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# Synthesis and Characterization of Dimeric Bile Acid Ester Derivatives

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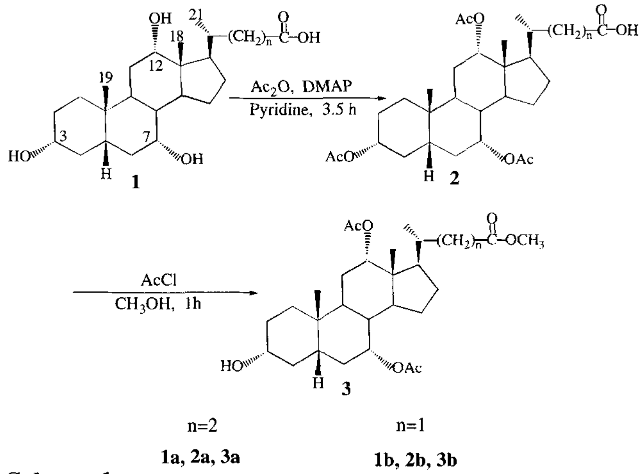
In continuation of our previous work on the synthesis of dimeric bile acid ester derivatives to study their binding properties with other components [1], we now report the synthesis of four bile acid dimers which represent all head-to-tail combinations of cholic and 24-norcholic acids that may exist either in a linear or semi-rigid molecular tweezer (folded) conformation. Here we regard the 3$\alpha$-OH group as the tail end and the C-24 (C-23) carboxyl group as the head of the cholic acid.



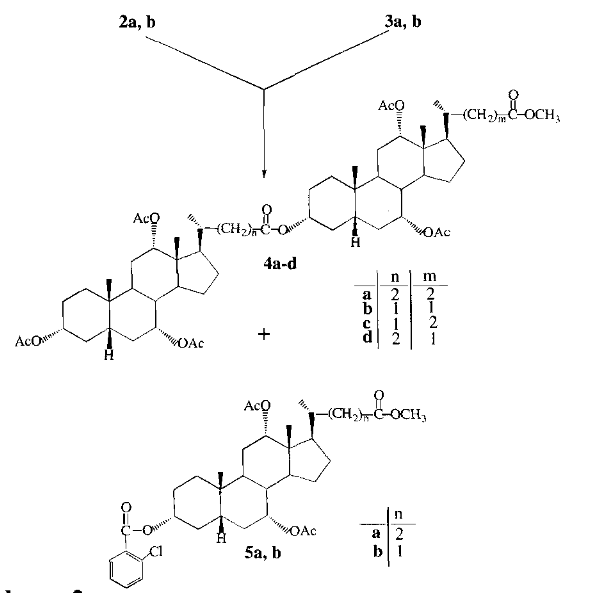
Scheme 1

## Preparation of Monomers for Coupling

The triacetoxycholanoic acid (**2a**) and triacetoxy-24-nor-cholic acid (**2b**) were synthesized from cholic acid (**1a**) and 24-norcholic acid (**1b**), as shown in Scheme 1. The reaction was carried out in acetic anhydride with pyridine as solvent and 4-dimethylaminopyridine (DMAP) as catalyst [2]. When methylene chloride was used instead of pyridine, there were several by-products, and the cholic acids did not react completely. Compound **3a** and **3b** were synthesized from **2a** or **2b** in one step. *In situ* generated hydrogen chloride [3] in methanol can selectively hydrolyze the 3-acetoxy group and simultaneously esterify the carboxylic group in overall yields of 95–96%.

## Dimerization

Dimeric steroids have been synthesized by using dicyclohexylcarbodiimide (DCC) and 4-dimethylaminopyridine (DMAP) [4]. Our group also successfully synthesized $\alpha$-dimer (73%) and $\beta$-dimer (47%) of a lithocholic acid derivative with these reagents [1]. Application of this method to the cholic acid system gave no product. We believe the reason is the increased steric effect of the 7$\alpha$-OAc and 12$\alpha$-OAc groups which inhibit esterification of the free acids. In 1979, Yamaguchi [5] reported a rapid and mild esterification method by using 2,4,6-trichlorobenzoic anhydrides in presence of DMAP. Later work [6–8] demonstrated that this is a good method to synthesize $\alpha$-dimers (51–88%) and cyclotrimers (22–47%) of cholic acid derivatives. We tried this method with 2-chlorobenzoyl chloride instead of 2, 4, 6-trichloro-benzoyl



Scheme 2

chloride in a one pot reaction as shown in Scheme 2. However, the yields (50% for cholic acid derivatives, 15% for 24-norcholic acid derivatives) were less satisfactory. The mechanism of the Yamaguchi [5] method shows two steps: the formation of the mixed anhydride and the alcoholysis of the anhydride. According to this mechanism, we first refluxed 2-chlorobenzoyl chloride and the acid **2a** or **2b** in THF with triethylamine, then added **3a** or **3b** and DMAP. The yields were improved to 74% for the cholic acid derivatives and to 41% for the 24-norcholic acid derivatives, and the production of transesterification by-products was reduced from 32% to 11%. The lower yields of dimers synthesized from 24-norcholic acid in comparison to those from cholic acid (–73%) seems to be the result of more steric effects of the shorter 17-side chain of the 24-norcholic acid.

## NMR Spectra

The hydrogens at C-22 of 24-norcholates give rise to a double doublet. Otherwise, the chemical shifts of the same functional groups on the two different monomers coincide. Compared with the monomers, the same functional groups on the dimers do not show significantly different chemical shifts. In the $^{13}C$ NMR spectra, both the mixed dimers, **4c** and **4d** show more peaks than those of the homodimers **4a** and **4b** because they have different monomeric units. In going from the cholate to the 24-norcholate system, the C-22 and C-20 carbons become more deshielded ($\delta$=30.9 to 33.1 and 34.7 to 41.0 ppm, respectively) because they are closer to the carboxyl group. The other carbons do not give obvious different chemical shifts between these cholic acid derivatives. For the five acetates in the dimers and the three acetates in the monomers, the axial ones can be distinguished from equatorial ones.

## Mass Spectra

Early research [9] demonstrated that loss of HOAc from bile acid acetate derivatives in the following order of decreasing preference: 12$\alpha$-OAc>7$\alpha$-OAc>3$\alpha$-OAc. According to our results, all MS spectra exhibited peaks corresponding to loss of 7$\alpha$-OAc, 12$\alpha$-OAc and the 17-side chain. For all the investigated intermediates, the 17-side chain can be lost before or after the 3$\alpha$-OAc is lost; 3$\alpha$-OAc is always lost after 7$\alpha$-OAc and 12$\alpha$-OAc. While all monomers could easily be characterized by EI mass spectrometry, the less volatile dimers required fast-atom-bombardment (FAB) mass spectral analysis. Three kinds of FAB mass spectral peaks $[MLi+LiI]^+$, $[MLi]^+$, $[MLi\text{-}HOAc]^+$ were present in all these spectra. Furthermore, the spectra show some minor peaks corresponding to the starting materials and other peaks, which belong to the protonated LiI (135.1) and the matrix components, the 3-nitrobenzyl alcohol and the lithium-ion (197.1).

We gratefully thank Dr. Peter Groner for recording the 250 MHz $^1H$ NMR and 63 MHz $^{13}C$ NMR spectra. The mass spectra were determined by the Nebraska Center for Mass Spectrometry.

## Experimental

Column chromatography was carried out using Grade 62 (60–200 mesh) silica gel and eluted by hexane/ethyl acetate solvent system. Melting points were determined on a Fisher–Johns melting point apparatus and are uncorrected. $^1H$ NMR and $^{13}C$ NMR spectra were measured at 250 MHz or 63 MHz (Bruker) in $CDCl_3$ as solvent and TMS as internal standard.

*3α,7α,12α-Triacetoxy-5β-cholan-24-oic acid* (**2a**)

To a cooled (0 °C) suspension of **1a** (10g; 0.0245 mol) in acetic anhydride (20 ml) and pyridine (30 ml), DMAP (1.80 g; 0.0147 mol; 0.6 eq.) was added. The reaction mixture was stirred at 25 °C for 3 h. The solvent was concentrated *in vacuo*, 500 ml diethyl ether added and the solution washed with 0.14 M HCl, $NaHCO_3$, and NaCl. The organic layer was dried with $Na_2SO_4$ and the solvent was evaporated. The residue was flash chromatographed on a silica-gel column (eluant: *n*-hexane/EtOAc) to afford 10.8g (82.5%) **2a** as a colorless solid with *m.p.* 78–80 °C ; [10] *m.p.* 105–108 °C. – $^1H$ NMR ($CDCl_3$): $\delta$ 0.73 (s, 3H, 18-$H_3$); 0.85 (d, 3H, 21-$H_3$); 0.91 (s, 3H, 19-$H_3$); 2.0 (s, 3H, 3-OAc); 2.10 (s, 3H, 7-OAc); 2.20 (s, 3H, 12-OAc); 2.35 (m, 2H, 22-$H_2$); 4.60 (m, 1H, 3$\beta$-H); 4.90 (broad s, 1H, 7$\beta$-H); 5.0 (broad s, 1H, 12$\beta$-H). – MS(EI): *m/e*(%): 534 $[M]^{+\cdot}$ (3), 474 $[M-HOAc]^{+\cdot}$ (5), 414 $[M-2HOAc]^{+\cdot}$ (32) 354 $[M-3HOAc]^{+\cdot}$ (78) 313 $[M-2HOAc\text{-}C_5H_9O_2]^+$ (33) 253 $[M-3HOAc\text{-}C_5H_9O_2]^+$ (100).

*3α,7α,12α-Triacetoxy-24-nor-5β-cholan-23-oic acid* (**2b**)

Prepared in analogous fashion, *m.p.* 108–110 °C; [3] *m.p.* 105–107 °C (81%). – $^1H$ NMR ($CDCl_3$): $\delta$ 0.77 (s, 3H, 18-$H_3$); 0.92 (d, 3H, 19-$H_3$); 0.94 (s, 3H, 21-$H_3$); 2.0 (s, 3H, 3-OAc); 2.10 (s, 3H, 7-OAc); 2.13 (s, 3H, 12-OAc); 2.40 (dd, 2H, 22-$H_2$); 4.60 (m, 1H, 3$\beta$-H); 4.90 (broad s, 1H, 7$\beta$-H); 5.0 (broad s, 1H, 12$\beta$-H). – MS(EI): *m/e*(%): 520 $[M]^{+\cdot}$ (4), 460 $[M-HOAc]^{+\cdot}$ (5), 400 $[M-2HOAc]^{+\cdot}$ (31), 340 $[M-3HOAc]^{+\cdot}$ (75), 286 (18), 253 $[M-3HOAc\text{-}C_4H_7O_2]^+$ (100).

*Methyl 7α,12α-diacetoxy-3α-hydroxy-5β-cholan-24-oate* (**3a**)

To a cooled (0 °C) solution of **2a** (5.5 g; 10.3 mmol) in methanol (60 ml), acetyl chloride (5.0 ml, 70.3 mmol) was added dropwise. The reaction mixture was stirred at 25 °C for 1 h, $NaHCO_3$ (5.88g) was added, and the reaction mixture extracted with ethyl acetate. The organic layers were washed with NaCl solution, dried with $Na_2SO_4$ and concentrated *in vacuo* to afford 5.0g (96%) **3a** with *m.p.* 70–72 °C; [3] *m.p.* 71–75 °C. – $^1H$ NMR ($CDCl_3$): $\delta$ 0.73 (s, 3H, 18-$H_3$); 0.81 (d, 3H, 21-$H_3$); 0.90 (s, 3H, 19-$H_3$); 2.07 (s, 3H, 7-OAc); 2.09 (s, 3H, 12-OAc); 2.30 (m, 2H, 22-$H_2$); 3.50 (m, 1H, 3$\beta$-H); 3.66 (s, 3H, $COOCH_3$); 4.90 (broad s, 1H, 7$\beta$-H); 5.0 (broad s, 1H, 12$\beta$-H). MS(EI): *m/e*(%): 506 $[M]^{+\cdot}$ (2), 446 $[M-HOAc]^{+\cdot}$ (3), 386 $[M-2HOAc]^{+\cdot}$ (89), 368 $[M-2HOAc\text{-}H_2O]^{+\cdot}$ (55), 353 $[M-2HOAc-H_2O\text{-}CH_3]^{+\cdot}$ (25), 271 $[M-2HOAc-C_6H_{11}O_2]^+$ (91), 253 $[M-2HOAc-H_2O\text{-}C_6H_{11}O_2]^+$ (100).

*Methyl 7α,12α-diacetoxy-3α-hydroxy-24-nor-5β-cholan-23-oate* (**3b**)

Prepared in analogous fashion, *m.p.* 148–150 °C; [3] *m.p.* 71–75 °C (94.7%). – $^1H$NMR ($CDCl_3$): $\delta$ 0.76 (s, 3H, 18-$H_3$); 0.86 (d, 3H, 21-$H_3$); 0.91 (s, 3H, 19-$H_3$); 2.06 (s, 3H, 7-OAc); 2.08 (s, 3H, 12-OAc); 2.4 (dd, 2H, 22-$H_2$); 3.49 (m, 1H, 3$\beta$-

H); 3.65 (s, 3H, $COOCH_3$); 4.90 (broad s, 1H, 7β-H); 5.0 (broad s, 1H, 12β-H). – MS(EI): *m/e*(%): 492 $[M]^{+\cdot}$ (4), 432 $[M-HOAc]^{+\cdot}$ (5), 372 $[M-2HOAc]^{+\cdot}$ (87), 354 $[M-2HOAc-H_2O]^{+\cdot}$ (44), 339 $[M-2HOAc-H_2O-CH_3]^+$ (23), 300, (14) 253 $[M-2HOAc-H_2O-C_5H_9O_2]^+$ (100), 226 (37).

### General procedure for the synthesis of the α-dimers

A mixture of 0.6 mmol of compounds **2**, 0.6 mmol of 2-chlorobenzoyl chloride, 0.6 mmol of triethylamine and 10 ml of THF was refluxed for 2 h. THF was evaporated *in vacuo*. The compounds **3** (0.6 mmol), DMAP 300 mg (2.46 mmol), and benzene (20 ml) were then added to this reaction mixture and continued to reflux for 12 h. The solvent was evaporated in vacuo, the residue flash chromatographed on a silica-gel column (eluant: *n*-hexane/EtOAc) to afford **4** and**5**.

*Dimer* **4a:** *m.p.* 105–107 °C, yield 74% (**4a**) and 11% (**5a**). – [1]H NMR ($CDCl_3$): δ 0.73 (s, 6H, 18-$H_3$, 18'-$H_3$); 0.81 (d, 6H, 21-$H_3$, 21'-$H_3$); 0.91 (s, 6H, 19-$H_3$, 19'-$H_3$); 2.07 (s, 3H, 3-OAc); 2.08 (s, 6H, 7-OAc, 7'-OAc); 2.13 (s, 6H, 12-OAc, 12'-OAc); 3.66 (s, 3H, $COOCH_3$); 4.57 (m, 2H, 3β-H, 3'β-H); 4.90 (broad s, 2H, 7β-H, 7'β-H); 5.08 (broad s, 2H, 12β-H, 12'β-H). – [13]C NMR ($CDCl_3$): δ 12.25 (18-C, 18'-C), 17.54 (21-C, 21'-C), 21.44 (axial-$\underline{CH_3}CO$), 21.59 (eq-$\underline{CH_3}CO$), 22.56 (19-C, 19'-C), 22.62 (15-C, 15'-C), 25.59 (11-C, 11'-C), 26.96 (2-C, 2'-C), 27.19 (16-C, 16'-C), 28.93 (9-C, 9'-C), 30.91 (23-C, 23'-C), 31.29 (22-C, 22'-C), 31.54 (6-C, 6'-C), 34.39 (10-C, 10'-C), 34.64 (1-C, 4-C; 1'-C, 4'-C; 20-C, 20'-C), 37.79 (8-C, 8'-C), 41.0 (5-C, 5'-C), 43.43 (14-C, 14'-C), 45.12 (13-C, 13'-C), 47.43, 47.54 (17-C, 17'-C), 51.55 (-$OCH_3$), 70.77 (7-C, 7'-C), 73.99, 74.11 (3-C, 3'-C), 75.45 (12-C, 12'-C), 170.61 (eq-$CH_3\underline{CO}$), 173.81 (axial-$CH_3\underline{CO}$), 173.63 (tail-24-C), 174.63 (head-24-C). FAB/MS (3-NBA+LiI): *m/e* (%): 1163.6 $[MLi+LiI]^+$, 1029.1 $[MLi]^+$, 969.5 $[MLi-HOAc]^+$, 369.3, 253.2, 197.1. – Anal. Calcd. for $C_{59}H_{90}O_{14}$: C 69.25, H 8.86. Found: C 69.45, H 8.99.

*Dimer* **4b:** *m.p.* 173–175 °C, yield 41% (**4b**) and 23% (**5b**). – [1]H NMR ($CDCl_3$): δ 0.77 (s, 6H, 18-$H_3$, 18'-$H_3$); 0.88 (d, 6H, 21-$H_3$, 21'-$H_3$); 0.92 (s, 6H, 19-$H_3$, 19'-$H_3$); 2.05 (s, 3H, 3-OAc); 2.06 (s, 3H, 7-OAc); 2.09 (s, 3H, 7'-OAc); 2.13 (s, 3H, 12-OAc); 2.14 (s, 3H, 12'-OAc); 2.40 (m, 4H, 22-$H_2$, 22'-$H_2$); 3.66 (s, 3H, $COOCH_3$); 4.59 (m, 2H, 3β-H, 3'β-H); 4.91 (broad s, 2H, 7β-H, 7'β-H); 5.10 (broad s, 2H, 12β-H, 12'β-H). – [13]C NMR ($CDCl_3$): δ 12.26 (18-C, 18'-C), 18.73 (21-C, 21'-C), 21.46 (axial-$\underline{CH_3}CO$), 21.59 (eq-$\underline{CH_3}CO$), 22.58 (19-C, 19'-C), 22.84 (15-C, 15'-C), 25.60 (11-C, 11'-C), 26.93, 27.05 (2-C, 2'-C), 27.34 (16-C, 16'-C), 28.93 (9-C, 9'-C), 31.29 (6-C, 6'-C), 33.06 (22-C, 22'-C), 34.39 (10-C, 10'-C), 34.65 (tail-1-C, 4-C), 34.85 (head-1-C, 4-C), 37.79 (8-C, 8'-C), 40.95 (20-C, 20'-C), 41.19, 41.62 (5-C, 5'-C), 43.50 (14-C, 14'-C), 45.19 (13-C, 13'-C), 47.45 (17-C, 17'-C), 51.43 (-$OCH_3$), 70.72 (7-C, 7'-C), 73.93, 74.13 (3-C, 3'-C), 75.29 (12-C, 12'-C), 170.0 (eq-$CH_3\underline{CO}$), 170.33 (axial-$CH_3\underline{CO}$), 172.61 (tail-23-C), 173.6 (head-23-C). – FAB/MS (3-NBA+LiI): *m/e*(%): 1135.6 $[MLi+LiI]^+$, 1001.2 $[MLi]^+$, 957.4, 941.5 $[MLi-HOAc]^+$, 355.3, 253.2, 160.1. – Anal. Calcd. for $C_{57}H_{86}O_{14}$: C 68.79, H 8.71. Found: C 68.68, H 8.77.

*Dimer* **4c:** *m.p.* 128–130 °C, yield 40.5% (**4c**) and 22% (**5a**). – [1]H NMR ($CDCl_3$): δ 0.73 (s, 3H, 18-$H_3$); 0.76 (s, 3H, 18'-$H_3$); 0.81 (d, 3H, 21-$H_3$); 0.87 (s, 3H, 21'-$H_3$); 0.92 (s, 6H, 19-$H_3$, 19'-$H_3$);2.04-2.13 (five peaks, 15H, 3-OAc, 7-OAc, 7'-OAc, 12-OAc, 12'-OAc); 3.66 (s, 3H, $COOCH_3$); 4.60 (m, 2H, 3β-H, 3'β-H); 4.91 (broad s, 2H, 7β-H, 7'β-H); 5.0 (broad s, 2H, 12β-H, 12'β-H). – [13]C NMR see Tab. 1. – FAB/MS (3-NBA+LiI): *m/e*(%): 1149.3 $[MLi+LiI]^+$, 1015.2 $[MLi]^+$, 971.4, 955.5 $[MLi-HOAc]^+$, 369.3, 253.2, 160.1. – Anal. Calcd. for $C_{58}H_{88}O_{14}$: C 69.02, H 8.79. Found: C 68.70, H 8.89.

**Table 1** [13]C NMR (63 MHz) data of the dimers **4c** and **4d**

| Assignment | 4c | | 4d | |
|---|---|---|---|---|
| C-18, 18' | 12.25 | 12.25 | 12.28 | 12.28 |
| C-21, 21' | 18.68 | 17.53 | 18.78 | 17.60 |
| $\underline{CH_3}CO$ (axial) | 21.43 | 21.43 | 21.46 | 21.46 |
| $\underline{CH_3}CO$ (eq) | 21.5 | 21.5 | 21.66 | 21.66 |
| C-19, 19' | 22.57 | 22.57 | 22.59 | 22.59 |
| C-15, 15' | 22.84 | 22.84 | 22.86 | 22.86 |
| C-11, 11' | 25.60 | 25.60 | 25.60 | 25.60 |
| C-2, 2' | 26.93 | 27.04 | 26.95 | 27.20 |
| C-16, 16' | 27.28 | 27.28 | 27.36 | 27.36 |
| C-9, 9' | 28.93 | 28.93 | 28.93 | 28.93 |
| C-23, 23' | – | 30.82 | – | 30.90 |
| C-6, 6' | 31.29 | 31.29 | 31.30 | 31.55 |
| C-22, 22' | 33.06 | 30.93 | 33.11 | 30.90 |
| C-10, 10' | 34.39 | 34.39 | 34.39 | 34.39 |
| C-1, 1' | 34.64 | 34.64 | 34.71 | 34.71 |
| C-4, 4' | 34.64 | 34.64 | 34.71 | 34.71 |
| C-8, 8' | 37.79 | 37.79 | 37.80 | 37.80 |
| C-20, 20' | 40.95 | 34.79 | 41.00 | 34.71 |
| C-5,5' | 41.63 | 40.95 | 41.19 | 41.0 |
| C-14, 14' | 43.48 | 43.48 | 43.46 | 43.46 |
| C-13, 13' | 45.16 | 45.16 | 45.14 | 45.14 |
| C-17, 17' | 47.46 | 47.46 | 47.60 | 47.44 |
| $OCH_3$ | – | 51.55 | 51.43 | – |
| C-7, 7' | 70.72 | 70.72 | 70.73 | 70.73 |
| C-3, 3' | 73.93 | 74.06 | 74.0 | 74.12 |
| C-12, 12' | 75.26 | 75.45 | 75.42 | 75.42 |
| $CH_3\underline{CO}$ | 170.32 | 170.32 | 170.12 | 170.12 |
| C-23, C-24 | 172.62 | 174.6 | 173.6 | 174.2 |

*Dimer* **4d:** *m.p.* 119–121°C, yield 71% (**4d**) and 10.5% (**5b**). – [1]H NMR ($CDCl_3$): δ 0.73 (s, 3H, 18-$H_3$); 0.77 (s, 3H, 18'-$H_3$); 0.81 (d, 3H, 21-$H_3$); 0.87 (s, 3H, 21'-$H_3$); 0.91 (s, 6H, 19-$H_3$, 19'-$H_3$); 2.07-2.13 (four peaks, 15H, 3-OAc, 7-OAc, 7'-OAc, 12-OAc, 12'-OAc); 3.65 (s, 3H, $COOCH_3$); 4.59 (m, 2H, 3β-H, 3'β-H); 4.90 (broad s, 2H, 7β-H, 7'β-H); 5.08 (broad s, 2H, 12β-H, 12'β-H). – [13]C NMR see Tab. 1. – FAB/MS (3-NBA+LiI): *m/e*(%): 1149.3 $[MLi+LiI]^+$, 1015.2 $[MLi]^+$, 971.5, 955.5 $[MLi-HOAc]^+$, 343.1, 283.1, 197.1. – Anal. Calcd. for $C_{58}H_{88}O_{14}$: C 69.02, H 8.79. Found: C 68.91, H 8.86.

**5a:** *m.p.* 65–67 °C. – [1]H NMR ($CDCl_3$): δ 0.74 (s, 3H, C-18); 0.81 (d, 3H, C-21); 0.95 (s, 3H, C-19); 2.07 (s, 3H, 7-OAc); 2.12 (s, 3H, 12-OAc); 3.66 (s, 3H, $COOCH_3$); 4.91 (broad, 2H, 3β-H, 7β-H); 5.09 (s, 1H, 12β-H); 7.40 (m, 3H, C-3, 4, 5 in benzene ring); 7.72 (d, 1H, C-6 in benzene ring).

– FAB/MS (3-NBA+LiI): *m/e*(%): 651.4 [MLi]$^+$, 591.4 [MLi–HOAc]$^+$, 583.4 [M–HOAc]$^+$, 525.3, 369.3 [M–2HOAc-$C_7H_4ClO_2$]$^+$, 253.2 [M–2HOAc–$C_7H_4ClO_2$–$C_6H_{11}O_2$]$^+$, 197.1, 135.1.

**5b:** *m.p.* 70–72°C. – $^1$H NMR ($CDCl_3$): $\delta$ 0.78 (s, 3H, C-18); 0.87 (d, 3H, C-21); 0.96 (s, 3H, C-19); 2.09 (s, 3H, 7-OAc); 2.14 (s, 3H, 12-OAc); 2.4 (dd, 2H, C-22); 3.65 (s, 3H, $COOCH_3$); 4.85 (broad, 2H, 3$\beta$-H, 7$\beta$-H); 5.09 (s, 1H, 12$\beta$-H); 7.41 (m, 3H, C-3, 4, 5 in benzene ring); 7.55 (d, 1H, C-6 in benzene ring). – FAB/MS (3-NBA+LiI): *m/e*(%): 637.4 [MLi]$^+$, 577.4 [MLi–HOAc]$^+$, 511.3 [M–HOAc]$^+$, 355.3 [M–2HOAc–$C_7H_4ClO_2$]$^+$, 283.1.

## References

[1] Y. Li, J. R. Dias, Org. Prep. Proc. Int. **28** (1996) 201
[2] a) D. Gargiulo, T. A. Blizzard, K. Nakanishi, Tetrahedron **45** (1989) 5423;
b) J. M. Harris, E. A. Bolessa, J. C. Vederas, J. Chem. Soc., Perkin Trans. 1 **1995**, 1951
[3] J. R. Dias, R. Ramachandra, Synth. Commun. **7** (1977) 293
[4] J. E. Herz, J. Sandoval, Org. Prep. Proc. Int. **17** (1985) 381
[5] J. Inanaga, K. Hirata, H. Seki, T. Katsuki, M. Yamaguchi, Bull. Chem. Soc. Jpn. **52** (1979) 1989
[6] R. P. Bonar–Law, J. K. M. Sanders, J. Chem. Soc., Chem. Commun. **1991,** 574
[7] R. P. Bonar–Law, L. G. Mackay, J. K. M. Sanders, J. Chem. Soc., Chem. Commun. **1993,** 456
[8] R. P. Bonar–Law, J. K. M. Sanders, Tetrahedron Lett. **33** (1992) 2071
[9] J. R. Dias, B. Nassim, Org. Mass Spectrom. **13** (1978) 402
[10] L. Djordjevic, D. U. Kilibarda, J. Serb. Chem. Soc. **53** (1988) 339

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