A comparative study of remote oxy-functionalization of unactivated carbons in 5β-steroids by dimethyldioxirane and 2,6-dichloropyridine *N*-oxide / ruthenium-porphyrin / HBr

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Dedicated to Professor Keiichiro Fukumoto on his 70th birthday

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Abstract

Remote oxy-functionalization of methyl 3α-acetoxy- and 3-oxo-5β-cholan-24-oates with 2,6-dichloropyridine (DCP) *N*-oxide catalyzed by (5,10,15,20-tetramesitylporphyrinate) ruthenium (II) carbonyl complex [Ru(TMP)CO] and HBr was compared with that with dimethyldioxirane (DMDO). Treatment of the 5β-steroids with DMDO afforded the corresponding 5β- and 17α-monohydroxylated and 5β,14α- and 5β,17α-dihydroxylated compounds. On the other hand, the corresponding 20*S*-mono- and 5β,20*S*-dioxygenated derivatives (as the γ-lactones), along with 5β-hydroxy compounds, were found to be the major oxidation products of the 5β-steroids with the DCP *N*-oxide / Ru(TMP)CO / HBr system. Both the reagents oxidized unactivated methine carbons stereoselectively, but the degree of regioselectivity depended upon the oxidants employed and the structure of the hydroxyl-protecting groups at C-3 (acetoxyl or carbonyl) of the substrates.

Keywords: 5β-Steroids, 2,6-dichloropyridine *N*-oxide, ruthenium porphyrin, HBr, dimethyldioxirane, remote oxy-functionalization, hydroxylation, ketonization

Introduction

The cytochrome P-450 oxidase-dependent system *in vivo* catalyses effectively the key transformation of unactivated carbon atoms of cholesterol to give various steroid hormones. In analogy with cytochrome P-450, the regio- and stereoselective remote oxy-functionalization (*i.e.*, hydroxylation and ketonization) of unactivated hydrocarbons by non-microbial or non-enzymic

methods is of particular interest from the viewpoint of biomimetic chemistry and/or artificial enzymes for obtaining bioactive steroids by short steps from abundantly available sterols and bile acids. For this purpose, a variety of versatile oxygen-transfer reagents and catalysts associated with cytochrome P-450 has been developed recently by many groups of workers.[1]

Our previous papers have reported the utility of dimethyldioxirane (DMDO; see Figure 1) as an effective oxygen-donating reagent against unactivated carbons in 5β-steroids.[2–4] However, the use of DMDO appears to be limited to oxidizing C-20~-23 side-chain carbons in 5β-cholanoic acid derivatives.

Meanwhile, a number of metalloporphyrins closely related to the iron porphyrin complex (heme) present in the active center of cytochrome P-450, has also been reported as attractive oxidant systems for oxidation reactions.[5] Recently, the successful use of a reagent system consisting of 2,6-dichloropyridine (DCP) *N*-oxide as an oxygen-transfer reagent and (5,10,15,20-tetramesitylporphyrinate) ruthenium (II) carbonyl complex [ruthenium porphyrin, Ru(TMP)CO] in the presence of HBr as catalyst, introduced by Higuchi *et al*.,[6,7] prompted us to examine the system in the biomimetic oxidation of 5β-steroids, because it resulted in effective remote oxy-functionalization of the side chain carbons in 5α-cholestane.

As part of our ongoing work on efficient and short-step syntheses of biologically important steroids, we report herein a comparative study of remote oxy-functionalization of unactivated methine and methylene carbons in methyl 3α-acetoxy-5β-cholan-24-oate (**1**) and methyl 3-oxo-5β-cholan-24-oate (**2**) by DMDO and DCP *N*-oxide / Ru(TMP)CO / HBr system.

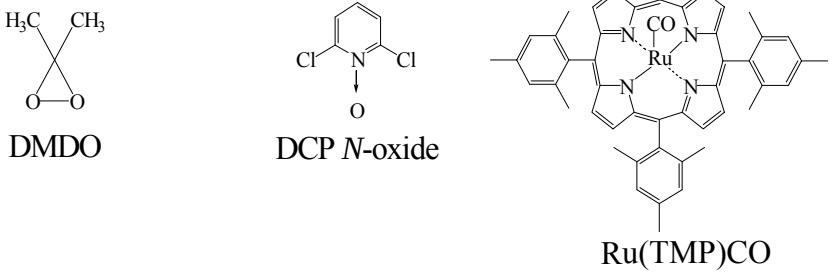


Figure 1

Results and Discussion

DMDO and DCP *N*-oxide were employed as oxygen-donating reagents, and Ru(TMP)CO and HBr as catalysts, for the DCP *N*-oxide oxidation[7] of the oxy-functionalization of unactivated methine and methylene carbons of the substrates, **1** and **2**. As shown in Scheme 1, oxidation of **1** with DMDO for 36h at room temperature afforded the expected 5β-monohydroxylated- (**3**) and

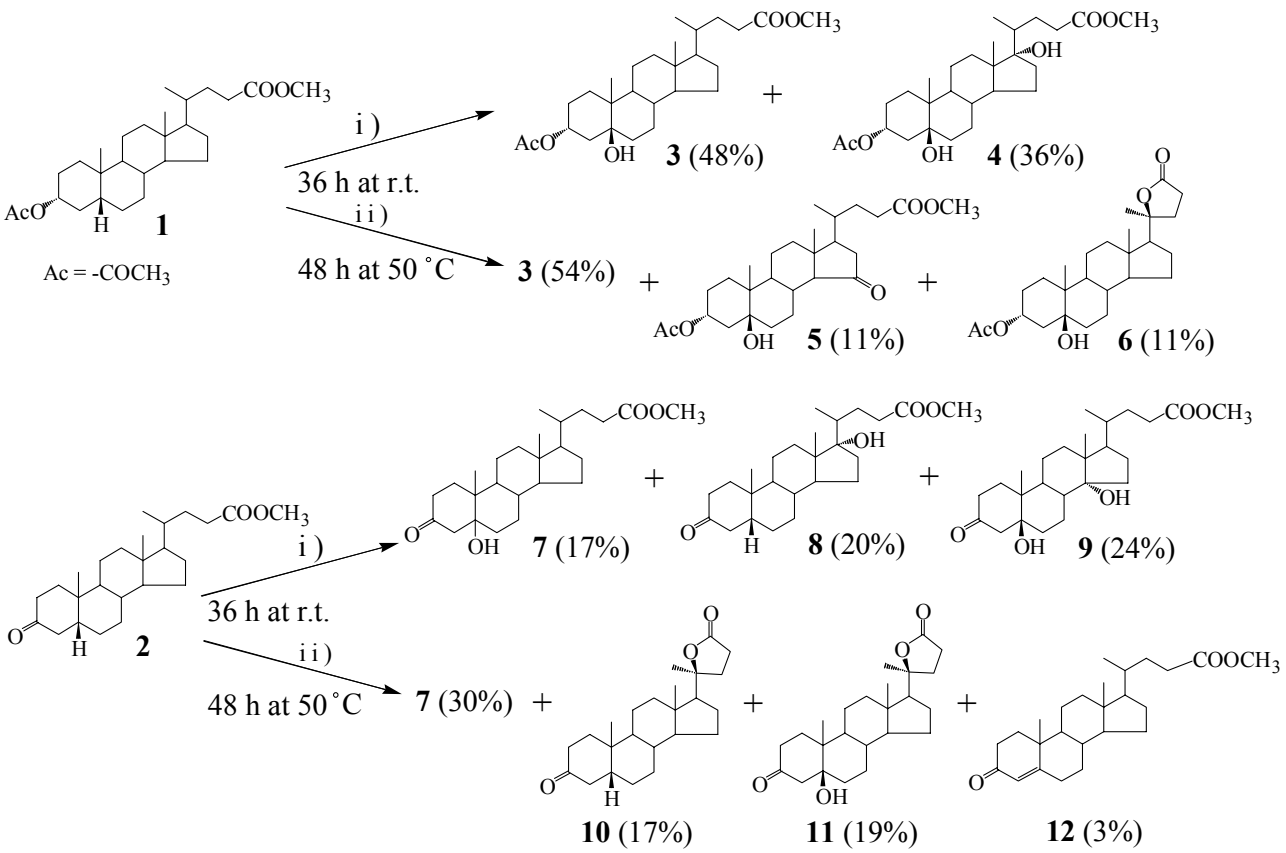
5β,17α-dihydroxylated- compounds (**4**)[3,8] as the major products in 48 and 36% yields, respectively.

The result for **1** with DMDO differed from that observed with the DCP *N*-oxide / Ru(TMP)CO / HBr system. Thus, treatment of **1** with the system for 48 h at 50 °C gave three oxidation products, one of which was identical with **3** (54%). However, the remaining two components were characterized as methyl 3α-acetoxy-5β-hydroxy-15-oxocholan-24-oate (**5**; 11%) and (20*S*)-3α-acetoxy-5β-hydroxy-cholane *O*-24,20-lactone (**6**; 11%). The number and positions of oxygenation, as well as γ-lactone formation, were confirmed by the ^{1}H- and ^{13}C-NMR (Table 1) and GC-MS analyses, compared with those of analogous steroid derivatives reported previously.[3,8] In **5**, the regioselective ketonization of the unactivated methylene carbon at C-15 in **1** was the sole example in this study, and may have occurred by successive oxidation of an intermediary 5β,15ξ-dihydroxy compound.[7] In **6**, the formation of the γ-lactone derivative probably arises from intramolecular esterification between the 24-carboxyl group and 20*S*-hydroxyl group *via* a possible (20*S*)-3α-acetoxy-5β,20-dihydroxy intermediate, in analogy with the direct 20*S*-hydroxylation of 5β-cholestane.[7] Alkaline hydrolysis of **6** with methanolic KOH, followed by acidification with H_2SO_4 yielded (20*S*)-3α,5β,20-trihydroxycholan-24-oic acid. Thus, the stereochemical configuration of the asymmetric center at C-20 was completely retained in the reaction (20β-H to 20β-OH).

When **2** was subjected to DMDO oxidation for 24 h at room temperature, three reaction products (**7**–**9**) were isolated in nearly equal amounts (17–24%), after careful chromatographic purification. Those compounds were identified as methyl 5β-hydroxy-3-oxocholan-24-oate (**7**; 17%), methyl 17α-hydroxy-3-oxo-5β-cholan-24-oate (**8**; 20%), and methyl 5β,14α-dihydroxy-3-oxocholan-24-oate (**9**; 24%).

On the other hand, oxidation of **2** with the DCP *N*-oxide / Ru(TMP)CO / HBr system for 12 h at 50°C yielded four major reaction products, one of which was identical with the 5β-hydroxylated derivative **7** (30%). After chromatographic purification, the three remaining components were characterized as (20*S*)-3-oxo-5β-cholan-*O*-24,20-lactone (**10**; 17%), (20*S*)-5β-hydroxy-3-oxocholan-*O*-24,20-lactone (**11**; 19%), and methyl 3-oxo-4-cholen-24-oate (**12**; 3%). The formation of a small amount of **12** may be derived by elimination of the 5β-hydroxyl group of **7**.

As mentioned above, the oxygen-transfer reaction induced by DCP *N*-oxide / Ru(TMP)CO / HBr produced a variety of novel mono- and di-oxygenated compounds in one step, and the resulting components differed from those obtained by DMDO. A comparison of the oxy-functionalization of the 5β-steroids, **1** and **2**, by the DMDO and DCP *N*-oxide / Ru(TMP)CO / HBr system revealed the following similarities and differences. As has been reported previously,[3,7] 5β-hydroxylation in 5β-steroids is essential for both the oxidants. In addition, 17α- and 14α-hydroxylations are characteristic for DMDO oxidation, while 20*S*-hydroxylation and 15-ketonization are given by DCP *N*-oxide / Ru(TMP)CO / HBr oxidation. In all cases, hydroxylation of a methine hydrogen (C-H) retains completely the stereochemical configuration of the resulting tertiary C-OH.



Reagents : i) DMDO ; ii) DCP *N*-oxide / Ru(TMP)CO / HBr
Values in parentheses refer to yields (%) determined by capillary GC.

Scheme 1

Particularly noteworthy in the DCP *N*-oxide / Ru(TMP)CO / HBr oxidation is 20*S*-hydroxylation *via* the corresponding *O*-24,20-γ-lactone, which is much more effective for **2** than for **1**. When the oxidant system is used, the presence of a carbonyl function at C-3 in **2** diminishes 5β-hydroxylation, but it accelerates remote 20*S*-oxygenation, as compared with that of **1** having an acetoxyl group. A similar trend was also found between **1** and **2** with DMDO oxidation. The above results suggest that variation of electron density caused by the electron-withdrawing function at C-3 on the 5β-steroid nucleus is important factor.[7]

Experimental Section

General Procedures. Melting points (mp) were determined on a microstage apparatus and are uncorrected. IR spectra were obtained in KBr discs on a Bio-Rad FTS-7 FTIR spectrometer. ^{1}H- and ^{13}C-NMR spectra were obtained on a JEOL JNM-EX 270 FT NMR instrument at 270 and

68.80 MHz, respectively. Electron ionization (EI) low-resolution mass spectra (LR-MS) were obtained on a JEOL JMS-Automass 150 gas chromatograph-mass spectrometer at 70 eV. High-resolution mass spectra (HR-MS) were measured using a JEOL LCmate double-focusing magnetic mass spectrometer equipped with an electrospray ionization (ESI) probe under the positive ion mode (PIM) or the negative ion mode (NIM). HR-MS was also obtained on a JEOL JMS-AX500 mass spectrometer with an EI probe under the PIM. A Shimadzu GC-17A gas chromatograph equipped with a FID was used isothermally at 280 ºC: it was fitted with an Ultra ALLOY-1 (HT) stainless-steel capillary column (30 m × 0.25 mm I.D.; film thickness, 0.15 μm; Frontier Lab. Ltd., Koriyama, Japan). The apparatus used for medium-pressure liquid chromatography (MPLC) consisted of a YRD-880 refractive index detector and a uf-3040 chromatographic pump (Shimamura Tech., Tokyo, Japan) using silica gel 60 (230–400 mesh, Nacalai Tesque, Kyoto, Japan) as the normal-phase (NP) adsorbent. TLC was performed on precoated silica gel plates (0.25 mm layer thickness; E. Merck, Darmstadt, Germany) using hexane/EtOAc/acetic acid mixtures (80:20:1–20:80:1, v/v/v) as developing solvents.

A solution (0.33 mol/L) of DMDO in $CHCl_3$ was prepared according to a literature method using Oxone®, $NaHCO_3$, and acetone.[3,8] DCP *N*-oxide was prepared according to the procedure of Rousseau and Robins.[9] The method of Lindsey *et al*. was used for the preparation of 5,10,15,20-tetrakis-(2,4,6-trimethylphenyl)-porphyrin.[10] Ruthenium porphyrin complex, Ru(TMP)CO, was prepared by a slight modification of the method of Rillema *et al*.[11]

General procedure for the oxidation with DMDO

To a solution of steroid (1 mmol) in CH_2Cl_2 (6 ml) was added a freshly prepared solution of DMDO (2 mmol; 6 ml) in $CHCl_3$. The mixture was left at room temperature for 12 h, and excess DMDO and solvent were evaporated off under reduced pressure. The above procedure was repeated for 2–3 runs (24–36 h) with monitoring by TLC. After the reaction, the product was purified by passage through an open column of silica gel (70–230 mesh, 60 g), eluting with benzene–EtOAc (9:1–6:4, v/v) mixtures and then by NP-MPLC on silica gel (230–400 mesh, 21 g), eluting with benzene–EtOAc (9:1, v/v).

General procedure for the oxidation with DCP *N*-oxide catalyzed by ruthenium porphyrin in the presence of HBr

To a magnetically stirred solution of steroid (1.3 mmol) and molecular sieves (850 mg; 4Å) in benzene (3 ml) were successively added DCP *N*-oxide (630 mg), ruthenium porphyrin complex (5 mg), and then HBr (50 μl). The mixture was stirred at 50 °C for 12–48 h, and the reaction product was extracted with benzene. The combined organic layer was washed with water, dried with Drierite, and evaporated to dryness. The oily residue was chromatographed on a column of silica gel (60 g), eluting with benzene–EtOAc (9:1–6:4, v/v) mixtures and then by NP-MPLC on silica gel (230–400 mesh, 21 g), eluting with benzene–EtOAc (95:5, v/v).

Oxidation Products of Methyl 3α-acetoxy-5β-cholan-24-oate with DMDO

Methyl 3α-acetoxy-5β,17α-dihydroxycholan-24-oate (4). Isolated as colorless needles [fraction 2 (Fr. 2)] recrystallized from aqueous acetone: mp, 189–191 °C.[3] IR, $\nu_{max.}$/cm^{-1}, 1712, 1731 (C=O), 3470 (OH). ^{1}H NMR, δ, 0.73 (s, 3H, 18-CH_3), 0.90 (d, 3H, *J* = 6.8 Hz, 21-CH_3), 0.91 (s, 3H, 19-CH_3), 2.02 (s, 3H, $OCOCH_3$), 3.67 (s, 3H, $COOCH_3$), 5.07 (brm 1H, 3β-H). LR-MS, *m/z*, 368 (15%, M-2H_2O-AcOH), 313 [18%, M-2H_2O-side chain (S.C.)], 281 (36%), 271 (15%, M-H_2O-AcOH-S.C.), 253 (69%, M-2H_2O-AcOH-S.C.), 207 (62%), 171 (100%).

Oxidation products of methyl 3α-acetoxy-5β-cholan-24-oate with DCP *N*-oxide/Ru(TMP)CO/ HBr

Methyl 3α-acetoxy-5β-hydroxycholan-24-oate (3). Isolated as colorless needles (Fr. 1), recrystallized from benzene–hexane: mp, 175–177 °C [lit.[3], mp, 165–167 °C, from aqueous acetone]. IR, ν_{max}/cm^{-1}, 1708, 1735 (C=O), 3454 (OH). ^{1}H NMR, δ 0.64 (s, 3H, 18-CH_3), 0.90 (s, 3H, 19-CH_3), 0.91 (d, 3H, *J* = 7.3 Hz, 21-CH_3), 2.02 (s, 3H, $OCOCH_3$), 3.67 (s, 3H, $COOCH_3$), 5.08 (brm 1H, 3β-H). LR-MS, *m/z*, 430 (8%, M-H_2O), 370 (16%, M-H_2O-AcOH), 334 (38%), 273 (23%, M-AcOH-S.C.), 255 (56%, M-H_2O-AcOH-S.C.), 228 (33%, M-H_2O-AcOH-S.C.-part of ring D), 213 (100%, M-H_2O-AcOH-S.C.–ring D).

Methyl 3α-acetoxy-5β-hydroxy-15-oxocholan-24-oate (5). Isolated as colorless needles (Fr. 2) recrystallized from ethyl acetate–hexane: mp, 163–165 °C. IR, $\nu_{max.}$/cm^{-1}, 1712, 1735 (C=O), 3467 (OH). ^{1}H NMR, δ 0.74 (s, 3H, 18-CH_3), 0.91 (s, 3H, 19-CH_3), 1.00 (d, 3H, *J* = 5.9 Hz, 21-CH_3), 2.02 (s, 3H, $OCOCH_3$), 3.67 (s, 3H, $COOCH_3$), 5.08 (brm, 1H, 3β-H). LR-MS, *m/z*, 444 (12%, M-H_2O), 402 (29%, M-AcOH), 384 (23%, M-H_2O-AcOH), 347 (49%, M-S.C.), 332 (23%, M-CH_3-S.C.), 320 (17%, M-S.C.-part of ring D), 305 (20%, M-CH_3-S.C.-part of ring D), 287 (21%, M-AcOH-S.C.), 269 (36%, M-H_2O-AcOH-S.C.), 251 (38%, M-H_2O-AcOH-211), 242 (30%, M-H_2O-AcOH-S.C.-part of ring D), 214 (100%, M-H_2O-AcOH-S.C.-ring D). HR-MS (ESI-PIM), Calcd. for $C_{27}H_{42}O_6Na$ $[M+Na]^+$: 485.2879. Found: *m/z*, 485.2898.

(20*S*)-3α-Acetoxy-5β-hydroxycholan-*O*-24,20-lactone (6). Isolated as colorless needles (Fr. 3) recrystallized from benzene–hexane: mp, 202–204 °C. IR, $\nu_{max.}$/cm^{-1}, 1736, 1767 (C=O), 3518 (OH). ^{1}H NMR, δ 0.80 (s, 3H, 18-CH_3), 0.91 (s, 3H, 19-CH_3), 1.00 (s, 3H, 21-CH_3), 2.02 (s, 3H, $OCOCH_3$), 5.09 (brm, 1H, 3β-H). LR-MS [as the trimethylsilyl (TMS) ether derivative], *m/z*, 490 (9%, M-CH_3), 444 (30%, M-AcOH), 429 (66%, M-CH_3-AcOH), 390 (78%, M-CH_3-S.C.), 354 [100%, M-AcOH-trimethylsilanol (TMSOH)], 339 (12%, M-CH_3-AcOH-TMSOH), 315 (12%, M-TMSOH-S.C.), 255 (48%, M-AcOH-TMSOH-S.C.), 228 (49%, M-AcOH-TMSOH-S.C.-part of ring D), 213 (64%, M-AcOH-TMSOH-S.C.-ring D). HR-MS (ESI-PIM), Calcd. for $C_{26}H_{40}O_5Na$ $[M+Na]^+$: 455.2773. Found: *m/z* 455.2811.

(20*S*)-3α,5β,20-Trihydroxycholan-24-oic acid. The usual alkaline hydrolysis of the lactone **6** with 5% methanolic KOH, followed by acidification with 10% H_2SO_4, gave the desired free acid, which was recrystallized from EtOAc as a colorless amorphous solids: mp, 296–298°C. IR, $\nu_{max.}$/cm^{-1}, 1731 (C=O), 3442, 3511 (OH). ^{1}H-NMR [as the methyl ester formed by reaction with diazomethane], δ 0.89 (s, 3H, 18-CH_3), 1.25 (s, each 3H, 19- and 21-CH_3), 3.67 (s, 3H, $COOCH_3$), 4.02 (brm, 1H, 3β-H). LR-MS [as the methyl ester-TMS ether derivative], *m/z*, 549

(15%, M-TMSOH), 534 (4%, M-CH_3-TMSOH), 459 (37%, M-2TMSOH), 444 (29%, M-CH_3-2TMSOH), 404 (31%), 369 (79%, M-3TMSOH), 354 (23%, M-CH_3-3TMSOH), 314 (23%), 255 (79%, M-3TMSOH-S.C.), 213 (100%, M-3TMSOH-S.C.-ring D). HR-MS (ESI-NIM), Calcd. for $C_{24}H_{39}O_5$ $[M-H]^-$: 407.2797. Found: *m/z*, 407.2791.

Oxidation products of methyl 3-oxo-5β-cholan-24-oate with DMDO

Methyl 5β-hydroxy-3-oxocholan-24-oate (7). Isolated as colorless amorphous solids (Fr. 1) recrystallized from aqueous acetone: mp, 170–172°C. IR, $\nu_{max.}/cm^{-1}$, 1702, 1741 (C=O), 3382 (OH). ^1H NMR, δ 0.68 (s, 3H, 18-CH_3), 0.91 (d, 3H, *J* = 6.5 Hz, 21-CH_3), 1.00 (s, 3H, 19-CH_3), 3.67 (s, 3H, $COOCH_3$). LR-MS, *m/z*, 386 (23%, M-H_2O), 355 (3%, M-$2H_2O$-CH_3), 329 (6%, M-H_2O-CH_3-CH_2CO), 229 (100%, M-H_2O-S.C.-ring D), 211 (24%, M-$2H_2O$-S.C.-ring D). HR-MS (ESI-PIM), Calcd. for $C_{25}H_{40}O_4Na$ $[M+Na]^+$: 427.2824. Found: *m/z*, 427.2810.

Methyl 17α-hydroxy-3-oxocholan-24-oate (8). Isolated as a non-crystalline substance (Fr. 2). IR, $\nu_{max.}/cm^{-1}$, 1714, 1735 (C=O), 3542 (OH). ^1H NMR, δ 0.68 (s, 3H, 18-CH_3), 1.00 (s, 3H, 19-CH_3), 0.90 (d, 3H, *J* = 6.5 Hz, 21-CH_3), 3.67 (s, 3H, $COOCH_3$). LR-MS, *m/z*, 404 (47%, M), 371 (23%, M-H_2O-CH_3), 353 (7%, M-$2H_2O$-CH_3), 329 (10%, M-H_2O-CH_3-CH_2CO), 289 (100%, M-S.C.), 229 (12%, M-H_2O-S.C.-ring D), 211 (19%, M-$2H_2O$-S.C.-ring D). HR-MS (ESI-PIM), Calcd. for $C_{25}H_{40}O_4Na$ $[M+Na]^+$: 427.2824. Found: *m/z*, 427.2810.

Methyl 5β,14α-dihydroxy-3-oxocholan-24-oate (9). Isolated as colorless amorphous solids (Fr. 3) recrystallized from acetone–hexane: mp, 185–187°C. IR, $\nu_{max.}/cm^{-1}$, 1705, 1729 (C=O), 3456, 3441 (OH). ^1H NMR, δ 0.82 (s, 3H, 18-CH_3), 0.90 (d, 3H, *J* = 6.8 Hz, 21-CH_3), 1.00 (s, 3H, 19-CH_3), 3.67 (s, 3H, $COOCH_3$). LR-MS, *m/z*, 402 (3%, M-H_2O), 384 (32%, M-$2H_2O$), 369 (7%, M-$2H_2O$-CH_3), 353 (6%), 338 (4%), 287 (5%, M-H_2O-S.C.), 269 (100%, M-$2H_2O$-S.C.), 251 (15%, M-$3H_2O$-S.C.), 227 (21%, M-$2H_2O$-S.C.-ring D), 208 (42%). HR-MS (ESI-PIM), Calcd. for $C_{25}H_{40}O_5Na$ $[M+Na]^+$: 443.2773. Found: *m/z*, 443.2768.

Oxidation products of methyl 3-oxo-5β-cholan-24-oate with DCP *N*-oxide / Ru(TMP)CO / HBr

Methyl 3-oxo-4-cholen-24-oate (12). Isolated as colorless amorphous solids (Fr. 1) recrystallized from aqueous acetone: mp, 124–126 °C [lit.,[12] mp, 125–126 °C]. IR, $\nu_{max.}/cm^{-1}$, 1677, 1736 (C=O), 1616, 3008 (C=C). ^1H NMR, δ 0.71 (s, 3H, 18-CH_3), 0.91 (d, 3H, *J* = 6.2 Hz, 21-CH_3), 1.18 (s, 3H, 19-CH_3), 3.67 (s, 3H, $COOCH_3$), 5.73 (s, 1H, 4-CH). LR-MS, *m/z*, 386 (24%, M^+), 371 (5%, M-CH_3), 344 (8%, M-CH_2CO), 329 (8%, M-CH_3-CH_2CO), 313 (4%), 271 (14%, M-S.C.-ring D), 229 (100%, M-S.C.-ring D), 211 (21%, M-H_2O- S.C.-ring D).

(20*S*)-3-Oxo-5β-cholan-*O*-24,20-lactone (10). Isolated as a non-crystalline substance (Fr. 3). IR, $\nu_{max.}/cm^{-1}$, 1735, 1771 (C=O). ^1H-NMR, δ, 0.84 (s, 3H, 18-CH_3), 1.03 (s, 3H, 19-CH_3), 1.46 (s, 3H, 21-CH_3). LR-MS, *m/z*, 372 (37%, M^+), 354 (24%, M-H_2O), 339 (63%, M-H_2O-CH_3), 321 (8%, M-$2H_2O$-CH_3), 302 (87%), 273 (51%, M-S.C.-ring D), 246 (96%, M-S.C.-part of ring D), 231 (95%, M-S.C.-ring D), 211 (100%, M-H_2O- S.C.-ring D). HR-MS (EI-PIM), Calcd. for $C_{24}H_{36}O_3$ $[M]^+$: 372.2664. Found: *m/z*, 372.2642.

(20*S*)-5β-Hydroxy-3-oxocholan-*O*-24,20-lactone (11). Isolated as colorless amorphous solids (Fr. 4) recrystallized from acetone–hexane: mp, 164–166 °C. IR, $\nu_{max.}/cm^{-1}$, 1736, 1773 (C=O), 3414 (OH). ^{1}H NMR, δ 0.84 (s, 3H, 18-CH_3), 1.01 (s, 3H, 19-CH_3), 1.47 (s, 3H, 21-CH_3). LR-MS, *m/z*, 370 (47%, M-H_2O), 355 (13%, M-H_2O-CH_3), 328 (43%, M-H_2O-CH_2CO), 313 (8%, M-H_2O-CH_3-CH_2CO), 271 (71%, M-H_2O-S.C.), 244, (60%, M-H_2O-S.C.-part of ring D), 229 (100%, M-H_2O-S.C.-ring D), 201 (31%). HR-MS (EI-PIM), Calcd. for $C_{24}H_{36}O_4$ $[M]^{+:}$ 388.2614. Found: *m/z*, 388.2592.

Table 1. ^{13}C-NMR chemical shifts of oxy-functionalization products

Carbon	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
1	29.4	29.3	29.4	29.3	31.1	37.2	31.3	37.2	31.1	35.7
2	26.1	26.1	26.1	26.1	37.3	37.0	37.3	36.9	37.3	33.9
3	71.4	71.3	71.2	71.4	211.6	213.3	211.5	213.3	211.3	199.6
4	38.1	38.0	38.2	38.1	49.3	42.3	49.4	42.3	49.3	123.7
5	75.4	75.3	74.9	75.2	78.4	44.4	78.5	44.2	78.5	171.6
6	36.9	36.7	36.5	36.7	36.1	25.7	36.0	25.6	36.2	32.9
7	28.6	28.5	27.1	28.4	29.0	26.6	23.7	26.5	28.9	32.0
8	34.9	35.1	31.3	34.3	34.7	35.7	37.7	35.0	34.2	35.6
9	43.2	42.8	43.0	43.1	43.6	40.3	36.1	40.7	43.7	53.7
10	39.6	39.6	39.7	39.6	40.1	34.8	40.2	34.9	40.1	38.6
11	21.1	20.9	20.6	20.9	21.6	21.0	20.7	21.0	21.4	21.0
12	39.8	32.4	39.7	39.9	39.7	32.6	32.0	40.1	39.8	39.6
13	42.5	47.4	42.2	42.9	42.5	47.7	46.6	43.2	43.0	42.4
14	56.5	51.0	65.8	56.5	56.4	50.9	85.4	56.5	56.5	55.8[a]
15	24.2	23.5	215.1	23.6	24.0	23.5	33.1	23.6	23.6	24.1
16	28.1	38.0	41.7	22.7	28.0	38.1	26.1	22.7	22.6	28.0
17	55.8	86.1	51.4	59.1	55.7	86.2	50.6	59.2	59.0	55.7[a]
18	12.0	13.5	12.9	13.2	12.0	14.5	15.7	13.3	13.3	11.9
19	16.3	16.2	16.3	16.3	16.1	22.6	15.7	22.6	16.1	17.3
20	35.3	39.1	35.0	88.5	35.2	39.1	35.2	88.5	88.4	35.3
21	18.2	14.4	18.5	26.5	18.2	13.5	18.2	26.6	26.5	18.2
22	31.0	27.4	30.7	33.6	30.9	27.4	31.1	33.7	33.6	30.9[b]
23	31.0	32.1	31.0	28.1	30.9	32.1	31.1	28.1	28.1	31.0[b]
24	174.7	174.4	174.1	177.4	174.6	174.4	174.6	177.5	177.4	174.7
$COO\underline{C}H_3$	51.5	51.5	51.6	–	51.4	51.5	51.5	–	–	51.5
$O\underline{C}OCH_3$	170.5	170.6	170.4	170.4	–	–	–	–	–	–
$OCO\underline{C}H_3$	21.4	21.4	21.4	21.4	–	–	–	–	–	–

[a,b] Assignments down a vertical column may be interchanged.

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