# Photochemical Transformation of Bufadienolide into 14β,21-Epoxycholanes *via* Photolytic Methanolysis[1]

**Takahiro Tanase, Nobutoshi Murakami, Akito Nagatsu and Jinsaku Sakakibara***
*Faculty of Pharmaceutical Sciences, Nagoya City University, 3-1, Tanabe-dori, Mizuho-ku, Nagoya 467, Japan*

A naturally occurring bufadienolide, proscillaridin **1a**, and its aglycone, scillarenin **1b**, were subjected to photolysis in MeOH with a high-pressure mercury arc lamp to afford novel 14β,21-epoxy-21-methoxycholadienes **2a–4a** and **2b–4b** and 14β,21-epoxy-22-methoxycholadienes **5a**, **5b**, **6a** and **6b**, along with 14β,21-epoxycholatrienes **7a** and **7b**. These structures were elucidated from spectroscopical evidence including NOE experiments.

Photochemical reactions of the α-pyrone ring[2] as well as the Diels–Alder reaction[3] have been investigated. Despite studies on the photochemical reactions of bufadienolides which have α-pyrone rings, the actual photoproducts have never been elucidated. In addition, photochemical behaviour of bufadienolide glycosides such as proscillaridin **1a**[4] and scillaren A[4] have never been studied. Therefore, we undertook investigation on the photochemical reaction of the bufadienolide glycoside, proscillaridin **1a**, as a part of our studies on its chemical transformations.[5] This report is the full account of the photochemical transformation of proscillaridin **1a** *via* photolytic alcoholysis.

## Results and Discussion

A solution of proscillaridin **1a** in MeOH was irradiated in a Pyrex vessel with a high-pressure mercury arc lamp (400 W) at room temperature for 5 h under nitrogen atmosphere to show disappearance of the spot of **1a** on TLC and to afford a photoproduct exhibiting one spot on TLC. The photoproduct was subjected to silica gel column chromatography followed by reversed phase high-performance liquid chromatography (HPLC) to furnish six photoproducts **2a** (20%), **3a** (17%), **4a** (8%), **5a** (4%), **6a** (4%) and **7a** (35%).

Compounds **2a–6a** were shown to have the molecular formula $C_{32}H_{48}O_9$ by their elemental analyses. The IR spectrum of **2a** exhibited an ester carbonyl absorption band at 1740 $cm^{-1}$ and lacked a conjugated carbonyl absorption. Compared with proscillaridin **1a**, the $^1H$ NMR spectrum of **2a** was devoid of the signals derived from the α-pyrone moiety [$\delta_H$ 6.23 (1 H, d, *J* 9.8 Hz, 23-H), 7.23 (1 H, d, *J* 2.5 Hz, 21-H) and 7.93 (1 H, dd, *J* 2.5 and 9.8 Hz, 22-H)]. Instead, the spectrum had new signals due to one methine proton [$\delta_H$ 4.88 (1 H, s)] indicating the presence of a ketal moiety, two methoxy protons [$\delta_H$ 3.38 and 3.68 (3 H each, both s)] and one olefinic proton [$\delta_H$ 5.55 (1 H, dd, *J* 6.8 and 7.9 Hz)]. As shown in the $^{13}C$ NMR ($\delta_C$ 101.9), the compound had a ketal moiety (Table 1).

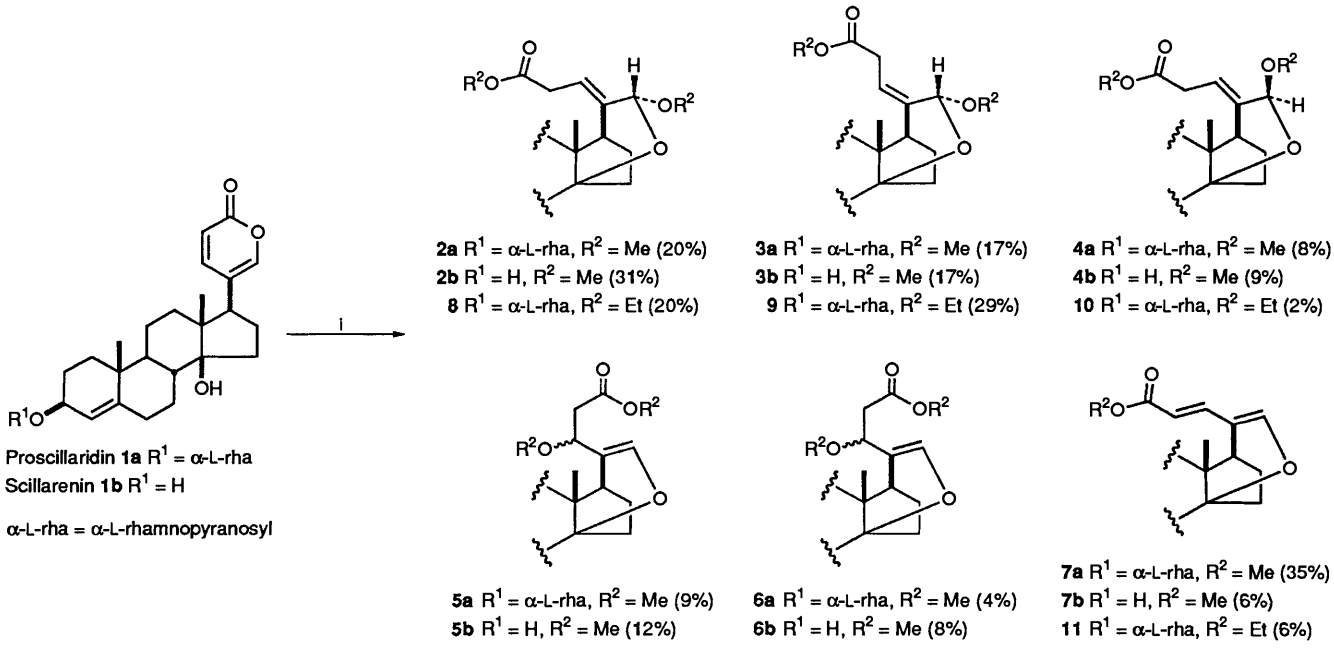
Wartburg and Ranz reported that bufogenin was converted into the methyl ester of isobufogenic acid by alkaline hydrolysis with KOH in MeOH followed by acidification.[6] In the conversion, cleavage of the α-pyrone ring and subsequent nucleophilic attack of 14-OH on C-21 would have resulted in the formation of a six-membered ring acetal (C-13–C-14–O–C-21–C-20–C-17). Dehydration of the acetal gave the methyl ester of isobufogenic acid. In view of both the report and the stereoscopic features of **2a**, the photoproduct **2a** was considered to have the same skeleton as the methyl ester, and was probably formed *via* a photo-pyrone intermediate.[7] Thus, the plane structure of **2a** was established as methyl 3β-[(6-deoxy-α-L-mannopyranosyl)oxy]-14β,21-epoxy-21-methoxychola-4,20-(22)-dien-24-oate. The $^1H$ and $^{13}C$ NMR spectra of **3a** and **4a** are fairly similar to those of **2a**, which indicated that compounds **3a** and **4a** are diastereoisomeric and/or geometrical isomers of **2a**.

Table 1 $^{13}C$ NMR data for **2a**, **3a**, **4a** and **5a**[a]

| | 2a | 3a | 4a | 5a |
|---|---|---|---|---|
| 1 | 32.2[b] | 32.2[b] | 32.2[b] | 32.4[b] |
| 2 | 29.1[c] | 28.9[c] | 28.6[c] | 27.8 |
| 3 | 74.2 | 74.2 | 74.2 | 74.2 |
| 4 | 120.5 | 120.4 | 120.3 | 120.7 |
| 5 | 147.5 | 147.7 | 147.9 | 147.2 |
| 6 | 35.5 | 35.5 | 35.5 | 35.5 |
| 7 | 27.0 | 27.0 | 27.0 | 27.0 |
| 8 | 38.7 | 38.8 | 38.2 | 37.9 |
| 9 | 49.4 | 49.5 | 49.5 | 49.9 |
| 10 | 37.6 | 37.6 | 37.6 | 37.5 |
| 11 | 19.9 | 19.8 | 19.9 | 20.2 |
| 12 | 24.8 | 25.8 | 25.4 | 31.5 |
| 13 | 44.8 | 44.6 | 45.4 | 40.6 |
| 14 | 87.2 | 87.2 | 86.4 | 91.7 |
| 15 | 32.0[b] | 31.8[b] | 31.6[b] | 31.9[b] |
| 16 | 28.4[c] | 28.4[c] | 28.3[c] | 30.7 |
| 17 | 46.9 | 54.1 | 47.0 | 43.4 |
| 18 | 16.1 | 16.6 | 15.9 | 15.4 |
| 19 | 18.8 | 18.8 | 18.9 | 18.9 |
| 20 | 142.9 | 142.7 | 141.8 | 120.8 |
| 21 | 101.9 | 97.2 | 98.4 | 150.0 |
| 22 | 118.0 | 117.7 | 113.2 | 143.6 |
| 23 | 32.3 | 32.4 | 32.4 | 109.3 |
| 24 | 172.0 | 172.1 | 172.4 | 168.5 |
| 1′ | 99.2 | 99.1 | 99.1 | 99.2 |
| 2′ | 71.5 | 71.5 | 71.5 | 71.5 |
| 3′ | 71.8 | 71.8 | 71.8 | 71.8 |
| 4′ | 73.0 | 73.5 | 73.5 | 73.2 |
| 5′ | 68.3 | 68.0 | 68.0 | 68.2 |
| 6′ | 17.6 | 17.5 | 17.5 | 17.5 |
| 21-OMe | 54.9 | 54.9 | 57.0 | |
| 24-OMe | 51.9 | 51.9 | 51.8 | 51.3 |

[a] Assignments for these compounds were made with the aid of DEPT and $^{13}C$–$^1H$ COSY data. [b,c] Assignment may be exchangeable within the same vertical column.

In order to determine the absolute stereochemistry of the photoproducts **2a–4a**, difference NOE experiments were examined. NOE enhancements between the ketal proton (21-H) and 22-H in **2a** indicated an *E*-configuration of the C-20–C-22 double bond and an *R*-configuration at C-21. For compound **3a**, NOEs appeared not only between 17-H and 22-H but also between 21-H and 23-$H_2$. Therefore, the configuration of the C-20–C-22 double bond and C-21 proved to be *Z* and *R*




**Scheme 1** *Reagents and conditions:* i, *hv*, MeOH or EtOH

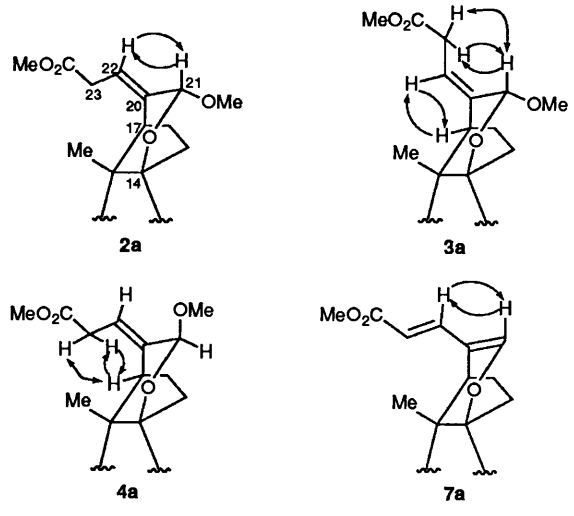



**Fig. 1** NOEs of **2a**, **3a**, **4a** and **7a**

respectively. Compound **4a** showed NOE enhancements between 17-H and 23-$H_2$, but it exhibited no NOE on irradiating 21-H. On the basis of the above spectral properties, these structures were consequently elucidated to be as shown in Fig. 1.

The molecular formula of the compound **5a** was determined to be $C_{32}H_{48}O_9$ by elemental analysis. The IR spectrum of **5a** showed a carbonyl absorption band at 1740 $cm^{-1}$ due to an ester group and lacked a conjugated carbonyl absorption. In the $^1H$ NMR spectrum of **5a**, the signals due to the α-pyrone moiety in proscillaridin **1a** were absent, and were replaced by an ABX system [$\delta_H$ 2.38 (1 H, dd, *J* 5.0 and 15.2 Hz), 2.68 (1 H, dd, *J* 9.0 and 15.2 Hz) and 3.90 (1 H, dd, *J* 9.0 and 5.0 Hz)]. In addition, a singlet olefinic proton signal at $\delta_H$ 6.11 and two methoxy protons at $\delta_H$ 3.26 and 3.68 (3 H each, both s) were observed. Taking these spectroscopic features and the mechanism of formation of **2a**–**4a** into consideration, compound **5a** was deduced to have a methyl 14β,21-epoxy-22-methoxychola-4,20-dien-24-oate skeleton.

Compound **6a** showed the same functional groups as **5a** in the $^1H$ NMR spectrum and the same molecular formula, and has the same structure as **5a**, *viz* a C-22 epimer of **5a**.*

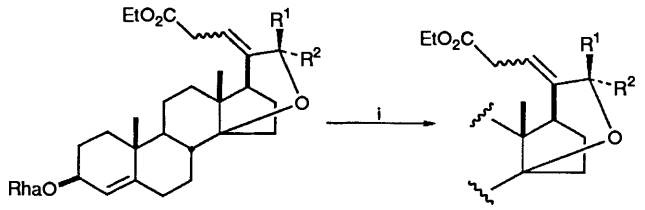
Compound **7a** was identified as methyl 14β,21-epoxychola-4,20,22-trien-24-oate, obtained by treatment of proscillaridin **1a** with KOH–MeOH. The geometry of the diene portion has, however, been ambiguous. In the NOESY spectrum of **7a**, a cross peak between 21-H and 22-H indicative of a transoid diene was observed. Consequently, the unambiguous chemical structure of **7a** was determined to be methyl (20*Z*,22*E*)-3β-[(6-deoxy-α-L-mannopyranosyl)oxy]-14β,21-epoxychola-4,20,22-trien-24-oate.

Next, a genuine aglycone of proscillaridin **1a**, scillarenin **1b**, was submitted to photolysis under the same conditions as **1a** to give six products **2b**–**7b** corresponding to the aglycones of the above glycoside compounds **2a**–**7a** in 31, 17, 9, 12, 8 and 6% respectively. The $^1H$ NMR spectra were very similar to those of **2a**–**7a** except for the signals due to the sugar moieties. Naringinase catalysed derhamnolysis of **2a**–**7a** afforded **2b**–**7b** quantitatively. Therefore, the structures of **2b**–**7b** were confirmed by spectral and chemical evidence.

In contrast, the irradiation of a solution of proscillaridin **1a** in EtOH for 5 h under the same reaction conditions as in MeOH provided four products **8**–**11** in 20, 29, 2 and 6% yield respectively. Among the four products, three (**8**–**10**) were found to have the molecular formula $C_{34}H_{52}O_9$ and the other (**11**) was shown to have $C_{32}H_{46}O_8$ by their elemental analyses. A non-conjugated carbonyl absorption (1735 $cm^{-1}$) appeared in the IR spectra of the three products **8**–**10**. Intensive analysis of the $^1H$ NMR spectra of **8**–**11** in comparison with those of **2a**, **3a**, **4a** and **7a** disclosed that the three products **8**–**10** were isomers of ethyl 3β-[(6-deoxy-α-L-mannopyranosyl)oxy]-14β,21-epoxy-21-ethoxychola-4,20(22)-dien-24-oate and the other one was ethyl 3β-[(6-deoxy-α-L-mannopyranosyl)oxy]-14β,21-epoxychola-4,20,22-trien-24-oate. Their absolute stereostructures were established as depicted in Scheme 1 by the NOE experiments (see Experimental section).

On heating under reflux in MeOH, **8**, **9** and **10** readily underwent acetal interchange to give two ethyl 3β-[(6-deoxy-α-L-mannopyranosyl)oxy]-14β,21-epoxy-21-methoxychola-4,20-(22)-dien-24-oates **12** and **13** (Scheme 2). The 21*R*-ethoxycholadienoates **8** and **9** afforded 21*R*-methoxy congeners quantitatively with retention of both the configuration at C-21

* The absolute configurations of **5** and **6** at C-22 are undetermined.




**8** 20*E*, $R^1$ = H, $R^2$ = OEt
**9** 20*Z*, $R^1$ = H, $R^2$ = OEt
**10** 20*E*, $R^1$ = OEt, $R^2$ = H

**12** 20*E*, $R^1$ = H, $R^2$ = OMe
**13** 20*Z*, $R^1$ = H, $R^2$ = OMe

**Scheme 2** *Reagents and conditions:* i, MeOH, reflux

**Table 2** Product distribution (%) in photolysis of **2a**, **3a** and **4a**[a]

| Substrate | 2a | 3a | 4a | 5a | 6a | 7a |
|---|---|---|---|---|---|---|
| **2a** | 42 | 6 | 13 | 17 | 17 | Trace |
| **3a** | 6 | 92 | 0 | Trace | Trace | Trace |
| **4a** | 36 | 5 | 29 | 12 | 12 | Trace |

[a] Isolated yield after 12 h.

and geometry of C-20–C-22 double bond. In contrast, 21*S*-ethoxycholadienoate **10** exclusively gave the 21*R*-methoxy derivative with inversion of configuration at C-21.

The photolysis of the three products **2a**, **3a** and **4a** was examined to eluciate the reaction pathway in the photolysis of **1a**. The product distributions from the photolyses of **2a**, **3a** and **4a** are summarized in Table 2. Two compounds (**2a** and **4a**) possessing 20*E* geometry afforded the five products **2a**–**6a** with recovery of the starting material after 12 h, while the 20*Z*-derivative **3a** was scarcely transformed to give small amount of the 20*E*-isomer **2a**. Thus, the 20*E*-21-alkoxycholadienoates are subject to isomerization of the double bond, acetal interchange and dealkoxylation and the 20*E*-isomer was nearly stable under the reaction conditions for the photolysis of **1a** in MeOH. On the other hand, the 22-methoxycholadienoates **5a** and **6a** and the cholatrienoate **7a** were recovered from the photochemical reaction.

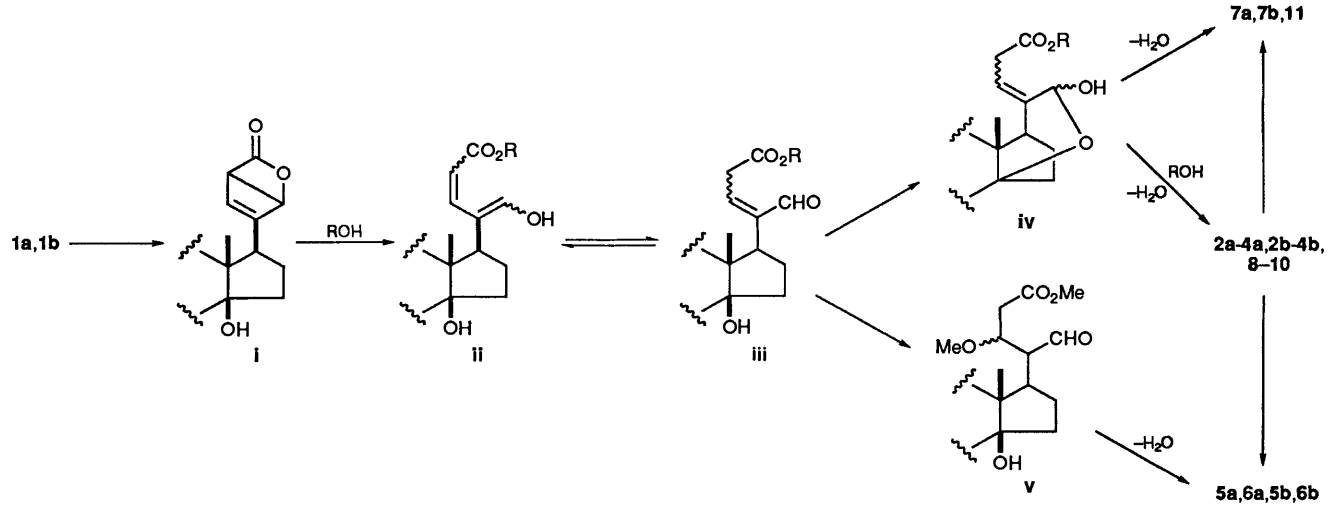
The present photochemical transformation may be rationalized by the involvement of a photo-pyrone intermediate **i**.[7] A plausible reaction mechanism for the transformation is depicted in Scheme 3. The photo-pyrone intermediate **i** was presumed to give the ketene aldehyde **ii** which would undergo alcoholysis to give the formyl ester **iii**. The formation of the ether ring between the 14-OH and the formyl group (C-21) presumably afforded the hemiacetal **iv** that would be converted into both the 21-alkoxycholadienoates **2a**–**4a**, **2b**–**4b** and **8**–**10** by acetalization and the cholatrienoates **7a**, **7b** and **11** by dehydration. The 22-methoxycholadienoates **5a**, **5b**, **6a** and **6b** were assumed to be generated by a Michael type addition followed by dehydration by way of **v**. Cholatrienoates and 21-methoxycholadienoates were also elaborated from the 21-alkoxy derivatives as mentioned above.

The stereochemical outcome of the 21-alkoxycholadienoates, the absolute configuration at C-21 and the geometry of the C-20–C-22 double bond, may be determined by a combination of the anomeric effect and steric repulsion. Namely, the anomeric effect on the newly formed six-membered ether ring would suggest a preference for an axial alkoxy substituent over an equatorial one. The 20*Z*-isomers of **4a**, **4b** and **10** were not formed presumably due to the steric repulsions between the alkoxy substituents and the C-23-methylene protons. Acetal interchange of **10** into **12** with the inversion of configuration at C-21 supported this view.

In conclusion, we have found a novel photochemical transformation of the bufadienolides **1a** and **1b** in which the α-pyrone moiety was cleaved to form 14β,21-epoxycholane derivatives. Among the photoproducts, the chemical and biological properties of 14β,21-epoxy-21-alkoxycholadienes may be of interest since they have never been found naturally or made synthetically. It seems noteworthy that this photochemical transformation requires no previous protection of the hydroxy groups in the sugar moiety.

## Experimental

M.p.s were determined on a Yanagimoto micro melting point apparatus and are uncorrected. UV spectra were recorded with a Shimadzu UV-2100 spectrophotometer and IR spectra with a JASCO IR-810 spectrophotometer. $^1H$ and $^{13}C$ NMR spectra were measured with JEOL GSX-400 (400 MHz) and EX-270 (270 MHz) spectrometers using tetramethylsilane as an internal standard. *J*-Values are given in Hz. Optical rotations were measured on a JASCO DIP-140 digital polarimeter and are given in units of $10^{-1}$ deg cm$^2$ g$^{-1}$. Fast-atom bombardment (FAB) and electron impact (EI) mass spectra were measured with a JEOL SX-102 or DX-300 mass spectrometer. High-performance liquid chromatography (HPLC) was performed using a JASCO 880-PU pump and 830-RI differential reflect-




**Scheme 3**

meter. TLC was carried out on Merck precoated Kieselgel $60F_{254}$ and spots were detected by illumination with an ultraviolet lamp, or spraying 1% $Ce(SO_4)_2$–10% $H_2SO_4$ followed by heating. Column chromatography was performed on silica gel BW-200 (Fuji Davison Chemicals). A high-pressure mercury arc lamp (AHH 400 S, 400 W) was employed from Shigemi standard. Naringinase (from *Penicillium decumbens*) was obtained from Sigma (St. Louis, USA).

*Photolysis of Proscillaridin* **1a** *in MeOH.*—A solution of proscillaridin **1a** (100 mg, 0.19 mmol) in MeOH (10 $cm^3$) was irradiated in a Pyrex vessel with a high-pressure mercury arc lamp (400 W) under a nitrogen atmosphere at room temperature for 5 h. After removal of the solvent under reduced pressure, the residue was purified by column chromatography ($SiO_2$, $CHCl_3$–MeOH, 12:1) followed by HPLC (Develosil ODS A-5, 10 mm i.d. × 250 mm, MeOH–$H_2O$, 9:1) to furnish compounds **2a** (22 mg, 20%), **3a** (18 mg, 17%), **4a** (9 mg, 8%), **5a** (4 mg, 4%), **6a** (4 mg, 4%) and **7a** (36 mg, 35%).

*Methyl* [21R,20(22)E]-3β-[(6-*deoxy*-α-L-*mannopyranosyl*)*oxy*]-14β,21-*epoxy*-21-*methoxychola*-4,20(22)-*dien*-24-*oate* **2a**. Colourless crystalline powder, m.p. 67–69 °C (from $Pr^i_2O$–MeOH) (Found: C, 66.7; H, 8.4. $C_{32}H_{48}O_9$ requires C, 66.6; H, 8.4%); $[\alpha]_D^{25}$ −71.2 (*c* 0.5 in $CHCl_3$); $\nu_{max}$(KBr)/$cm^{-1}$ 3425 (OH) and 1740 (CO); $\delta_H$(400 MHz, $CDCl_3$) 0.86 (3 H, s, 13-$CH_3$), 1.07 (3 H, s, 10-$CH_3$), 1.30 (3 H, d, *J* 6.2, 5′-$CH_3$), 2.63 (1 H, d, *J* 4.2, 17-H), 3.07 (1 H, dd, *J* 6.8 and 17.0, 23-H), 3.15 (1 H, dd, *J* 7.9 and 17.0, 23-H), 3.38 (3 H, s, 21-$OCH_3$), 3.42 (1 H, dd, *J* 9.3 and 9.3, 4′-H), 3.68 (3 H, s, 24-$CO_2CH_3$), 3.70–3.80 (2 H, m, 3′-H and 5′-H), 3.92 (1 H, s, 2′-H), 4.12 (1 H, dd, *J* 5.9 and 9.9, 3-H), 4.88 (1 H, s, 21-H), 4.96 (1 H, s, 1′-H), 5.30 (1 H, s, 4-H) and 5.55 (1 H, dd, *J* 6.8 and 7.9, 22-H) (assignments were made with the aid of $^{13}C$–$^1H$ COSY data); NOE (400 MHz, $CDCl_3$, %) 21-H→22-H (8.6) and 22-H→21-H (8.9); *m/z* (FAB) 583 $[(M + Li)^+$, 85%] and 160 (100).

*Methyl* [21R,20(22)Z]-3β-[(6-*deoxy*-α-L-*mannopyranosyl*)*oxy*]-14β,21-*epoxy*-21-*methoxychola*-4,20(22)-*dien*-24-*oate* **3a**. Colourless crystalline powder, m.p. 70–72 °C (from $Pr^i_2O$–MeOH) (Found: C, 66.6; H, 8.4. $C_{32}H_{48}O_9$ requires C, 66.6; H, 8.4%); $[\alpha]_D^{25}$ −109.9 (*c* 0.7 in $CHCl_3$); $\nu_{max}$(KBr)/$cm^{-1}$ 3425 (OH) and 1740 (CO); $\delta_H$(400 MHz, $CDCl_3$) 0.87 (3 H, s, 13-$CH_3$), 1.07 (3 H, s, 10-$CH_3$), 1.30 (3 H, d, *J* 6.2, 5′-$CH_3$), 2.30 (1 H, d, *J* 5.5, 17-H), 3.02 (1 H, dd, *J* 6.6 and 17.6, 23-H), 3.11 (1 H, dd, *J* 7.9 and 17.6, 23-H), 3.40 (3 H, s, 21-$OCH_3$), 3.44 (1 H, dd, *J* 9.5 and 9.5, 4′-H), 3.68 (3 H, s, 24-$CO_2CH_3$), 3.74–3.80 (2 H, m, 3′-H and 5′-H), 3.93 (1 H, br s, 2′-H), 4.13 (1 H, dd, *J* 5.9 and 9.9, 3-H), 4.93 (1 H, d, *J* 1.3, 1′-H), 5.11 (1 H, d, *J* 0.7, 21-H), 5.30 (1 H, s, 4-H) and 5.43 (1 H, ddd, *J* 0.7, 6.6 and 7.9, 22-H) (assignments were made with the aid of $^{13}C$–$^1H$ COSY data); NOE (400 MHz, $CDCl_3$, %) 17-H→22-H (5.4), 22-H→17-H (9.4), 21-H→23-H (3.02 ppm) (2.2), 21-H→23-H (3.11 ppm) (5.3), 23-H (3.02 ppm)→21-H (4.4) and 23-H (3.11 ppm)→21-H (5.4); *m/z* (FAB) 583 $[(M + Li)^+$, 12%] and 154 (100).

*Methyl* [21S,20(22)E]-3β-[(6-*deoxy*-α-L-*mannopyranosyl*)*oxy*]-14β,21-*epoxy*-21-*methoxychola*-4,20(22)-*dien*-24-*oate* **4a**. Colourless crystalline powder, m.p. 88–90 °C (from $Pr^i_2O$–MeOH) (Found: C, 66.6; H, 8.4. $C_{32}H_{48}O_9$ requires C, 66.6; H, 8.4%); $[\alpha]_D^{25}$ −31.5 (*c* 0.6 in $CHCl_3$); $\nu_{max}$(KBr)/$cm^{-1}$ 3440 (OH) and 1745 (CO); $\delta_H$(400 MHz; $CDCl_3$) 0.92 (3 H, s, 13-$CH_3$), 1.06 (3 H, s, 10-$CH_3$), 1.30 (3 H, d, *J* 6.0, 5′-$CH_3$), 2.70 (1 H, d, *J* 5.3, 17-H), 3.02 (1 H, dd, *J* 6.8 and 15.4, 23-H), 3.10 (1 H, dd, *J* 8.2 and 15.4, 23-H), 3.45 (1 H, dd, *J* 9.0 and 9.0, 4′-H), 3.55 (3 H, s, 21-$OCH_3$), 3.67 (3 H, s, 24-$CO_2CH_3$), 3.70–3.80 (2 H, m, 3′-H and 5′-H), 3.92 (1 H, s, 2′-H), 4.12 (1 H, dd, *J* 7.5 and 8.1, 3-H), 4.95 (1 H, s, 1′-H), 5.00 (1 H, d, *J* 1.5, 21-H), 5.29 (1 H, s, 4-H) and 5.66 (1 H, ddd, *J* 1.5, 6.8 and 8.2, 22-H) (assignments were made with the aid of $^{13}C$–$^1H$ COSY data); NOE (400 MHz, $CDCl_3$, %) 17-H→23-H (3.02 ppm) (7.0), 17-H→23-H (3.11 ppm) (6.3), 23-H (3.02 ppm)→17-H (13.2) and 23-H (3.11 ppm)→17-H (8.5); *m/z* (FAB) 583 $[(M + Li)^+$, 17%] and 160 (100).

*Methyl* 3β-[(6-*deoxy*-α-L-*mannopyranosyl*)*oxy*]-14β,21-*epoxy*-22-*methoxychola*-4,20-*dien*-24-*oate* **5a**. Colourless crystalline powder, m.p. 83–85 °C (from $Pr^i_2O$–MeOH) (Found: C, 66.6; H, 8.45. $C_{32}H_{48}O_9$ requires C, 66.6; H, 8.4%); $[\alpha]_D^{25}$ −92.9 (*c* 0.5 in $CHCl_3$); $\nu_{max}$(KBr)/$cm^{-1}$ 3400 (OH) and 1740 (CO); $\delta_H$(400 MHz, $CDCl_3$) 0.97 (3 H, s, 13-$CH_3$), 1.08 (3 H, s, 10-$CH_3$), 1.30 (3 H, d, *J* 6.2, 5′-$CH_3$), 2.38 (1 H, dd, *J* 5.0 and 15.2, 23-H), 2.68 (1 H, dd, *J* 9.0 and 15.2, 23-H), 3.26 (3 H, s, 22-$OCH_3$), 3.45 (1 H, dd, *J* 9.3 and 9.3, 4′-H), 3.68 (3 H, s, 24-$CO_2CH_3$), 3.74–3.80 (2 H, m, 3′-H and 5′-H), 3.90 (1 H, dd, *J* 5.0 and 9.0, 22-H), 3.92 (1 H, s, 2′-H), 4.13 (1 H, dd, *J* 7.3 and 8.0, 3-H), 4.95 (1 H, s, 1′-H), 5.30 (1 H, s, 4-H) and 6.11 (1 H, s, 21-H); *m/z* (FAB) 599 $[(M + Na)^+$, 15%] and 154 (100).

*Methyl* 3β-[(6-*deoxy*-α-L-*mannopyranosyl*)*oxy*-14β,21-*epoxy*-22-*methoxychola*-4,20-*dien*-24-*oate* **6a**. Colourless crystalline powder, m.p. 67–69 °C (from $Pr^i_2O$–MeOH) (Found: C, 66.5; H, 8.5. $C_{32}H_{48}O_9$ requires C, 66.6; H, 8.4%); $[\alpha]_D^{25}$ −58.0 (*c* 0.6 in $CHCl_3$); $\nu_{max}$(KBr)/$cm^{-1}$ 3425 (OH) and 1740 (CO); $\delta_H$(400 MHz, $CDCl_3$) 1.06 and 1.09 (2 × 3 H, 2 × s, 10-$CH_3$ and 13-$CH_3$), 1.30 (3 H, d, *J* 6.2, 5′-$CH_3$), 2.47 (1 H, dd, *J* 4.4 and 15.0, 23-H), 2.65 (1 H, dd, *J* 9.6 and 15.0, 23-H), 3.23 (3 H, s, 22-$OCH_3$), 3.44 (1 H, dd, *J* 9.3 and 9.3, 4′-H), 3.70 (3 H, s, 24-$CO_2CH_3$), 3.76–3.80 (2 H, m, 3′-H and 5′-H), 3.87 (1 H, dd, *J* 4.4 and 9.6, 22-H), 3.92 (1 H, d, *J* 1.3, 2′-H), 4.13 (1 H, dd, *J* 7.7 and 7.7, 3-H), 4.95 (1 H, d, *J* 1.3, 1′-H), 5.30 (1 H, s, 4-H) and 6.11 (1 H, s, 21-H); *m/z* (FAB) 599 $[(M + Na)^+$, 34%] and 154 (100).

*Methyl* 3β-[(6-*deoxy*-α-L-*mannopyranosyl*)*oxy*]-14β,21-*epoxychola*-4,20,22-*trien*-24-*oate* **7a**.[5b] $[\alpha]_D^{25}$ −97.9 (*c* 0.6 in $CHCl_3$); $\lambda_{max}$(MeOH)/nm (ε) 302.3 (23 000); *m/z* (FAB) 567 $[(M + Na)^+$, 10%] and 115 (100).

*Photolysis of Scillarenin* **1b** *in MeOH.*—A solution of scillarenin **1b** (100 mg, 0.26 mmol) in MeOH (14 $cm^3$) was irradiated at room temperature under a nitrogen atmosphere for 6 h. After removal of the solvent under reduced pressure, the residue was purified by column chromatography ($SiO_2$, hexane–EtOAc, 2:1) followed by HPLC (Develosil ODS-5, 10 mm i.d. × 250 mm, MeOH–$H_2O$, 9:1 and Develosil ODS A-5, 10 mm i.d. × 250 mm, MeCN–$H_2O$, 8:2) to furnish the compounds **2b** (35 mg, 31%), **3b** (19 mg, 17%), **4b** (10 mg, 9%), **5b** (13 mg, 12%), **6b** (9 mg, 8%) and **7b** (7 mg, 6%).

*Methyl* [21R,20(22)E]-14β,21-*epoxy*-3β-*hydroxy*-21-*methoxychola*-4,20(22)-*dien*-24-*oate* **2b**. Colourless crystalline powder, m.p. 95–97 °C (from $Pr^i_2O$–MeOH) (Found: C, 72.6; H, 8.8. $C_{26}H_{38}O_5$ requires C, 72.5; H, 8.9%); $[\alpha]_D^{25}$ −31.0 (*c* 0.5 in $CHCl_3$); $\nu_{max}$(KBr)/$cm^{-1}$ 3445 (OH) and 1740 (CO); $\delta_H$(400 MHz, $CDCl_3$) 0.87 (3 H, s, 13-$CH_3$), 1.07 (3 H, s, 10-$CH_3$), 2.63 (1 H, dd, *J* 2.7 and 3.2, 17-H), 3.06 (1 H, dd, *J* 6.6 and 16.8, 23-H), 3.14 (1 H, dd, *J* 7.8 and 16.8, 23-H), 3.39 (3 H, s, 21-$OCH_3$), 3.68 (3 H, s, 24-$CO_2CH_3$), 4.16 (1 H, br s, 3-H), 4.89 (1 H, s, 21-H), 5.30 (1 H, d, *J* 1.5, 4-H) and 5.55 (1 H, dd, *J* 6.6 and 7.8, 22-H); *m/z* (EI) 398 $[(M - MeOH)^+$, 100].

*Methyl* [21R,20(22)Z]-14β,21-*epoxy*-3β-*hydroxy*-21-*methoxychola*-4,20(22)-*dien*-24-*oate* **3b**. Colourless crystalline powder, m.p. 115–117 °C (from $Pr^i_2O$–MeOH) (Found: C, 72.5; H, 8.9. $C_{26}H_{38}O_5$ requires C, 72.5; H, 8.9%); $[\alpha]_D^{25}$ −17.5 (*c* 0.6 in $CHCl_3$); $\nu_{max}$(KBr)/$cm^{-1}$ 3520 (OH) and 1740 (CO); $\delta_H$(400 MHz, $CDCl_3$) 0.88 (3 H, s, 13-$CH_3$), 1.07 (3 H, s, 10-$CH_3$), 2.31 (1 H, dd, *J* 2.0 and 3.7, 17-H), 3.01 (1 H, dd, *J* 6.6 and 17.6, 23-H), 3.11 (1 H, dd, *J* 7.9 and 17.6, 23-H), 3.40 (3 H, s, 21-$OCH_3$), 3.68 (3 H, s, 24-$CO_2CH_3$), 4.15 (1 H, dd, *J* 5.7 and 7.5, 3-H), 5.12 (1 H, d, *J* 0.7, 21-H), 5.30 (1 H, d, *J* 1.5, 4-H) and 5.43 (1 H, ddd, *J* 0.7, 6.6 and 7.9, 22-H); *m/z* (EI) 398 $[(M - MeOH)^+$, 2.4%] and 57 (100).

*Methyl* [21S,20(22)E]-14β,21-*epoxy*-3β-*hydroxy*-21-*methoxychola*-4,20(22)-*dien*-24-*oate* **4b**. Colourless crystalline powder, m.p. 62–64 °C (from $Pr^i_2O$–MeOH) (Found: C, 72.6; H, 8.8. $C_{26}H_{38}O_5$ requires C, 72.5; H, 8.9%); $[\alpha]_D^{25}$ −40.9 (*c* 0.5 in $CHCl_3$); $\nu_{max}$(KBr)/$cm^{-1}$ 3440 (OH) and 1740 (CO); $\delta_H$(400 MHz, $CDCl_3$) 0.92 (3 H, s, 13-$CH_3$), 1.06 (3 H, s, 10-$CH_3$), 2.70 (1 H, d, *J* 5.6, 17-H), 3.02 (1 H, dd, *J* 7.1 and 16.8, 23-H), 3.10 (1 H, dd, *J* 8.1 and 16.8, 23-H), 3.55 (3 H, s, 21-$OCH_3$), 3.67 (3 H, s, 24-$CO_2CH_3$), 4.15 (1 H, dd, *J* 7.7 and 7.9, 3-H), 5.00 (1 H, d, *J* 1.2, 21-H), 5.29 (1 H, d, *J* 1.4, 4-H) and 5.66 (1 H, ddd, *J* 1.2, 7.1 and 8.1, 22-H); *m/z* (EI) 398 [(M − MeOH)$^+$, 3.4%] and 57 (100).

*Methyl* 14β,21-*epoxy*-3β-*hydroxy*-22-*methoxychola*-4,20-*dien*-24-*oate* **5b**. Colourless crystalline powder, m.p. 100–102 °C (from $Pr^i_2O$–MeOH) (Found: C, 72.4; H, 9.0. $C_{26}H_{38}O_5$ requires C, 72.5; H, 8.9%); $[\alpha]_D^{25}$ −50.0 (*c* 0.5 in $CHCl_3$); $\nu_{max}$(KBr)/$cm^{-1}$ 3500 (OH) and 1730 (CO); $\delta_H$(400 MHz, $CDCl_3$) 0.97 (3 H, s, 13-$CH_3$), 1.08 (3 H, s, 10-$CH_3$), 2.38 (1 H, dd, *J* 4.9 and 15.3, 23-H), 2.69 (1 H, dd, *J* 9.0 and 15.3, 23-H), 3.26 (3 H, s, 22-$OCH_3$), 3.68 (3 H, s, 24-$CO_2CH_3$), 3.90 (1 H, dd, *J* 4.9 and 9.0, 22-H), 4.15 (1 H, dd, *J* 5.7 and 7.5, 3-H), 5.30 (1 H, d, *J* 1.5, 4-H) and 6.11 (1 H, s, 21-H); *m/z* (EI) 430 ($M^+$, 2.1%) and 57 (100).

*Methyl* 14β,21-*epoxy*-3β-*hydroxy*-22-*methoxychola*-4,20-*dien*-24-*oate* **6b**. Colourless crystalline powder, m.p. 68–70 °C (from $Pr^i_2O$–MeOH) (Found: C, 72.55; H, 8.9. $C_{26}H_{38}O_5$ requires C, 72.5; H, 8.9%); $[\alpha]_D^{25}$ −14.0 (*c* 0.5 in $CHCl_3$); $\nu_{max}$(KBr)/$cm^{-1}$ 3480 (OH) and 1730 (CO); $\delta_H$(400 MHz, $CDCl_3$) 1.06 and 1.09 (3 H, each, both s, 10-$CH_3$ and 13-$CH_3$), 2.47 (1 H, dd, *J* 4.5 and 15.1, 23-H), 2.66 (1 H, dd, *J* 9.6 and 15.1, 23-H), 3.23 (3 H, s, 22-$OCH_3$), 3.70 (3 H, s, 24-$CO_2CH_3$), 3.87 (1 H, dd, *J* 4.5 and 9.6, 22-H), 4.15 (1 H, dd, *J* 5.9 and 7.6, 3-H), 5.31 (1 H, d, *J* 1.5, 4-H) and 6.61 (1 H, s, 21-H); *m/z* (EI) 430 ($M^+$, 2.6%), 398 [(M − MeOH)$^+$, 100].

*Methyl* 14β,21-*epoxy*-3β-*hydroxychola*-4,2,22-*trien*-24-*oate* **7b**. Colourless crystalline powder, m.p. 69–71 °C (from $Pr^i_2O$–MeOH) (Found: C, 75.4; H, 8.55. $C_{25}H_{34}O_4$ requires C, 75.3; H, 8.6%); $[\alpha]_D^{25}$ −34.0 (*c* 0.6 in $CHCl_3$); $\nu_{max}$(KBr)/$cm^{-1}$ 3430 (OH) and 1710 (CO); $\lambda_{max}$(MeOH)/nm (ε) 302.0 (22 000); $\delta_H$(400 MHz, $CDCl_3$) 1.01 (3 H, s, 13-$CH_3$), 1.09 (3 H, s, 10-$CH_3$), 2.25 (1 H, d, *J* 4.4, 17-H), 3.72 (3 H, s, 24-$CO_2CH_3$), 4.16 (1 H, m, 3-H), 5.32 (1 H, d, *J* 1.4, 4-H), 5.63 (1 H, d, *J* 15.6, 23-H), 6.56 (1 H, s, 21-H) and 7.21 (1 H, d, *J* 15.6, 22-H); *m/z* (EI) 398 ($M^+$, 18%) and 91 (100).

*Enzymatic hydrolysis of* **2a**–**7a** *with Naringinase*.—A solution of **2a** (5.0 mg, 8.7 μmol) and naringinase (1.6 mg) in a mixture of EtOH (90 $mm^3$) and acetate buffer (pH 4.0, 270 $mm^3$) was stirred at 40 °C for 6.5 h. After addition of EtOH (0.7 $cm^3$) to quench the reaction followed by concentration of the reaction mixture under reduced pressure, the residue was chromatographed on silica gel (hexane–EtOAc, 1:1) to give **2b** (3.7 mg, quant.). Using the same procedure, **3b**–**7b** were prepared in quantitative yield from **3a**–**7a**.

*Photolysis of Proscillaridin* **1a** *in EtOH*.—A solution of proscillaridin **1a** (100 mg, 0.19 mmol) in EtOH (10 $cm^3$) was irradiated at room temperature under a nitrogen atmosphere for 6 h. After removal of the solvent at reduced pressure, the residue was purified by column chromatography ($SiO_2$, $CHCl_3$–EtOH, 10:1) followed by HPLC (Develosil ODS-5, 10 mm i.d. × 250 mm, EtOH–$H_2O$, 7:3) to furnish compounds **8** (23 mg, 20%), **9** (33 mg, 29%), **10** (2 mg, 2%) and **11** (6 mg, 6%).

*Ethyl* [21R,20(22)E]-3β-[(6-*deoxy*-α-L-*mannopyranosyl*)-*oxy*]-14β,21-*epoxy*-21-*ethoxychola*-4,20(22)-*dien*-24-*oate* **8**. Colourless crystalline powder, m.p. 120–122 °C (from $Pr^i_2O$–EtOH) (Found: C, 67.6; H, 8.6. $C_{34}H_{52}O_9$ requires C, 67.5; H, 8.7%); $[\alpha]_D^{25}$ −30.9 (*c* 0.5 in $CHCl_3$); $\nu_{max}$(KBr)/$cm^{-1}$ 3435 (OH) and 1735 (CO); $\delta_H$(400 MHz, $CDCl_3$) 0.83 and 0.86 (2 × 3 H, 2 × s, 10-$CH_3$ and 13-$CH_3$), 1.19–1.28 (6 H, m, 2 × $OCH_2CH_3$), 1.30 (3 H, d, *J* 6.3, 5′-$CH_3$), 2.63 (1 H, d, *J* 5.1, 17-H), 3.04 (1 H, dd, *J* 6.4 and 16.8, 23-H), 3.13 (1 H, dd, *J* 7.9 and 16.8, 23-H), 3.43–3.51 (2 H, m, 4′-H and CH in 21-$OCH_2CH_3$), 3.76–3.83 (3 H, m, 3′-H, 5′-H and CH in 21-$OCH_2CH_3$), 3.93 (1 H, s, 2′-H), 4.11–4.17 (3 H, m, 3-H and 24-$OCH_2CH_3$), 4.96 (1 H, s, 1′-H), 5.00 (1 H, s, 21-H), 5.30 (1 H, s, 4-H) and 5.54 (1 H, dd, *J* 6.4 and 7.9, 22-H); NOE (270 MHz, $CDCl_3$, %) 17-H→23-H (3.04 ppm) (9.6), 17-H → 23-H (3.13 ppm) (5.6), 23-H (3.04 ppm)→17-H (15.8), 23-H (3.13 ppm)→17-H (20.0), 21-H→22-H (19.2) and 22-H→21-H (16.9); *m/z* (FAB) 627 [(M + Na)$^+$, 19%] and 154 (100).

*Ethyl* [21R,20(22)Z]-3β-[(6-*deoxy*-α-L-*mannopyranosyl*)-*oxy*]-14β,21-*epoxy*-21-*ethoxychola*-4,20(22)-*dien*-24-*oate* **9**. Colourless crystalline powder, m.p. 104–106 °C (from $Pr^i_2O$–EtOH) (Found: C, 67.6; H, 8.6. $C_{34}H_{52}O_9$ requires C, 67.5; H, 8.7%); $[\alpha]_D^{25}$ −73.4 (*c* 0.5 in $CHCl_3$); $\nu_{max}$(KBr)/$cm^{-1}$ 3410 (OH) and 1735 (CO); $\delta_H$(400 MHz, $CDCl_3$) 0.87 and 0.88 (2 × 3 H, 2 × s, 10-$CH_3$ and 13-$CH_3$), 1.20–1.27 (6 H, m, 2 × $OCH_2CH_3$), 1.29 (3 H, d, *J* 6.3, 5′-$CH_3$), 2.30 (1 H, d, *J* 5.4, 17-H), 2.99 (1 H, dd, *J* 6.5 and 17.5, 23-H), 3.09 (1 H, dd, *J* 7.8 and 17.5, 23-H), 3.46 (2 H, dd, *J* 9.3 and 9.3, 4′-H), 3.50 (1 H, dd, *J* 7.1 and 9.9, CH in 21-$OCH_2CH_3$), 3.72–3.78 (2 H, m, 3′-H and 5′-H), 3.84 (1 H, dd, *J* 7.1, and 9.9, CH in 21-$OCH_2CH_3$), 3.93 (1 H, s, 2′-H), 4.10–4.17 (3 H, m, 3-H, 24-$OCH_2CH_3$), 4.93 (1 H, s, 1′-H), 5.24 (1 H, s, 21-H), 5.29 (1 H, s, 4-H) and 5.41 (1 H, dd, *J* 6.5 and 7.8, 22-H); NOE (270 MHz, $CDCl_3$, %) 21-H→23-H (2.99 ppm) (6.2), 21-H→23-H (3.09 ppm) (4.8), 23-H (2.99 ppm)→21-H (4.5), 23-H (3.09 ppm)→21-H (10.4), 17-H→22-H (11.9) and 22-H→17-H (10.3); *m/z* (FAB) 627 [(M + Na)$^+$, 24%] and 154 (100).

*Ethyl* [21S,20(22)E]-3β-[(6-*deoxy*-α-L-*mannopyranosyl*)-*oxy*]-14β,21-*epoxy*-21-*ethoxychola*-4,20(22)-*dien*-24-*oate* **10**. Colourless crystalline powder, m.p. 115–117 °C (from $Pr^i_2O$–EtOH) (Found: C, 67.4; H, 8.7. $C_{34}H_{52}O_9$ requires C, 67.5; H, 8.7%); $[\alpha]_D^{25}$ −89.9 (*c* 0.5 in $CHCl_3$); $\nu_{max}$(KBr)/$cm^{-1}$ 3420 (OH) and 1735 (CO); $\delta_H$(400 MHz, $CDCl_3$) 1.04 (6 H, s, 10-$CH_3$ and 13-$CH_3$), 1.24–1.28 (6 H, m, 2 × $OCH_2CH_3$), 1.29 (3 H, d, *J* 5.9, 5′-$CH_3$), 2.77 (1 H, d, *J* 6.1, 17-H), 3.02 (1 H, dd, *J* 7.0 and 16.8, 23-H), 3.10 (1 H, dd, *J* 8.2 and 16.8, 23-H), 3.43–3.50 (2 H, m, 4′-H and CH in 21-$OCH_2CH_3$), 3.77–3.84 (3 H, m, 3′-H, 5′-H and CH in 21-$OCH_2CH_3$), 3.91 (1 H, s, 2′-H), 4.08–4.18 (3 H, m, 3-H and 24-$OCH_2CH_3$), 4.94 (1 H, s, 1′-H), 5.01 (1 H, s, 21-H), 5.29 (1 H, s, 4-H) and 5.66 (1 H, dd, *J* 7.0 and 8.2, 22-H); NOE (270 MHz, $CDCl_3$, %) 17-H→23-H (3.02 ppm) (10.9), 17-H→23-H (3.10 ppm) (7.9), 23-H (3.02 ppm)→17-H (7.1) and 23-H (3.10 ppm)→17-H (6.3); *m/z* (FAB) 627 [(M + Na)$^+$, 4%] and 154 (100).

*Ethyl* 3β-[(6-*deoxy*-α-L-*mannopyranosyl*)*oxy*]-14β,21-*epoxy*-*chola*-4,20,22-*trien*-24-*oate* **11**. Colourless crystalline powder, m.p. 130–132 °C (from $Pr^i_2O$–EtOH) (Found: C, 68.8; H, 8.25. $C_{32}H_{46}O_8$ requires C, 68.8; H, 8.3%); $[\alpha]_D^{25}$ −81.4 (*c* 0.5 in $CHCl_3$); $\nu_{max}$(KBr)/$cm^{-1}$ 3445 (OH) and 1705 (CO); $\lambda_{max}$(MeOH)/nm (ε) 302.2 (14 000); $\delta_H$(400 MHz; $CDCl_3$) 1.00 and 1.09 (3 H each, both s, 10-$CH_3$ and 13-$CH_3$), 1.28 (3 H, t, *J* 7.1, $OCH_2CH_3$), 1.30 (3 H, d, *J* 6.3, 5′-$CH_3$), 2.26 (1 H, d, *J* 4.8, 17-H), 3.44 (1 H, dd, *J* 9.6 and 9.6, 4′-H), 3.75–3.81 (2 H, m, 3′-H and 5′-H), 3.92 (1 H, d, *J* 2.0, 2′-H), 4.10–4.22 (2 H, m, $OCH_2CH_3$), 4.96 (1 H, s, 1′-H), 5.31 (1 H, s, 4-H), 5.62 (1 H, d, *J* 15.5, 23-H), 6.56 (1 H, s, 21-H) and 7.21 (1 H, d, *J* 15.5, 22-H); *m/z* 581 [(M + Na)$^+$, 11%] and 154 (100).

*Heating* **8**, **9** *and* **10** *under Reflux in MeOH to give* **12** *and* **13**.—A solution of **8** (20 mg, 0.033 mmol) in MeOH (6 $cm^3$) was heated under reflux for 1 h. Removal of the solvent under reduced pressure, gave compound **12** quantitatively. Com-

pounds **9** and **10** were converted into **13** and **12** respectively in the same manner.

*Ethyl* [21R,20(22)E]-3β-[(6-*deoxy*-α-L-*mannopyranosyl*)-*oxy*]-14β,21-*epoxy*-21-*methoxychola*-4,20(22)-*dien*-24-*oate* **8a**. Colourless crystalline powder, m.p. 144–146 °C (from $Pr^i_2O$–EtOH) (Found: C, 67.1; H, 8.5. $C_{33}H_{50}O_9$ requires C, 67.1; H, 8.5%); $[\alpha]_D^{25}$ −73.5 (*c* 0.5 in $CHCl_3$); $\nu_{max}$(KBr)/cm$^{-1}$ 3420 (OH) and 1740 (CO); $\delta_H$(400 MHz, $CDCl_3$) 0.86 (3 H, s, 13-$CH_3$), 1.07 (3 H, s, 10-$CH_3$), 1.25 (3 H, t, *J* 7.0, $OCH_2CH_3$), 1.30 (3 H, d, *J* 6.2, 5′-$CH_3$), 2.64 (1 H, d, *J* 4.0, 17-H), 3.05 (1 H, dd, *J* 6.6 and 16.9, 23-H), 3.13 (1 H, dd, *J* 7.9 and 16.9, 23-H), 3.38 (3 H, s, 21-$OCH_3$), 3.45 (1 H, dd, *J* 9.4 and 9.4, 4′-H), 3.74–3.80 (2 H, m, 3′-H and 5′-H), 3.92 (1 H, s, 2′-H), 4.10–4.17 (3 H, m, 3-H, $OCH_2CH_3$), 4.89 (1 H, s, 21-H), 4.96 (1 H, s, 1′-H), 5.30 (1 H, s, 4-H) and 5.55 (1 H, dd, *J* 6.6 and 7.9, 22-H); *m*/*z* (FAB) 613 [(M + Na)$^+$, 2%] and 154 (100).

*Ethyl* [21R,20(22)Z]-3β-[(6-*deoxy*-α-L-*mannopyranosyl*)-*oxy*]-14β,21-*epoxy*-21-*methoxychola*-4,20(22)-*dien*-24-*oate* **9a**. Colourless crystalline powder, m.p. 129–131 °C (from $Pr^i_2O$–EtOH) (Found: C, 67.1; H, 8.5. $C_{33}H_{50}O_9$ requires C, 67.1; H, 8.5%); $[\alpha]_D^{25}$ −68.5 (*c* 0.5 in $CHCl_3$); $\nu_{max}$(KBr)/cm$^{-1}$ 3440 (OH) and 1735 (CO); $\delta_H$(400 MHz, $CDCl_3$) 0.88 (3 H, s, 13-$CH_3$), 1.07 (3 H, s, 10-$CH_3$), 1.25 (3 H, t, *J* 7.1, $OCH_2CH_3$), 1.30 (3 H, d, *J* 6.2, 5′-$CH_3$), 2.30 (1 H, d, *J* 5.5, 17-H), 2.99 (1 H, dd, *J* 6.5 and 17.5, 23-H), 3.09 (1 H, dd, *J* 8.0 and 17.5, 23-H), 3.40 (3 H, s, 21-$OCH_3$), 3.44 (1 H, dd, *J* 9.3 and 9.3, 4′-H), 3.74–3.78 (2 H, m, 3′-H and 5′-H), 3.93 (1 H, s, 2′-H), 3.91–4.18 (3 H, m, 3-H and $OCH_2CH_3$), 4.96 (1 H, s, 1′-H), 5.12 (1 H, s, 21-H), 5.30 (1 H, s, 4-H) and 5.43 (1 H, dd, *J* 6.5 and 8.0, 22-H); *m*/*z* (FAB) 613 [(M + Na)$^+$, 16%] and 154 (100).

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