 (q, 21-Me), 21.2 (q, AcO), 21.8 (t), 22.5 (q, 19-Me), 22.8 (q, 26-Me), 22.8 (q, 27-Me), 23.6 (t), 25.6 (t), 27.8 (t), 28.0 (d), 30.7 (t), 31.7 (t), 35.0 (d), 35.8 (t), 39.4 (t), 40.3 (d), 40.4 (t), 41.5 (s), 42.0 (s), 50.8 (s), 51.3 (s), 52.1 (q, COOMe), 52.5 (q, COOMe), 55.3 (d), 56.0 (d), 69.4 (s, 9-C), 73.1 (d, 3-C), 132.2 (d, 7-C), 142.1 (d), 145.7 (s), 145.8 (s), 165.9 (s), 167.0 (s), 170.0 (s) ppm. MS (EI): *m*/*z* = 582.6 (19) [M$^+$], 550.6 (60) [M$^+$ − CH_4O], 522.6 (38) [M$^+$ − AcOH], 490.5 (100) [M$^+$ − AcOH − CH_4O], 458.5 (58) [M$^+$ − AcOH − 2 × CH_4O]. HRMS (EI) [M$^+$] ($C_{35}H_{50}O_7$): calcd. 582.3557; found 582.3546.

5α,8α-[1′,2′-*cis*-Bis(ethoxycarbonyl)etheno]-9α,11α-epoxycholest-6-en-3β-yl Acetate (3b): M.p. 132−133 °C (from methanol). $[\alpha]_D^{20}$ = −87.3 (*c* = 0.795, $CHCl_3$). IR (Diamant-ATR): nu (tilde) = 1720 (s), 1255 (s), 1236 (s), 1030 (s) cm^{-1}. ^{1}H NMR (400 MHz): δ = 0.77 (s, 3 H, 18-Me), 0.86 (d, *J* = 2.2 Hz, 3 H, 26-Me), 0.88 (d, *J* = 2.2 Hz, 3 H, 27-Me), 0.91 (d, *J* = 6.3 Hz, 3 H, 21-Me), 1.26 (t, *J* = 7.1 Hz, 3 H, COOEt), 1.31 (t, *J* = 7.2 Hz, 3 H, COOEt), 2.02 (s, 3 H, AcO), 2.10 (m, 1 H, 12-H), 2.80 (m, 1 H, 2-H), 2.88 (m, 1 H, 4-H), 3.05 (d, *J* = 5.5 Hz, 1 H, 11-H), 4.17 (q, *J* = 7.0 Hz, 2 H, COOEt), 4.23 (m, 1 H, COOEt), 4.33 (m, 1 H, COOEt), 4.78 (m, 1 H, 3-H), 6.29 (d, *J* = 7.5 Hz, 1 H, 7-H), 6.39 (d, *J* = 7.6 Hz, 1 H, 6-H) ppm. ^{13}C NMR(100 MHz): δ = 13.8 (q, COOEt), 13.9 (q, COOEt), 16.1 (q, 18-Me), 18.4 (q, 21-Me), 21.2 (q, AcO), 21.8 (t), 22.5 (q, 26-Me), 22.7 (q, 27-Me), 22.8 (q, 19-Me), 23.6 (t), 25.6 (t), 27.8 (t), 27.9 (d), 30.6 (t), 31.6 (t), 35.0 (d), 35.8 (t), 39.4 (t), 40.2 (d), 40.5 (t), 41.5 (s), 42.0 (s), 50.6 (s), 51.2 (s), 55.2 (d), 56.1 (d), 61.1 (t, COOEt), 61.6 (t, COOEt), 69.5 (d), 73.1 (s), 132.2 [d,C(7)], 142.1 [d, C(8)], 145.3 (s), 145.4 (s), 165.5 (s), 166.6 (s), 169.9 (s) ppm. MS (EI): *m*/*z* = 610 (18) [M$^+$], 564 (64) [M$^+$ − C_2H_6O], 550 (25) [M$^+$ − AcOH], 504 (100) [M$^+$ − AcOH − C_2H_6O], 458 (68) [M$^+$ − AcOH − 2 × C_2H_6O]. $C_{37}H_{54}O_7$ (610.83): calcd. C 72.74, H 8.93; found C 73.13, H 9.10.

5α,8α-[1′,2′-*cis*-Bis(ethoxycarbonyl)etheno]-6,7β,9α,11α-diepoxycholest-3β-yl Acetate (3b'):[16] M.p. 146 °C. $[\alpha]_D^{20}$ = −72.0 (*c* = 1.00, $CHCl_3$). IR (ATR): nu (tilde) = 1737 (m), 1714 (s), 1382 (m), 1365 (m), 1256 (s), 1020 (s) cm^{-1}. ^{1}H NMR (200 MHz): δ = 0.87 (d, 3 H, 26-Me), 0.90 (d, 3 H, 27-Me), 0.90 (d, 3 H, 21-Me), 0.90 (s, 3 H, 18-Me), 1.25−1.34 (m, 7 H, 19-Me), 2 × COOEt), 2.60 (m, 1 H, 12-H), 3.10 (m, 1 H, 4-H), 3.08 (d, *J* = 5.4 Hz, 1 H, 11-H), 3.15 (d, *J* = 4.0 Hz, 1 H, 7-H), 3.58 (d, *J* = 4.1 Hz, 1 H, 6-H), 4.12−4.39 (m, 4 H, COOEt), 4.60(m, 1 H, 3-H) ppm. ^{13}C NMR (50 MHz): δ = 13.9 (q), 13.9 (q), 17.7 (q), 18.3 (q), 19.9 (q), 21.2 (q), 21.6 (t), 22.5 (q), 22.8 (q), 23.6 (t), 25.8 (t), 27.6 (t), 28.0 (d), 31.5 (t), 34.9 (d), 35.7 (t), 39.4 (t), 39.6 (s), 40.1 (t), 40.2 (d), 41.7 (s), 45.4 (d),

47.4 (s), 47.9 (s), 52.1 (d), 55.6(d), 55.9 (d), 61.3 (t), 61.6 (t), 69.4 (d), 70.1 (s), 134.7 (s), 137.2 (s), 164.7 (s), 166.0 (s), 169.9 (s) ppm. MS(EI): *m*/*z* = 626.5 (11) [M^+], 610.5 (10) [$M^+ - O$], 598.5 (45) [$M^+ - CO$] 581.4 (100) [$M^+ - C_2H_5O$]. HRMS (EI) [M^+] ($C_{37}H_{54}O_8$): calcd. 626.3819; found 626.3804.

5α,8α-(3,5-Dioxo-4-oxacyclopentane-1,2-diyl)-9α,11α-epoxycholest-6-en-3β-yl Acetate (3c): M.p. 170 °C (from methanol). $[\alpha]_D^{20}$ = +98.9 (*c* = 1.00, $CHCl_3$). IR (Diamant-ATR): nu (tilde) = 1846 (w), 1780 (s), 1736 (s), 1720 (s), 1240 (s), 1209 (m) cm^{-1}. ^1H NMR (400 MHz): δ = 0.69 (s, 3 H, 18-Me), 0.86 (d, *J* = 1.9 Hz, 3 H, 26-Me), 0.87 (d, *J* = 1.9 Hz, 3 H, 27-Me), 0.91 (d, *J* = 6.5 Hz, 3 H, 21-Me), 1.04 (s, 3 H, 19-C), 2.06 (s, 3 H AcO), 2.76 (m, 1 H, 4-H_α), 3.12 (d, *J* = 5.9 Hz, 1 H, 11-H), 3.48 (d, *J* = 8.5 Hz, 1 H, 1′-H), 3.57 (d, *J* = 8.5 Hz, 1 H, 2′- H), 5.10 (m, 1 H, 3-H), 5.97 (d, *J* = 8.6 Hz, 1 H, 7-H), 6.35 (d, *J* = 8.7 Hz, 1 H, 6-H) ppm. ^{13}C NMR (100 MHz): δ = 15.0 (q, 18-Me), 18.7 (q, 21-Me), 21.3 (q, AcO), 21.6 (t), 21.9 (q, 19-Me), 22.5 (q, 26-Me), 22.8 (q, 27-Me), 23.7 (t), 25.8 (t), 27.4 (t), 28.0 (t), 30.9 (t), 34.9 (d), 35.8 (t), 39.1 (s), 39.4 (t), 39.6 (t), 42.8 (s), 43.3 (d), 44.6 (s), 45.4 (s), 46.0 (d), 50.6 (d), 55.3 (d), 57.5 (d), 68.7 (d, 3-C), 70.1 (s, 9-C), 130.7 (d, 7-C), 136.1 (d, 6-C), 170.2 (s), 170.7 (s), 170.9 (s) ppm. MS (EI): *m*/*z* = 538 (100) [M^+], 520 (68) [$M^+ - H_2O$], 505 (63) [$M^+ - H_2O - CH_3$]. HRMS (EI) [M^+] ($C_{33}H_{46}O_6$): calcd. 538.3294; found 538.3282.

5α,8α-(3,5-Dioxo-4-phenyl-1,2,4-triazolidine-1,2-diyl)-9α,11α-epoxycholest-6-en-3β-yl Acetate (3d): M.p. 150−152 °C (from ether). $[\alpha]_D^{20}$ = +77.4 (*c* = 1.00, $CHCl_3$). IR (Diamant-ATR): nu (tilde) = 1762 (m), 1731 (m), 1701 (s), 1399 (s), 1239 (s) cm^{-1}. ^1H NMR (400 MHz): δ = 0.79 (s, 3 H, 18-Me), 0.88 (d, *J* = 1.8 Hz, 3 H, 26-Me), 0.90 (d, *J* = 1.9 Hz, 3 H, 27-Me), 0.95 (d, *J* = 6.2 Hz, 3 H, 21-Me), 1.13 (s, 3 H, 19-Me), 2.04 (s, 3 H, AcO), 3.28 (d, *J* = 5.4 Hz, 1 H, 11-H), 5.44 (m, 1 H, 3-H), 6.32 (d, *J* = 8.3 Hz, 1 H, 7-H), 6.58 (d, *J* = 8.4 Hz, 1 H, 6-H), 7.30−7.34 (m, 1 H, Ph), 7.40−7.50 (m, 4 H, Ph) ppm. ^{13}C NMR (100 MHz): δ = 15.9 (q, 18-Me), 18.6 (q, 21-Me), 21.2 (q, AcO), 21.4 (q, q, 19-Me), 22.2 (t), 22.5 (q, 26-Me), 22.7 (q, 27-Me), 23.6 (t), 25.3 (t), 27.4 (t), 27.6 (t), 27.9 (d), 31.5 (t), 34.8 (d), 35.7 (t), 39.3 (t), 39.4 (t), 40.3 (s), 42.2 (d), 43.4 (s), 55.3 (d), 57.9 (d, 11-C), 63.9 (s), 66.4 (s), 68.4 (s), 70.1 (d, 3-C), 126.1 (d, Ph), 127.7 (d, Ph), 128.7 (d, Ph), 129.4 (d, 6-C), 131.6 (s, Ph), 134.5 (d, 7-C), 148.4(s, CO), 150.3(s, CO), 169.7 (s, AcO) ppm. MS (EI): *m*/*z* = 615 (2) [M^+], 440 (8) [$M^+ - C_8H_5N_3O_2$], 380 (59) [$M^+ - C_8H_5N_3O_2 - AcOH$], 365 (100) [$M^+ - C_8H_5N_3O_2 - AcOH - CH_3$]. HRMS (EI) [$M^+$] ($C_{37}H_{49}N_3O_5$): calcd. 615.3672; found 615.3643.

General Procedure for the Hydrogenation:[15] The adduct (0.5 g) was dissolved in EtOAc (30 mL) and PtO_2 (50 mg) was added followed by hydrogenation at room temp. and atmospheric pressure. The reaction of the acetylenic adduct **4a** was complete after 3 h, and the maleic anhydride adduct **4c** was to 90% hydrogenated after 50 h, and was recrystallized from ether, CH_2Cl_2, and methanol.

5α,8α-[1′,2′-*cis*-Bis(methoxycarbonyl)etheno]-9α,11α-epoxycholest-3β-yl Acetate (4a): M.p. 65 °C (from methanol). $[\alpha]_D^{20}$ = −70.0 (*c* = 0.60, $CHCl_3$). IR (Diamant.ATR): nu (tilde) = 1724 (s), 1247 (s), 1032 (m), 1018 (m) cm^{-1}. ^1H NMR (200 MHz): δ = 0.63 (s, 3 H 27-Me), 0.66 (s, 3 H, 26-Me), 0.66 (s, 3 H, 18-Me), 0.68 (s, 3 H, 21-Me), 0.95 (s, 3 H, 19-Me), 1.79 (s, 3 H, AcO), 2.86 (d, *J* = 5.1 Hz, 1 H, 11-H), 3.50 (s, 3 H, COOMe), 3.56 (s, 3 H, COOMe), 4.41 (m, 1 H, 3-H) ppm. ^{13}C NMR (50 MHz): δ = 17.8 (q), 18.2 (q), 20.6 (t), 21.2 (q), 21.3 (q), 21.5 (t), 22.5 (q), 22.8 (q), 23.7 (t), 26.1 (t), 27.3 (t), 27.9 (d), 30.9 (t), 31.1 (t), 33.4 (t), 35.2 (d), 35.6 (t), 38.2 (s), 39.4 (t), 40.2 (t), 41.3 (s), 41.5 (d), 43.1 (s), 44.3 (s), 51.1 (q, COOMe), 52.3 (q, COOMe), 56.2 (d), 56.2 (d), 56.3 (d, 3-C), 70.1 (d, 11-C), 70.8 (s, 9-C), 141.8 (s), 142.3 (s), 166.0 (s), 167.2 (s), 170.0 (s) ppm. MS (EI): *m*/*z* = 584 (5) [M^+], 552 (35) [$M^+ -$ MeOH], 492 (50) [$M^+ -$ MeOH − AcOH], 460 (70) [$M^+ - 2 \times$ MeOH − AcOH]. HRMS (EI) [M^+] ($C_{35}H_{52}O_7$): calcd. 584.3713; found 584.3717.

5α,8α-(3,5-Dioxo-4-oxacyclopentane-1,2-diyl)-9α,11α-epoxycholestan-3β-yl Acetate (4c): M.p. 186 °C (from methanol). $[\alpha]_D^{20}$ = +6.8 (*c* = 1.00, $CHCl_3$). IR (Diamant-ATR): nu (tilde) = 1778 (s), 1735 (s), 1721 (s), 1241 (s), 1213 (s), 1026 (s), 939 (s) cm^{-1}. ^1H NMR (200 MHz): δ = 0.82 (s, 3 H, 18-Me), 0.83 (s, 3 H, 27-M), 0.86 (s, 3 H, 26-Me), 0.86 (d, *J* = 10.7 Hz, 3 H, 21-Me), 1.24 (s, 3 H, 19-Me), 2.01 (s, 3 H, AcO), 3.14 (d, *J* = 5.8 Hz, 1 H, 11-H), 3.26 (d, *J* = 10.1 Hz, 1 H, 1′-H), 3.52 (d, *J* = 10.1 Hz, 1 H, 2′-H), 4.94 (m, 1 H, 3-H) ppm. ^{13}C NMR (50 MHz): δ = 16.3 (q), 18.5 (q), 20.7 (q), 21.1 (t), 21.3 (q), 22.5 (q), 22.7 (q), 23.7 (t), 26.3 (t), 26.4 (t), 26.9 (t), 27.4 (t), 27.9 (d), 34.1 (t), 35.1 (d), 35.7 (t), 37.3 (s), 38.4 (s), 39.4 (t), 39.6 (t), 39.6 (s), 42.7 (s), 45.0 (d), 48.3 (d), 50.8 (d), 55.5 (d), 57.2 (d), 68.5 (s), 69.0 (d), 170.1 (s), 171.3 (s), 171.7 (s) ppm. MS (EI): *m*/*z* = 540 (37) [M^+], 480 (10) [$M^+ -$ AcOH], 442 (100) [$M^+ -$ maleic anhydride ($C_4H_2O_3$)]. HRMS (EI): *m*/*z* = [M^+] ($C_{33}H_{48}O_6$): calcd. 540.3451; found 540.3451.

General Procedure for the Rearrangement: About 0.5 mmol of the adduct was dissolved in a dry solvent (benzene, CH_2Cl_2 or Et_2O; Table 2) (25 mL) and $BF_3{\cdot}Et_2O$ (0.5 mL) was added under nitrogen or argon and the mixture left at room temp. In benzene solution a fast color change from pink-violet to blue was observed. The reaction was monitored by TLC in CH_2Cl_2/Et_2O (9:1). Following completion, ice was added and the mixture extracted with diethyl ether. The organic solution was washed with solutions of $NaHCO_3$, NaCl, and dried with anhydrous $MgSO_4$. The solution was filtered and the solvents evaporated to dryness. The residue was chromatographed on silica gel if necessary (CH_2Cl_2/Et_2O, 95:5).

5α,9α-[1′,2′-*cis*-Bis(methoxycarbonyl)etheno]-11α-hydroxycholesta-6,8(14)-dien-3β-yl Acetate (5a): M.p. 128 °C (from methanol/pentane). $[\alpha]_D^{20}$ = +272.4 (*c* = 1.00, $CHCl_3$). UV (ethanol): $\lambda_{max.}$ (log ε) = 238 (4.23), 312 (3.70). IR (KBr): nu (tilde) = 3501 (m), 1734 (s), 1725 (s), 1707 (s), 1620 (w), 1265 (m), 1244 (s), 1222 (m). ^1H NMR (400 MHz): δ = 0.86 (s, 3 H, 27-Me), 0.87 (s, 3 H, 26-Me), 0.92 (s, 3 H, 19-Me), 0.95 (d, *J* = 6.4 Hz, 3 H, 21-Me), 0.96 (s, 3 H, 18-Me), 2.01 (s, 3 H, AcO), 2.21 (m, 2 H, 12α-H), 2.37 (t, *J* = 6.7 Hz, 2 H), 2.45 (m, 1 H, 4α-H), 3.73 (d, *J* = 12 Hz, 1 H, 11α-OH), 3.74 (s, 3 H, COOMe), 3.80 (s, 3 H, COOMe), 3.95 (dt, *J* = 4.4, 12.1 Hz, 1 H, 11β-H), 4.60 (m, 1 H, 3-H), 5.61 (d, *J* = 9.5 Hz, 1 H, 7-H), 5.98 (d, *J* = 9.4 Hz, 1 H, 6-H) ppm. ^{13}C NMR (400 MHz): δ = 14.7 (q, 19-Me), 18.7 (q, 21-Me), 19.6 (q, 18-Me), 21.3 (q, AcO), 22.5 (q, COOMe), 22.7 (q, COOMe), 23.8 (t), 25.2 (t), 27.2 (t), 27.7 (t), 27.9 (d), 31.2 (t), 31.5 (t), 34.7 (d), 35.7 (t), 39.4 (t), 43.8 (t), 45.7 (s), 51.2 (s), 52.1 (d), 52.7 (d), 54.3 (s), 56.1 (d), 63.0 (s), 65.7 (d, 11-C), 71.1 (d, 3-C), 120.6 (s), 123.6 (d, 6-C), 131.3 (d, 7-C), 134.9 (s), 148.1 (s), 154.3 (s), 164.9 (s), 169.2 (s), 170.1 (s) ppm. MS (EI): *m*/*z* = 582.6 (18) [M^+], 550.6 (95) [$M^+ -$ MeOH], 518.5 (55) [$M^+ - 2 \times$ MeOH], 490.5 (27) [$M^+ - 2 \times$ MeOH − CO], 458.5 (45) [$M^+ - 2 \times$ MeOH − AcOH], 431.5 (65) [$M^+ - 2 \times$ MeOH − AcOH − C_2H_3]. HRMS (EI) [M^+] ($C_{35}H_{50}O_7$): calcd. 582.3557; found 582.3547.

5α,9α-[1′,2′-*cis*-Bis(ethoxycarbonyl)etheno]-11α-hydroxycholesta-6,8(14)-dien-3β-yl Acetate (5b): Pale yellow oil (resin). $[\alpha]_D^{20}$ = +219.7 (*c* = 1.00, $CHCl_3$). UV (ethanol): $\lambda_{max.}$ (log ε) = 238 (4.12), 316 (3.64). IR (KBr): nu (tilde) = 3468 (w), 1734 (s), 1702 (s), 1617 (w), 1280 (s), 1266 (s), 1242 (s), 1054 (s), 1030 (s) cm^{-1}. ^1H NMR

(400 MHz): δ = 0.85 (d, *J* = 0.94 Hz, 3 H, 27-Me), 0.87 (d, *J* = 0.94 Hz, 3 H, 26-Me), 0.93 (s, 3 H 19-Me), 0.95 (d, *J* = 6.32 Hz, 3 H, 21-Me), 0.96 (s, 3 H, 18-Me), 1.25 (t, *J* = 7.1 Hz, 3 H, COOEt), 1.30 (t, *J* = 7.2 Hz, 3 H, COOEt), 2.01 (s, 3 H, AcOH), 2.16−2.30 (m, 2 H, 12-H), 2.37 (t, *J* = 6.5 Hz, 2 H), 2.46 (m, 1 H, 4α-H), 3.81 (d, *J* = 11.7 Hz, 1 H, 11α-OH), 3.94 (dt, *J* = 4.2, 12.0 Hz, 1 H, 11-H), 4.13−4.31 (m, 4 H, COOEt), 4.63 (m, 1 H, 3-H), 5.61 (d, *J* = 9.5 Hz, 1 H, 7-H), 5.97 (d, *J* = 9.4 Hz, 1 H, 6-H) ppm. ^{13}C NMR (100 MHz): δ = 13.9 (q, COOEt), 14.0 (q, COOEt), 14.7 (q, 19-Me), 18.7 (q, 21-Me), 19.6 (q, 18-Me), 21.2(q, AcO), 22.5 (q, 27-Me), 22.7 (q, 26-Me), 23.6 (t), 25.2 (t), 27.2 (t), 27.8 (t), 27.9 (d), 31.2 (t), 31.5 (t), 34.6 (d), 35.7 (t), 39.4 (t), 43.9 (t), 45.7 (s), 51.1 (s), 54.3 (s), 56.0 (d), 61.1 (t, COOEt), 61.9 (t, COOEt), 63.1 (s), 65.7 (d, 11-C), 71.1 (d, 3-C), 120.8 (s), 123.6 (d, 6-C), 131.4 (d, 7-C), 134.8 (s), 147.6 (s), 153.9 (s), 164.5 (s), 168.9 (s), 170.0 (s) ppm. MS (EI): *m*/*z* = 610 (15) [M$^+$], 564 (85) [M$^+$ − EtOH], 518 (35) [M$^+$ − 2 × EtOH], 504 (22) [M$^+$ − EtOH −AcOH], 458 (40) [M$^+$ − 2 × EtOH − AcOH], 431 (55) [M$^+$ − 2 × EtOH − AcOH − C_2H_3]. HRMS (EI) [M$^+$] ($C_{37}H_{54}O_7$): calcd. 610.3870; found 610.3873.

5α,9α-[3,5-Dioxo-4-oxacyclopentane-1,2-diyl]-11α-hydroxycholesta-6,8(14)-dien-3β-yl Acetate (5c): Pale yellow oil (resin). $[\alpha]_D^{20}$ = +34.6 (*c* = 1.00, $CHCl_3$). UV (ethanol): $\lambda_{max.}$ (log ε) = 260 (4.13). IR (Diamant-ATR): nu (tilde) = 1856 (w), 1773 (s), 1721 (m), 1242 (s) cm^{-1}. ^{1}H NMR (400 MHz): δ = 0.89 (d, *J* = 2.1 Hz, 3 H 27-Me), 0.90 (d, *J* = 2.1 Hz, 3 H, 26-Me), 0.97 (s, 3 H, 19-Me), 0.98 (s, 3 H, 18-Me), 1.00 (d, *J* = 5.8 Hz, 3 H, 21-Me), 2.08 (s, 3 H, AcO), 2.29−2.45 (m, 3 H, 2-H, 4-H), 3.86 (d, *J* = 10.0 Hz, 1 H, 1′-H), 4.05 (dd, *J* = 3.7, 12.1 Hz, 1 H, 11-H), 4.32 (d, *J* = 10.0 Hz, 1 H, 2′-H), 5.08 (m, 1 H, 3-H), 5.39 (d, *J* = 9.6 Hz, 1 H, 7-H), 6.24 (d, *J* = 9.6 Hz, 1 H, 6-H) ppm. ^{13}C NMR (100 MHz): δ = 16.2 (q, 19-Me), 18.7 (q, 21-Me), 19.6, (q, 18-Me), 21.2 (q, AcO), 22.5 (q, 26-Me), 22.8 (q, 27-Me), 23.9 (t), 25.3 (t), 27.0 (t), 27.4 (t), 27.9 (d), 30.5 (t), 32.3 (t), 34.6 (d), 35.6 (t), 39.4 (t), 43.5 (t), 45.1 (s), 47.1 (d), 50.3 (s), 50.9 (s), 54.5 (d), 55.1 (d), 59.6 (s), 64.9 (d, 11-C), 69.1 (d, 3-C), 124.4 (s, 8-C), 127.3 (d, 6-C), 130.9 [d, C(7)], 152.0 [s, C(14)], 170.4 (s), 171.9 (s), 172.6 (s) ppm. MS (EI): *m*/*z* = 538 (100) [M$^+$], 520 (95) [M$^+$ − H_2O], 505 (90) [M$^+$ − H_2O − CH_3], 460 (20) [M$^+$ −H_2O − AcOH]. HRMS (EI) [M$^+$] ($C_{33}H_{46}O_6$): calcd. 538.3294; found 538.3292.

5α,8α-(3,5-Dioxo-4-oxacyclopentane-1,2-diyl)-11-oxocholest-6-en-3β-yl Acetate (6c): M.p. 223 °C (from ether). $[\alpha]_D^{20}$ = +40.0 (*c* = 1.00, $CHCl_3$). IR (Diamant-ATR): nu (tilde) = 1861 (w), 1835 (w), 1776 (s), 1720 (s), 1261 (s), 1222 (s), 1027 (s) cm^{-1}. ^{1}H NMR (400 MHz): δ = 0.86 (d, *J* = 2.4 Hz, 3 H, 27-Me), 0.86 (d, *J* = 6.0 Hz, 3 H, 21-H), 0.88 (d, *J* = 2.3 Hz, 3 H, 26-Me), 1.06 (s, 3 H, 18-Me), 1.15 (s, 3 H, 19-Me), 2.05 (s, 3 H, AcO), 2.34 (d, *J* = 7.3 Hz, 1 H), 2.56 (d, *J* = 7.29 Hz, 1 H 12-H), 2.86 (s, 1 H, 9-H), 2.89 (d, *J* = 8.8 Hz, 1 H, 1′-H), 3.58 (d, *J* = 8.7 Hz, 1 H, 2′-H), 5.16 (m, 1 H, 3-H), 6.02 (d, *J* = 8.6 Hz, 1 H, 7-H), 6.42 (d, *J* = 8.6 Hz, 1 H, 6-H) ppm. ^{13}C NMR (100 MHz): δ = 17.3 (q), 18.3 (q), 21.3 (q), 22.5 (q), 22.7 (t), 22.8 (q), 23.8 (t), 26.5 (t), 27.5 (q), 28.0 (d), 28.4 (t), 28.9 (t), 30.0 (t), 35.4 (t), 35.5 (d), 38.5 (s), 39.4 (t), 43.9 (d), 44.2 (s), 44.7 (s), 45.6 (s), 47.7 (d), 51.7 (d), 57.9 (d), 58.9 (d), 59.0 (t), 68.3 (d, 3-C), 130.6 (d, 6-C), 137 (d, 7-C), 170.2 (s), 170.8 (s), 170.9 (s), 211.4 (s, 11-C) ppm. MS (EI): *m*/*z* = 538 (4) [M$^+$], 478 (35) [M$^+$ − AcOH], 380 (100) [M$^+$ − AcOH − maleic anhydride ($C_4H_2O_3$)]. HRMS (EI) [M$^+$] ($C_{33}H_{46}O_6$): calcd. 538.3294; found 538.3276.

5α,9α-[1′,2′-*cis*-Bis(methoxycarbonyl)etheno]-11α-hydroxycholest-8(14)-en-3β-yl Acetate (5a′): Colorless oil (resin). $[\alpha]_D^{20}$ = +197.9 (*c* = 1.00, $CHCl_3$). IR (Diamant-ATR): nu (tilde) = 3441 (w), 1729 (s), 1697 (s), 1275 (s), 1241 (s), 1062 (m), 1031 (s). ^{1}H NMR (400 MHz): δ = 0.86 (d, *J* = 1.5 Hz, 3 H, 26-Me), 0.87 (d, *J* = 1.5 Hz, 3 H, 27-Me), 0.88 (s, 3 H, 19-Me) 0.93 (s, 3 H, 18-Me), 0.95 (d, *J* = 6.7 Hz, 3 H, 21-Me), 1.99 (s, 3 H, AcO), 3.62 (d, *J* = 11.0 Hz, 1 H, 11-OH), 3.75 (s, 3 H, COOMe), 3.82 (s, 3 H, COOMe), 3.96 (dt, *J* = 4.5, 11.8 Hz, 1 H, 11-H), 4.65 (m, 1 H, 3-H) ppm. ^{13}C NMR (100 MHz): δ = 15.4 (q, 18-Me), 18.6 (q, 19-Me), 18.8 (q, 21-Me), 21.3 (q, AcO), 22.5 (q, 26-Me), 22.8 (q, 27-Me), 22.8 (t), 23.8 (t), 26.0 (t), 27.2 (t), 27.9 (t), 28.0 (d), 28.4 (t), 31.1 (t), 34.0 (t), 34.5 (d), 35.8 (t), 39.5 (t), 44.5 (s), 45.4 (t), 50.2 (s), 52.0 (q, COOMe), 52.7 (q, COOMe), 53.3 (s), 57.2 (d), 63.6 (s), 66.1 (d, 11-C), 71.3 (d, 3-C), 120.0 (s), 139.3 (s), 146.2 (s), 146.6 (s), 165.9 (s), 168.3 (s), 170.1 (s) ppm. MS (EI): *m*/*z* = 584 (5) [M$^+$] 566 (20) [M$^+$ − H_2O], 552 (50) [M$^+$ − MeOH], 534 (22) [M$^+$ − MeOH − H_2O], 506 (30) [M$^+$ − H_2O − AcOH], 474 (45) [M$^+$ − MeOH − H_2O − AcOH], 460 (50) [M$^+$ − 2 × MeOH − AcOH], 446 (100) [M$^+$ − MeOH − H_2O − AcOH − CO]. HRMS (EI) [M$^+$] ($C_{33}H_{48}O_6$): calcd. 584.3713; found 584.3712.

5α,8α-(3,5-Dioxo-4-oxacyclopentan-1,2-diyl)-11-oxocholestan-3β-yl Acetate (6c′): M.p. 201 °C (from ether). $[\alpha]_D^{20}$ = +60.4 (*c* = 1.00, $CHCl_3$). IR (Diamant-ATR): nu (tilde) = 1859 (w), 1833 (w), 1773 (s), 1716 (s), 1257 (s), 1222 (s), 1022 cm^{-1}. ^{1}H NMR (400 MHz): δ = 0.88 (d, *J* = 5.9 Hz, 3 H, 21-Me), 0.89 (d, *J* = 2.3 Hz, 3 H, 26-Me), 0.89 (s, 3 H, 18-Me), 0.90 (d, *J* = 2.3 Hz, 3 H, 27-Me), 1.21 (s, 3 H, 19-Me), 2.05 (s, 3 H, AcO), 2.60 (d, *J* = 17.4 Hz, 1 H, 12-H), 2.88 (dd, *J* = 1.9, 10.3 Hz, 1 H, 1′-H), 3.13 (s, 1 H, 9-H), 3.60 (dd, *J* = 2.5, 10.3 Hz, 1 H, 2′-H), 5.08 (m, 1 H, 3-H) ppm. ^{13}C NMR (100 MHz): δ = 17.3 (q, 19-Me), 18.1 (q, 21-Me +18-Me), 21.2 (q, AcO), 21.5 (t), 22.5 (q, 26-Me), 22.8 (q, 27-Me), 23.7 (t), 25.2 (t), 25.5 (d), 26.2 (t), 26.4 (t), 27.8 (t), 28.0 (d), 28.9 (t), 32.0 (t), 35.3 (t), 37.9 (s), 38.0 (s), 39.3 (s), 43.7 (d), 45.4 (s), 48.7 (d), 52.3 (d), 57.3 (d), 57.9 (t), 58.3 (d), 68.6 [d, C(3)], 170.2 (s), 171.9 (s), 212.1 (s, 11-C) ppm. MS (EI): *m*/*z* = 540 (4) [M$^+$], 522 (2) [M$^+$ − H_2O], 480 (100) [M$^+$ − AcOH]. HRMS (EI) [M$^+$] ($C_{33}H_{48}O_6$): calcd. 540.3451; found 540.3452.

5α,9α-(3,5-Dioxo-4-oxacyclopentane-1,2-diyl)-11α-hydroxycholest-8(14)-en-3β-yl Acetate (5c′): Colorless oil (resin). $[\alpha]_D^{20}$ = +75.5 (*c* = 1.02, $CHCl_3$). IR (Diamant-ATR): nu (tilde) = 3454 (w), 1853 (w), 1773 (s), 1718 (s), 1238 (s), 1210 (s), 1027 (s) cm^{-1}. ^{1}H NMR (400 MHz): δ = 0.89 (d, *J* = 2.2 Hz, 3 H, 27-Me), 0.91 (d, *J* = 2.2 Hz, 3 H, 26-Me), 0.93 (s, 3 H, 19-Me), 0.98 (d, *J* = 6.9 Hz, 3 H, 21-Me), 0.99 (s, 3 H, 18-Me), 2.06 (s, 3 H AcO), 3.74 (d, *J* = 11.5 Hz, 1 H, 1′-H), 4.03 (t, *J* = 8.1 Hz, 1 H, 11-H), 4.42 (d, *J* = 11.5 Hz, 1 H, 2′-H), 5.00 (m, 1 H, AcO) ppm. ^{13}C NMR (100 MHz): δ = 17.2 (q, 18-Me), 18.7 (q, 21-Me), 19.0 (q, 19-Me), 21.2 (q, AcO), 22.2 (t), 22.5 (q, 26-Me), 22.8 (q, 27-Me), 23.9 (t), 26.1 (t), 27.0 (t), 27.6 (t), 27.9 (d), 29.9 (t), 31.1 (t), 34.6 (d), 35.7 (t), 36.0 (t), 39.4 (t), 44.2 (s), 44.7 (t), 46.5 (d, 2′-C), 49.1 (s), 49.7 (d. 1′-C)), 50.4 (s), 56.0 (d), 60.1 (s), 65.2 (d, 11-C), 69.3 (d, 3-C), 122.0 (s, 8-C), 146.9 (s, 14-C), 170 (s), 172.6 (s), 172.9 (s) ppm. MS (EI): *m*/*z* = 540 (10) [M$^+$], 522 (36) [M$^+$ − H_2O], 447 (100) [M$^+$ − H_2O − AcOH − CH_3]. HRMS (EI) [M$^+$] ($C_{33}H_{48}O_6$): calcd. 540.3451; found 540.3447.

5α,9α-(3,5-Dioxo-4-phenyl-1,2,4-triazolidine-1,2-diyl)-11α-hydroxycholest-6,8(14)-dien-3β-yl Acetate (5d): Colorless oil (resin). $[\alpha]_D^{20}$ = +404.0 (*c* = 0.85, $CHCl_3$). UV (ethanol): $\lambda_{max.}$ (log ε) = 204 (5.28), 222 (4.29), 270 (4.17). IR (Diamant-ATR): nu (tilde) = 3478 (w), 1762 (m), 1710 (s), 1398 (s), 1362 (m), 1238 (s) cm^{-1}. ^{1}H NMR (400 MHz): δ = 0.85 (d, *J* = 1.9 Hz, 3 H, 26-Me), 0.87 (d, *J* = 1.9 Hz, 3 H, 27-Me), 0.93 (s, 3 H, 19-Me), 0.98 (d, *J* = 0.98 Hz, 3 H, 21-Me), 1.03 (s, 3 H, 18-Me), 2.04 (s, 3 H, AcO), 2.92-2-97 (m, 1 H, 4-H), 4.04 (dd, *J* = 4.7, 12.2 Hz, 1 H, 11-H), 5.26 (m, 1 H, 3-

H), 5.28 (d, J = 16.6 Hz, 1 H, 11-OH), 5.60 (d, J = 9.6 Hz, 1 H, 7-H), 6.30 (d, J = 9.5 Hz, 1 H, 6-H), 7.30−7.37 (m, 1 H, Ph), 7.38−7.45 (m, 4 H, Ph) ppm. ^{13}C NMR(100 MHz): δ = 15.0 (q, 18-Me), 18.7 (q, 21-Me), 18.8 (q, 19-Me), 21.2 (q, AcO), 22.5 (q, 26-Me), 22.8 (q, 27-Me), 23.9 (t), 25.5 (t), 26.9 (t), 27.7 (t), 28.0 (d), 29.6 (t), 32.8 (t), 34.5 (d), 35.7 (t), 39.4 (t), 42.5 (t), 45.0 (s), 49.2 (s), 55.5 (d), 64.4 [d, C(11)], 68.7 (s, 5-C), 70.0 (d, 3-C), 71.8 (s, 9-C), 121.6 (s), 125.6 (d, 7-C), 125.7 (d, Ph), 128.0 (d, 6-C), 128.2 (d, Ph), 129.0 (d, Ph), 131.6 (s, Ph), 153.3 (s), 155.3 (s, CO), 155.7 (s, CO), 170.1 (s, AcO) ppm. MS (EI): m/z = 615 (75) [M$^+$], 379 (62) [M$^+$ − AcOH − $C_8H_6N_3O_2$]. HRMS (EI) [M$^+$] ($C_{37}H_{49}N_3O_5$): calcd. 615.3672; found 615.3666.

General Procedure for the Lactonization: A solution of the alcohol adduct was heated at reflux in benzene or xylene with or without addition of a catalytic amount of *p*-toluenesulfonic acid (Table 3). The reaction was monitored by TLC in CH_2Cl_2/Et_2O (9:1). After completion of the reaction, diethyl ether was added to the mixture resulting solution was washed with water, solutions of $NaHCO_3$ and NaCl, and dried with anhydrous $MgSO_4$. The mixture was purified by preparative TLC developing several times in CH_2Cl_2/Et_2O (95:5).

5α,9α-[1′-*cis*-Bis(methoxycarbonyl)etheno]-11α,2′-lactonocholesta-6,8(14)-dien-3β-yl Acetate (7a): M.p. 129−130 °C (pale yellow crystals from ethanol/pentane). $[\alpha]_D^{20}$ = +5.7 (c = 0.92, $CHCl_3$). UV (ethanol): $\lambda_{max.}$ (log ε) = 210 (4.01), 244 (4.38), 348 (3.30). IR (KBr): nu (tilde) = 1765 (s), 1737 (s), 1716 (s), 1244 (s), 1231 (s), 1099 (s), 1076 (m), 1030 (s) cm^{-1}. ^{1}H NMR (400 MHz): δ = 0.86 (d, J = 1.3 Hz, 3 H, 27-Me), 0.88 (d, J = 1.4 Hz, 3 H, 26-Me), 089 (s, 3 H, 19-Me), 0.97 (d, J = 6.5 Hz, 3 H, 21-Me), 1.04 (s, 3 H, 18-Me), 2.02 (s, 3 H, AcO), 2.33−2.50 (m, 3 H, 2-H, 4-H), 2.64 (q, J = 7.0 Hz, 1 H, 12-H), 3.89 (s, 3 H, COOMe), 4.68 (m, 1 H, 3-H), 4.76 (dd, J = 7.0, 8.9 Hz, 1 H, 11-H), 5.64 (d, J = 9.5 Hz, 1 H, 7-H), 6.01 (d, J = 9.4 Hz, 1 H, 6-H) ppm. ^{13}C NMR (100 MHz): δ = 17.1 (q, 18-Me), 18.9 (q, 21-Me), 19.0 (q, 19-Me), 21.2 (q, AcO), 22.5 (q, 27-Me), 22.8 (q, 26-Me), 23.7 (t), 25.7 (t), 27.0 (d), 27.3 (t), 28.0 (d), 28.7 (t), 31.3 (t), 34.5 (d), 35.8 (t), 39.4 (t), 43.2 (s), 43.7 (t), 52.5 (d), 55.2 (d), 58.1 (s), 60.6 (s), 60.8 (s), 70.4 [d, C(3)], 74.3 (d, 11-C), 120.9 (s), 123.9 (d, 6-C), 130.5 (d, 7-C), 139.3 (s), 148.3 (s), 152.6 (s), 162.8 (s), 163.1 (s), 170.0 (s) ppm. MS (EI): m/z = 550 (33) [M$^+$], 518 (60) [M$^+$ − MeOH], 431 (100) [M$^+$ − MeOH − $MeOCOHCH_2$]. HRMS (EI) [M$^+$] ($C_{34}H_{46}O_6$): calcd. 550.3294; found 550.3287.

5α,9α-[1′-*cis*-Bis(ethoxycarbonyl)etheno)]-11α,2′-lactonocholesta-6,8(14)-dien-3β-yl Acetate (7b): M.p. 147−148 °C (pale yellow crystals from ethanol/pentane). $[\alpha]_D^{20}$ = +7.8 (c = 0.42, $CHCl_3$).UV (ethanol): $\lambda_{max.}$ (log ε) = 212 (2.96), 244 (3.34), 350 (2.31). IR (KBr): nu (tilde) = 1763 (s), 1739 (s), 1710 (s), 1295 (s), 1245 (s), 1091 (s), 1076 (s), 1027 (s) cm^{-1}. ^{1}H NMR (400 MHz): δ = 0.79 (d, J = 1.4 Hz, 3 H, 27-Me), 0.81 (d, J = 1.4 Hz, 3 H, 26-Me), 0.82 (s, 3 H, 19-Me), 0.91 (d, J = 6.5 Hz, 3 H, 21-Me), 0.97 (s, 3 H, 18-Me), 1.29 (t, J = 7.1 Hz, 3 H, COOEt), 1.94 (s, 3 H, AcO), 2.26−2.43 (m, 3 H, 2-H, 4-H), 2.56 (q, J = 7.0 Hz, 1 H, 12-H), 4.28 (q, J = 7.1 Hz, 2 H, COOEt), 4.64 (m, 1 H, 3-H), 4.68 (dd, J = 7.0, 8.8 Hz, 1 H, 11-H), 5.57 (d, J = 9.5 Hz, 1 H, 7-H), 5.93 (d, J = 9.4 Hz, 1 H, 6-H) ppm. ^{13}C NMR (100 MHz): δ = 14.0 (q, COOEt), 17.1 (q, 18-Me), 18.9 (q, 21-Me), 19.1 (q, 19-Me), 21.2 (q, AcO), 22.5(q, 27-Me), 22.7 (q, 26-Me), 23.7 (t), 25.7 (t), 27.0 (t), 27.3 (t), 27.9 (d), 28.6 (t), 31.3 (t), 34.5 (d), 35.7 (t), 39.4 (t), 43.1 (s), 43.6 (t), 55.1 (d), 57.9 (s), 60.6 (s), 60.7 (s), 61.7 (t), 70.4 (d, 3-C), 74.2 (d, 11-C), 120.9 (s), 123.8 (d), 130.6 (d), 139.0 (s), 148.6 (s), 152.4 (s), 162.6 (s), 162.7 (s), 169.9 (s) ppm. MS (EI): m/z = 564.4 (50) [M$^+$], 518.4 (58) [M$^+$ − EtOH], 504.4 (30) [M$^+$ − AcOH], 458.4 (40) [M$^+$ − AcOH − EtOH], 431.4 (100) [M$^+$ − AcOH − EtOH − C_2H_3]. $C_{35}H_{48}O_6$ (564.35): calcd. C 74.44, H 8.57; found C 74.60, H 8.57.

5α,9α-[1′-*cis*-Bis(ethoxycarbonyl)etheno]-11α,2′-lactonocholesta-7,14-dien-3β-yl Acetate (8b): Pale yellow oil. IR (KBr): nu (tilde) = 1771 (s), 1734 (s), 1266 (s), 1242 (s) cm^{-1}. ^{1}H NMR (400 MHz): δ = 0.79 (d, J = 2.4 Hz, 3 H, 27-Me), 0.81 (d, J = 2.4 Hz, 3 H, 26-Me), 0.83 (s, 3 H, 19-Me), 0.88 (d, J = 6.6 Hz, 3 H, 21-Me), 1.12 (s, 3 H, 18-Me), 1.27 (t, J = 7.1 Hz, 3 H, COOEt), 1.95 (s, 3 H, AcO), 2.08 (dd, J = 3.1, 20.0 Hz, 1 H, 6-H), 2.45 (dd, J = 3.8, 19.9 Hz, 1 H, 6-H), 2.29−2.39 (m, 2 H 16-H), 2.43−2.58 (m, 2 H, 12-H), 4.23 (dq, J = 1.7, 7.1 Hz, 2 H, COOEt), 4.54−4.64 (m, 2 H, 11-H, 3-H), 5.53 (d, J = 1.7 Hz, 1 H, 15-H), 5.60 (dd, J = 3.4, 3.7 Hz 1 H, 7-H) ppm. ^{13}C NMR (100 MHz): δ = 14.0 (q, COOEt), 15.8 (q, 18-Me), 18.7 (q, 21-Me), 21.2 (q, AcO), 22.5 (q, 26-Me), 22.8 (q, 27-Me), 23.1 (q, 19-Me), 23.9 (t), 28.0 (d), 28.1 (t), 30.2 (t), 33.3 (t), 34.1 (t), 34.4 (d), 35.6 (t), 35.8 (t), 39.5 (t), 39.7 (t), 43.6 (s), 47.4 (s), 58.1 (d), 59.4 (s), 61.5 (s), 62.4 (t, CH_3CH_2OCO), 70.5 (d), 77.0 (d, 11-C), 120.7 (d), 123.6 (d), 134.3 (s), 135.9 (s), 146.4 (s), 150.1 (s), 161.8 (s), 162.9 (s), 170.0 (s) ppm. MS (EI): m/z = 564 (25) [M$^+$], 458 (24) [M$^+$ − AcOH − EtOH,], 411 (100). HRMS (EI) [M$^+$] ($C_{35}H_{48}O_6$): calcd. 564.3451; found 564.3424.

X-ray Crystallography Data Collection and Structure Refinement for 5a: A colorless single crystal (0.28 × 0.22 × 0.14 mm) of $C_{35}H_{50}O_7$ (582.75) was measured at 203(2) K with a Siemens SMART CCD 1 K system. Cell dimensions: a = 7.709(2), b = 8.647(3), c = 12.797(4), α = 73.939(6), β = 85.231(6), γ = 82.784(6), V = 812.3(4) Å^3, ρ = 1.191 g·cm^{-3}. Triclinic space group $P1$, 9776 intensities collected ($\theta_{max.}$ = 28.46°), 7012 unique (R_{int} = 0.0196), 6108 observed [$I > 2\sigma(I)$], empirical absorption correction (Bruker AXS SADABS program multiscan V2.03) max/min transmission 1.00/0.91, R_{merg} before/after correction 0.0926/0.0293, absorption coefficient 0.081 mm^{-1}, structure solution with direct methods and refinement on F^2 with Bruker AXS SHELXTL Vers. 5.10 DOS/WIN95/NT, 379 parameters, GOF = 1.118, $R1$ = 0.0472, $wR2$ = 0.1188, all data: $R1$ = 0.0557, $wR2$ = 0.1300, $w = 1/[\sigma^2(F_o^2) + (0.0842 \cdot P)^2]$, where $P = (F_o^2 + 2F_c^2)/3$, absolute structure parameter 0.1(7) (absolute structure not reliably determined), residual electron density 0.370 and −0.200 e·Å^{-3}, hydrogen treatment: riding model based on idealized geometries with the 1.2-fold (1.5-fold for methyl and hydroxy groups) isotropic displacement parameters of the equivalent U_{ij} values of the corresponding carbon atom. CCDC-231711 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; Fax: (internat.) + 44-1223-336-033; or E-mail: deposit@ccdc.cam.ac.uk].

Acknowledgments

Financial support of this work by the Deutsche Forschungsgemeinschaft (fellowship to L. B.) and Prof. H. Hopf is gratefully acknowledged.

[1] H. B. Henbest, T. I. Wrigley, *J. Chem. Soc.* **1957**, 4596−4604.
[2] [2a] V. Cornel, in *Handbook of Reagents for Organic Synthesis: Acidic and Basic Reagents* (Ed.: J. Reich, J. H. Rigby), Wiley, Chichester **2000**, p. 50−59. [2b] K. Ishihara, in: *Lewis Acid in Organic Synthesis* (Ed.: H. Yamamoto),Wiley-VCH, Weinheim, **2000**, vol. 1, p. 101−104. [2c] J. G. Smith, *Synthesis* **1984**, 629−656.
[3] [3a] M. Nakatani, M. Nakamura, A. Suzuki, M. Inoue, T. Ka-

toh, *Org. Lett.* **2002**, *4*, 4483−4486. [3b] Q. Cheng, T. Oritani, T. Horiguchi, *Tetrahedron* **1999**, *55*, 12099−12108. [3c] H. Hideyuki, S. Jun'ichi Kobayashi, *Tetrahedron Lett.* **1999**, *40*, 2149−2152. [3d] F. J. Parodi, N. H. Fischer, *J. Chem. Soc., Chem. Commun.* **1986**, 1405−1405. [3e] M. Taran, B. Delmond, *J. Chem. Soc., Cem. Commun.* **1984**, 716−718. [3f] T. Nakano, A. C. Spinelli, A. Martín, A. Usubillaga, A. T. McPail, K. D. Onan, *Tetrahedron Lett.* **1982**, *23*, 3627−3630.

[4] J. Wölfling, E. Frank, G. Schneider, L. F. Tietze, *Eur. J. Org. Chem.* **2004**, 90−100.

[5] [5a] J. F. Zeelen, *Princ. Med. Biol.* **1997**, *8B*, 427−463. [5b] J. F. Zeelen, *Medicinal Chemistry of Steroids*, Elsevier, Amsterdam, **1990**. [5c] R. T. Blickenstaff, *Antitumor Steroids*, Academic Press, New York, **1992**.

[6] [6a] J. Fried, J. A. Edwards, *Organic Reactions in Steroid Chemistry*, Van Nostrand Reinhold Company, New York, **1972**, vol. 1−2. [6b] R. Skoda-Földes, L. Kollár, *Chem. Rev.* **2003**, *103*, 4095−4129.

[7] [7a] S. Bäurle, T. Blume, A. Mengel, C. Parchmann, W. Skuballa, S. Bäsler, M. Schäfer, D. Sülzle, H-P. Wrona-Metzinger, *Angew. Chem.* **2003**, *115*, 4091−4094. [7b] E. Winterfeldt, *Chimia* **1993**, *47*, 39−45. [7c] Lj. Lorenc, L. Bondarenko-Gheorghiu, N. Krstić, H. Fuhrer, J. Kalvoda, M. Lj. Mihailović, *Helv. Chim. Acta* **1995**, *78*, 891−898. [7d] Lj. Lorenc, L. Bondarenko, V. Pavlović, H. Fuhrer, G. Rihs, J. Kalvoda, M. Lj. Mihailović, *Helv. Chim. Acta* **1989**, *72*, 608−623.

[8] J. W. Morzyeki, *Pol. J. Chem.* **1995**, *69*, 321−340.

[9] The 6,19-bridges: [9a] E. Petrera, M. Joselevich, A. Ghini, G. Burton, C. E. Coto, *Antiviral Chem. Chemother.* **2003**, *14*, 243−248. [9b] M. Joselevich, A. Ghini, G. Burton, *Org. Biomol. Chem.* **2003**, *1*, 939−943.

[10] The 2,19-bridges: [10a] N. P. Peet, J. O. Johnston, J. P. Burkhart, *US 5491136*, **1996**; *Chem. Abstr.* **1996**, *124*, 289995. [10b] N. P. Peet, J. O. Johnston, J. P. Burkhart, L. C. Wright, *J. Steroid Biochem. Mol. Biol.* **1993**, *44*, 409−420. [10c] J. P. Burkhart, E. W. Huber, F. M. Laskovics, N. P. Peet, *J. Org. Chem.* **1992**, *57*, 5150−5154. [10d] J. O. Johnston, N. P. Peet, J. P. Burkhart, *EP 488383*, **1992**; *Chem. Abstr.* **1992**, *117*, 131436.

[11] The 10,11-bridges: [11a] W. Schewede, W. Halfbrodt, J. Kuhnke, R. Krattenmacher, H.-P. Muhn, K.-H. Fritzemier, *DE 4413184*, **1995**; *Chem. Abstr.* **1996**, *124*, 56404. [11b] W. Schwede, K.-H. Fritzemeier, W. Halfbrodt, R. Krattenmacher, P. Muhn, G. Neef, E. Ottow, K. Schollkopf, *Steroids* **1998**, *63*, 166−177. [11c] W. Halfbrodt, A. Clewe, K. Schoellkopf, W. Schwede, K.-H. Fritzemier, C. Hegele-Hartung, H.-P. Muhn-Seipoldy, *DE 4337416*, **1995**; *Chem. Abstr.* **1995**, *123*, 83834. [11d] E. Ottow, R. Wiechert, G. Neef, S. Beier, W. Elger, D. A. Henderson, *US 5095129*, **1992**; *Chem. Abstr.* **1992**, *117*, 131435.

[12] The 7α,15α-bridges: [12a] U. Egner, K.-H. Fritzmeier, W. Halfbrodt, N. Heinrich, J. Kuhnke, A. Muller-Fahrnow, G. Neef, *Tetrahedron* **1999**, *55*, 11267−11274. [12b] W. K. Chong, W.-R. Chao, D. M. Yasuda, D. M. Johansson, M. A. Avery, M. Tanabe, *WO 93/255,568*, **1993**; *Chem. Abstr.* **1994**, *121*, 57783. [12c] L. G. Bondarenko-Gheorghiu, Lj. B. Lorenc, M. Lj. Mihailović, *J. Serb. Chem. Soc.* **2000**, *65*, 147−156.

[13] [13a] V. Dave, R. Farwaha, P. de Mayo, J. B. Stothers, *Can. J. Chem.* **1985**, *63*, 2401−2405. [13b] J. F. Blount, G. D. Gray, K. S. Atwal, T. Y. R. Tsai, K. Wiesner, *Tetrahedron Lett.* **1980**, *21*, 4413−4416.

[14] J. P. Connolly, S. F. O Muircheartaigh, J. B. Thomson, *J. Chem. Soc. C* **1970**, 508−513.

[15] [15a] F. Ramirez, J. Marecek, S. S. Yemul, *J. Org. Chem.* **1983**, *48*, 1417−1420. [15b] A. van der Gen, J. Lakeman, M. A. M. P. Gras, H. O. Huisman, *Tetrahedron* **1964**, *20*, 2521−2530. [15c] M. Inhoffen, *Chem. Ber.* **1954**, *87*, 146−159. [15d] A. Windaus, M. Deppe, C. Roosen-Runge, *Justus Liebigs Ann. Chem.* **1939**, *537*, 1−10.

[16] [16a] A. van der Gen, W. A. Zunnebeld, U. K. Pandit, *Tetrahedron* **1965**, *21*, 3651−3659. [16b] D. W. Guest, D. H. Williams, *J. Chem. Soc., Perkin Trans. 1* **1979**, 1695−1697. [16c] A. Abramovitch, P. W. Le Quesne, *J. Org. Chem.* **1974**, *39*, 2197−2201

[17] The use of 77% *m*CPBA gave also some 9,11:6,7-diepoxides (**3b′**) causing purification problems. With 70% *m*CPBA monoepoxide is the only product.

[18] J. Brynjolffssen, A. Emke, D. Hands, J. M. Midgley, W. Basil Whalley, *J. Chem. Soc., Chem. Commun.* **1975**, 633−633.

[19] H. Seto, S. Fujioka, H. Koshino, S. Takatsuto, S. Yoshida, *J. Chem. Soc., Perkin Trans. 1* **2000**, 1697−1703.

[20] [20a] Gregory S. Hamilton, in *Handbook of Reagents for Organic Synthesis: Acidic and Basic Reagents* (Ed.: J. Reich, J. H. Rigby), Wiley, Chichester, **2000**, p. 402−405. [20b] E. J. Cory, D. J. Brunelle, K. C. Nicolaou, *J. Am. Chem. Soc.* **1977**, *99*, 7359−7360.

Received February 23, 2004

