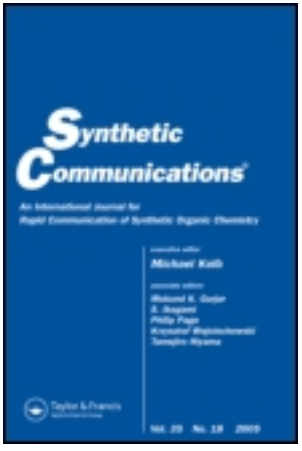


Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

Synthesis and Plant Growth-Activity of three New Brassinosteroids Analogues

Luis Espinoza [a], Felipe Bulat [a], Danahe Coll [b], Francisco Coll [b], Marcelo D. Preite [a] & Manuel Cortés [a]

[a] Facultad de Química, Pontificia Universidad Católica de Chile, Casilla 306, Correo 22, Santiago, Chile
[b] Laboratorio de Productos Naturales, Facultad de Química, Universidad de La Habana, Zapata y G, La Habana, 10400, Cuba E-mail:
Published online: 04 Dec 2007.

To cite this article: Luis Espinoza, Felipe Bulat, Danahe Coll, Francisco Coll, Marcelo D. Preite & Manuel Cortés (2000) Synthesis and Plant Growth-Activity of three New Brassinosteroids Analogues, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 30:11, 1963-1974, DOI: 10.1080/00397910008087246

To link to this article: http://dx.doi.org/10.1080/00397910008087246

SYNTHETIC COMMUNICATIONS, 30(11), 1963–1974 (2000)

SYNTHESIS AND PLANT GROWTH-ACTIVITY OF THREE NEW BRASSINOSTEROIDS ANALOGUES

Luis Espinoza[a], Felipe Bulat[a], Danahe Coll[b], Francisco Coll[b], Marcelo D. Preite[a]*, and Manuel Cortés[a]*.

[a] Facultad de Química, Pontificia Universidad Católica de Chile, Casilla 306, Correo 22, Santiago, Chile.
[b] Laboratorio de Productos Naturales, Facultad de Química, Universidad de La Habana, Zapata y G, La Habana 10400, Cuba.

E-mail: mpreite@puc.cl

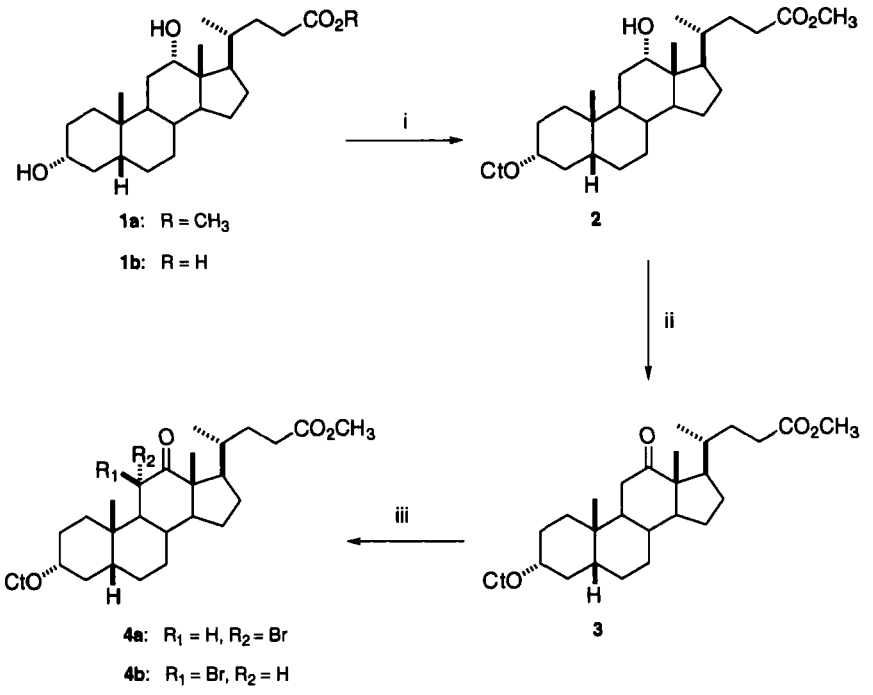
Abstract: The chemical synthesis, starting from deoxycholic acid methyl ester, of several brassinosteroids analogues with different oxygenated functions in ring C, is described. Three of them showed growth-promoting activity.

INTRODUCTION

Brassinosteroids are a very important class of steroidal phytohormones with a high growth-promoting and antistress activity[1]. The synthesis of novel

* To whom correspondence should be addressed.

Scheme 1



i) EtOCOCl/Pyr/CH_2Cl_2, 0°C, 2 h; ii) Jones reagent/ acetone, 10°C, 2 h; iii) Br_2/PhH, r.t., 4 d

analogues is a very important task, not only for structure-activity studies, but also to develop new compounds with improved biological properties. New biologically active brassinosteroids sporting a cis-A/B ring junction,[2,3] different side chains,[4,5] and a carbonyl function on C ring,[6] have been synthesized in the last few years. We report here the synthesis and a biological activity study of several brassinosteroids analogues with 5β-cholanic acid skeleton and oxygen functions at C-11 and/or C-12.

RESULTS AND DISCUSSION

Methyl deoxycholate **(1a)** was obtained in almost quantitative yield from deoxycholic acid **(1b)** by a standard procedure. (Scheme 1) Diol **1a** was selectively

cathylated at C-3 by treatment with ethyl chloroformate and pyridine in CH_2Cl_2, to give **2** (85% yield). Jones oxidation of **2** produced ketone **3** (88% yield), which was α-brominated to afford a 3.8:1.0 mixture, respectively, of chromatographically separable epimeric bromoketones **4a** and **4b** (98% combined yield). The ^{1}HNMR spectrum of **4a** showed a signal at δ 4.95 (d, J=10.7 Hz) consistent with an α-bromine atom at C-11.[8] Compound **4b** shows a signal at δ 4.31 (d, J=5.0 Hz), consistent with a β-bromine atom at C-11. ^{13}CNMR analysis of compounds **4a** and **4b** was also consistent with the assigned stereochemistries (see Table 1 below).

Treatment of either **4a**, **4b**, or a mixture of both, with NaOH in a 1.0:1.0 mixture of t-BuOH and water at reflux temperature for 6h,[9] and further esterification with acidic MeOH, afforded a chromatographically separable mixture of **5a**, **6a** and **7a** (65%, 10%, 4% isolated yield, respectively). (Scheme 2)

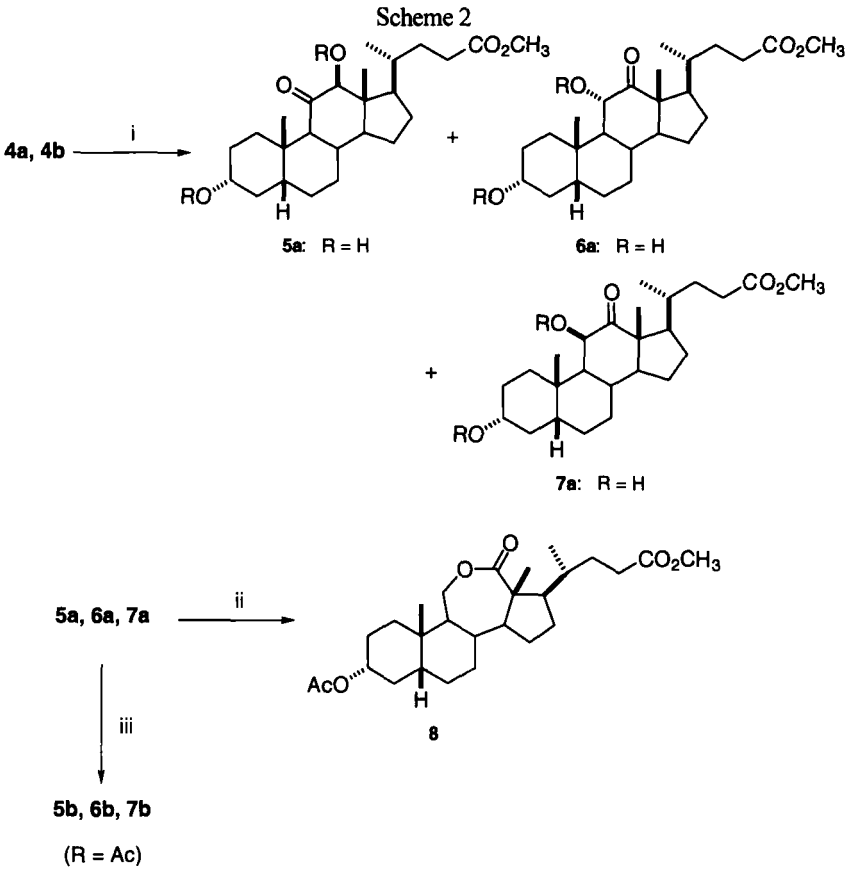
NMR analysis of compound **5a** demonstrated that its structure is as depicted in the formula, as ^{1}H and ^{13}C signals were very similar to those of a previously reported compound bearing a 3α-benzoate group.[10] The structures of **6a** and **7a** were obtained by a similar NMR analysis. Compound **6a** showed a signal at 4.47 (d, J=9.5 Hz), assigned to H-11, and compound **7a** showed a signal at 4.16 (d, J=3.5 Hz) also assigned to its H-11. The coupling constant values are consistent with the stereochemistries showed in the formulae. ^{13}CNMR analysis was also consistent with these stereochemistries (see Table 1).

Next, we turned our attention to try the conversion of α-hydroxyketones **5a**, **6a** and **7a** into the corresponding lactones by oxidative cleavage followed by reduction and further acid-mediated lactonization. Direct oxidation of a mixture of **5a**, **6a** and **7a** with $NaIO_4$ in a 1.0:1.0 mixture of THF/water at room temperature showed, after 72 h, the disappearance of **6a** and **7a** by TLC. Unreacted **5a** was

Table 1: ^{13}C NMR data ($CDCl_3$, 50.3 MHz)

Carbon	2	3	4a	4b	5a	6a	7a	5b	6b	7b	8
1	34.79	34.85	37.05	33.79	36.28	37.63	36.10	33.93	37.59	37.59	34.93
2	23.60	26.32	27.65	27.14	29.68	30.34	30.51	27.01	27.49	27.49	24.93
3	77.96	77.41	77.44	76.89	71.12	71.59	71.39	73.72	73.81	73.81	73.54
4	32.08	32.12	33.05	31.85	34.26	36.66	34.86	32.30	32.57	32.57	32.06
5	41.82	41.35	43.68	44.43	42.52	42.83	44.00	42.40	42.58	42.58	41.60
6	26.39	25.99	26.54	26.82	26.72	27.55	27.22	26.70	27.32	27.32	27.86
7	26.00	24.33	24.93	24.29	26.55	27.55	26.83	26.33	26.86	26.86	26.77
8	35.07	35.62	38.04	32.52	36.94	35.36	31.94	36.38	35.41	35.41	39.27
9	33.55	46.45	51.56	45.83	49.91	47.11	46.37	50.20	46.91	46.91	40.76
10	34.09	35.32	37.93	36.55	34.05	36.70	35.79	34.13	36.72	36.72	34.88
11	28.64	38.06	58.56	52.17	211.89	73.26	78.79	203.98	75.83	80.45	68.60
12	73.00	214.41	203.52	204.21	84.09	214.45	213.57	85.88	206.57	206.57	177.62
13	46.49	57.48	57.04	56.82	52.46	55.90	57.19	50.08	56.64	56.64	52.21
14	48.19	58.56	56.07	58.57	56.59	57.92	59.80	55.89	57.17	57.17	53.35
15	27.41	27.51	27.65	26.97	24.74	26.17	26.42	25.02	26.29	26.29	26.28
16	26.93	26.96	27.30	26.66	23.28	24.60	24.18	23.26	24.73	24.73	25.52
17	47.30	43.99	48.09	47.65	52.41	52.33	47.17	53.96	46.91	46.91	52.53
18	12.74	11.70	11.40	15.75	8.71	11.05	10.87	9.70	10.68	10.68	10.42
19	23.03	22.72	23.13	25.30	23.31	23.35	26.62	23.15	23.15	23.15	23.09
20	35.98	35.64	35.33	35.77	32.08	35.12	35.62	32.58	35.34	35.34	35.15
21	17.30	18.58	18.51	18.38	20.50	18.42	18.61	20.51	18.45	18.45	19.19
22	30.88	30.50	30.32	30.53	31.07	31.20	30.84	29.61	30.37	30.37	30.18
23	31.06	31.31	31.14	31.32	32.17	31.38	31.35	32.13	31.20	31.20	31.58
24	174.67	174.65	174.55	174.62	174.73	174.56	174.77	174.26	174.59	174.60	174.57
OMe	51.48	51.46	51.48	51.48	51.47	51.52	51.53	51.50	51.48	51.48	51.47
OEt	63.56	63.64	63.73	63.73							
OEt	14.26	14.26	14.28	14.26							
CO_3	156.66	154.62	154.62	154.52							
AcO								170.54	170.69	170.58	170.65
AcO								20.77	20.87	20.87	21.38
AcO								170.16	169.94	170.30	
AcO								21.38	21.44	21.41	

Scheme 2



i) NaOH/*t*-BuOH-H_2O (1:1), r.t., 6 h; ii) a) $NaIO_4$/THF-H_2O (1:1), r.t., 72 h (at this stage, unreacted **5a** was separated); b) $NaBH_4$/MeOH, r.t., 1 h; c) 12N HCl/THF (1:1), 24 h; d) MeOH/H_2SO_4 (cat.), reflux, 1 h; e) Ac_2O/Pyr, r.t., 1 h; iii) Ac_2O/Pyr/DMAP, refl., 2 h

quantitatively recovered from the reaction mixture by taking advantage of its low solubility, and the remaining mother liquors were concentrated and reduced with $NaBH_4$, with acidic workup to lactonize, and subsequent re-esterification, with acidic MeOH first, and then, with acetic anhydride and pyridine, to give lactone **8** (11.8% overall yield from the mixture of **5a**, **6a** and **7a**). Unfortunately, ketol **5a** was completely non-reactive towards $NaIO_4$ oxidation and, consequently, the

corresponding lactone was impossible to be obtained. This lack of reactivity of **5a** could be attributed to its enolization, whose structure would be stabilized by intramolecular hydrogen bonding.

The above mixture of **5a**, **6a** and **7a** was acetylated with acetic anhydride in pyridine to afford **5b**, **6b** and **7b**, respectively, which were chromatographically separated by column chromatography.

The biological activities of compounds **6a**, **6b**, and **8** were tested by the cotyledons expansion of radish bioassay.[11] A mother solution of the compound to test in EtOH was prepared, and the samples were applied in a concentration range of 10^{-4} to 10^{-8} mg/mL. The best growth-promoting activity was observed at 10^{-5} mg/mL at which the radish cotyledons treated with **8** and **6b** increased their weight 38.6% and 20% respectively, over the control. No growth promoting activity was observed for compound **6a** at 10^{-5} mg/mL concentration, but a significant phytotoxicity was evident, instead.

The activities of products **5a**, **5b**, **7a** and **7b** were also examined but no activity was observed at tested dosage. Finally, we wish to remark that ketol **5a** has been transformed in an active brassinosteroids analogue that will be reported in due time.

EXPERIMENTAL

Melting points were measured on a Stuart-Scientific SMP3 apparatus and are uncorrected. Optical rotations were obtained for $CHCl_3$ solutions on a Perkin-Elmer 241 polarimeter, and their concentrations are expressed in g/ 100 mL. NMR spectra were recorded on a Bruker AM-200 spectrometer. Chemical shifts are expressed in ppm downfield relative to TMS (δ scale) in $CDCl_3$ solutions. Carbon multiplicity was established by a DEPT pulse sequence. IR spectra were recorder as KBr disks in a Bruker FT-IR Vector-22 and frequencies are in cm^{-1}. Elemental

analyses were obtained on a Fisons-Carlo-Erba FA-1108 Automost microanalyzer. For analytical TLC, Merck silica gel 60 in 0.25 mm layer was used. Chromatographic separations were carried out by conventional column on Merck silica gel 60 (230-400 Mesh) using hexane-EtOAc gradients of increasing polarity.

All reactions were routinely run under an N_2 atmosphere. All organic extracts were dried over anhydrous magnesium sulfate and evaporated under reduced pressure, below 65° C.

Methyl 3α-cathyloxy-12α-hydroxy-5β-cholan-24-oate (2)

A magnetically stirred solution of **1a** (24 g, 59.1 mmol) and pyridine (20 mL) in CH_2Cl_2 (100 mL) was cooled to 0°C in and ice bath. The stirring was stopped, and ethyl chloroformate was slowly added dropwise during a 2 h period. The solvent was evaporated, the residue was cooled to 0°C and 10% HCl was added until the mixture resulted frankly acidic. The resulting suspension was extracted when still cool with EtOAc (2 × 100 mL). The combined organic extracts were washed with H_2O (2 × 50 mL), dried, and evaporated. The crude residue was chromatographed to yield pure **2** (24.01 g, 85%) as a colorless solid: m.p. 148-149°C (hexane/EtOAc); $[\alpha]_D^{25}$ +50.2° (c=0.528); analysis: found C, 69.69%; H, 9.81%; $C_{28}H_{46}O_6$ requires C, 70.26%; H, 9.69%; IR: 3537, 1737; ^{1}HNMR: 0.66 (s, 3H, H-18), 0.90 (s, 3H, H-19), 0.96 (d, J=6.0 Hz, 3H, H-21), 1.28 (t, J=7.2 Hz, 3H, $OCH_2C\underline{H}_3$), 2.25 (m, 2H, H-23), 3.65 (s, 3H, $CO_2C\underline{H}_3$), 3.95 (bs, 1H, H-12), 4.15 (q, J=7.2 Hz, 2H, $OC\underline{H}_2CH_3$), 4.55 (m, 1H, H-3).

Methyl 3α-cathyloxy-12-oxo-5β-cholan-24-oate (3)

Jones reagent (10 mL) was added dropwise to a solution of **2** (21.04 g, 44.1 mmol) in acetone (150 mL) at 10°C. The reaction mixture was stirred at that temperature, followed by addition of MeOH to destroy the excess of reagent. The

resulting green mixture was evaporated, and the residue was diluted with H_2O (50 mL) and extracted with EtOAc (2 × 50 mL). The organic phase was washed with H_2O (2 × 50 mL), dried and evaporated. The concentrate was chromatographed to afford **3** (18.43 g, 88%) as a white solid: m.p. 167-169°C; $[\alpha]_D^{25}$ +98.9° (c=0.454); analysis: found C, 70.03%, H, 9.40%, $C_{28}H_{44}O_6$ requires C, 70.55%, H, 9.31%; IR: 1737, 1705; ^{1}HNMR: 0.84 (d, J=6.4 Hz, 3H, H-21), 1.00 (s, 3H, H-18), 1.02 (s, 3H, H-19), 1.29 (t, J=7.1 Hz, 3H, $OCH_2C\underline{H}_3$), 2.33 (m, 2H, H-23), 2.50 (d, J=12.4 Hz, 1H, H-11), 3.66 (s, 3H, $CO_2C\underline{H}_3$), 4.16 (q, J=7.1 Hz, $OC\underline{H}_2CH_3$), 4.55 (m, 1H, H-3).

Methyl 3α-cathyloxy-11α-bromo-12-oxo-5β-cholan-24-oate (4a) and methyl 3α-cathyloxy-11β-bromo-12-oxo-5β-cholan-24-oate (4b).

To a solution of **3** (18.03 g, 37.8 mmol) in benzene (200 mL), a bromine solution (25 mL, 2M in benzene) was slowly added with stirring, at room temperature and in the dark. After 4 days, TLC analysis showed the total consumption of the starting material. The solvent was evaporated, and the residue, chromatographed to yield **4a** (16.28 g, 78%), and **4b** (4.30 g, 21%). **4a**: colorless crystals: m.p. 104-105°C (hexane/EtOAc), $[\alpha]_D^{25}$ +52.8° (c=0.108); analysis: found C, 60.35%, H, 7.89%, $C_{28}H_{43}BrO_6$ requires C, 60.54%, H, 7.80%; IR: 1732, 1262; ^{1}HNMR: 0.82 (d, J=6.2 Hz, 3H, H-21), 1.00 (s, 3H, H-18), 1.17 (s, 3H, H-19), 1.27 (t, J=7.1 Hz, 3H, $OCH_2C\underline{H}_3$), 2.28 (m, 2H, H-23), 2.30 (d, J=10.3 Hz, 1H, H-9), 2.97 (dt, J=2.8, 14.9 Hz, 1H, H-1α), 3.64 (s, 3H, $CO_2C\underline{H}_3$), 4.14 (q, J=7.1 Hz, 2H, $OC\underline{H}_2CH_3$), 4.61 (m, 1H, H-3), 4.95 (d, J=10.7 Hz, 1H, H-11), **4b**: white solid: m.p. 164-166°C; $[\alpha]_D^{25}$ +34° (c=0.582); analysis: found C, 60.44%, H, 8.18%, $C_{28}H_{43}BrO_6$ requires C, 60.54%, H, 7.80%; IR: 1737, 1270; ^{1}HNMR: 0.92 (d, J=6.2 Hz, 3H, H-21), 1.29 (t, J=7.1 Hz, 3H,

OCH_2CH_3), 1.35 (s, 3H, H-18), 1.36 (s, 3H, H-19), 3.66 (s, 3H, CO_2CH_3), 4.16 (q, J=7.1 Hz, 2H, OCH_2CH_3), 4.31 (d, J=5.0 Hz, 1H, H-11), 4.57 (m, 1H, H-3).

Methyl 3α-12β-dihydroxy-11-oxo-5β-cholan-24-oate (5a), methyl 3α-11α-dihydroxy-12-oxo-5β-cholan-24-oate (6a) and methyl 3α-11β-dihydroxy-12-oxo-5β-cholan-24-oate (7a).

A mixture of **4a** (15 g, 27 mmol) and **4b** (5 g, 9 mmol), was heated to reflux for 6 h, with a stirred solution of NaOH (25 g) in t-butyl alcohol (500 mL) and water (500 mL). After removal of the alcohol under reduced pressure, the mixture was treated with 10% HCl (50 mL), water (50 mL), and extracted with EtOAc (4 × 50 mL). The combined organic extracts were washed with water (2 × 50 mL), dried and evaporated. The residue was esterified with MeOH (100 mL) in the presence of H_2SO_4 (0.5 mL) at reflux temperature. The excess of MeOH was evaporated, water (100 mL) was added and the resulting suspension extracted with EtOAc (4 × 50 mL). The combined organic extracts were washed with H_2O (2 × 50 mL) dried, and evaporated. The residue was chromatographed to yield **6a** (1.55 g, 10%), **5a** (9.84 g, 65%) and **7a** (0.58 g, 4%). **6a** (oil): $[\alpha]_D^{25}$ +44.6° (c=4.926); IR: 3583, 3433, 1732, 1705; ^{1}HNMR: 0.88 (d, J=6.3 Hz, 3H, H-21), 1.05 (s, 3H, H-18), 1.98 (s, 3H, H-19), 2.40 (m, 2H, H-23), 2.41 (m, 1H, H-1), 3.71 (s, 3H, CO_2CH_3), 3.74 (m, 1H, H-3), 4.47 (d, J=9.5 Hz, 1H, H-11). **5a** (white solid): m.p. 135-138.7°C (hexane/EtOAc); $[\alpha]_D^{25}$ +58.9° (c=0.472); analysis; found C, 71.45%, H, 9.58%, $C_{25}H_{40}O_5$ requires C, 71.39%, H, 9.59%; IR: 3473, 1737, 1694. ^{1}HNMR: 0.54 (s, 3H, H-18), 1.09 (d, J=6.4 Hz, 3H, H-21), 1.22 (s, 3H, H-19), 3.65 (m, 1H, H-3), 3.71 (s, 3H, CO_2CH_3), 3.90 (s, 1H, H-12). **7a** (white solid): m.p. 118-119°C (hexane/EtOAc); $[\alpha]_D^{25}$ +104.1° (c=0.508); analysis: found, C, 71.30%, H, 9.65% $C_{25}H_{40}O_5$ requires C, 71.39%, H, 9.59%;

IR: 3485, 1720, 1702; ^{1}HNMR: 0.82 (d, J=6.0 Hz, 3H, H-21), 1.20 (s, 3H, H-18), 1.24 (s, 3H, H-19), 2.30 (m, 2H, H-23), 3.59 (m, 1H, H-3), 3.64 (s, 3H, $CO_2C\underline{H}_3$), 4.16 (d, J=3.5 Hz, 1H, H-11).

Methyl 3α-acetoxy-C-homo-12-oxa-13-oxo-5β-cholan-24-oate (8).

To a stirred solution of a mixture of ketols **5a**, **6a** and **7a** (4.4 g, 10.5 mmol) in a mixture of THF (100 mL) and water (100 mL), $NaIO_4$ (1.5 g, 19.4 mmol) at room temperature, was added . The mixture was stirred for three days, filtered and concentrated. The residue was extracted with EtOAc (2 × 50 mL), the organic phase was washed with water (2 × 25 mL), dried and concentrated. The solid was recrystallised from EtOAc-hexane to afford unreacted **5a** (3.31 g, 7.87 mmol). The mother liquors were concentrated to give an oil (1.03 g) which was dissolved in MeOH (40 mL) and treated with $NaBH_4$ (0.15 g, 4 mmol) at room temperature for 1h. The solvent was removed, the residue was acidified with 12N HCl (50 mL) in THF (50 mL) and the mixture was stirred for 24 h. After concentration, the residue was extracted with EtOAc (2 × 50 mL). The organic phase was washed with water (3 × 50 mL), dried and concentrated. The concentrate was dissolved in MeOH (50 mL), H_2SO_4 (two drops) was added, and the mixture was boiled under reflux for 1 h. The reaction mixture was evaporated, redissolved in EtOAc (50 mL), washed with water (2 × 50 mL), dried, and evaporated. The crude residue was dissolved in a mixture of acetic anhydride (5 mL) and pyridine (1 mL). After 1 h, the reaction mixture was poured into water (50 mL) and extracted with EtOAc (3 × 50 mL). The organic phase was washed with 10% $KHSO_4$ (20 mL), dried and concentrated. The residue was chromatographed to afford lactone **8** (0.57 g, 11.8% from the mixture of ketols **5a**, **6a** y **7a**), as a colorless solid: m.p. 153-154°C (hexane/EtOAc), $[\alpha]_D^{25}$ +53° (c=0.236); analysis: found C, 70.14%, H, 9.13%, $C_{27}H_{42}O_6$ requires C, 70.10%,

H, 9.15%; IR: 1733, 1058; ^{1}HNMR: 0.87 (s, 3H, H-18), 0.91 (d, J=6.6 Hz, 3H, H-21), 1.22 (s, 3H, H-19), 2.01 (s, 3H, $COCH_3$), 2.37 (m, 2H, H-17, H-23), 3.65 (s, 3H, CO_2CH_3), 4.14 (d, J=13 Hz, 1H, H-11), 4.40 (dd, J=13, 8.2 Hz, 1H, H-11), 4.70 (m, 1H, H-3).

Methyl 3α-12β-diacetoxy-11-oxo-5β-cholan-24-oate (5b), methyl 3α-11α-diacetoxy-12-oxo-5β-cholan-24-oate (6b), and methyl 3α-11β-diacetoxy-12-oxo-5β-cholan-24-oate (7b).

A mixture of ketols **5a, 6a** and **7a** (from 18 g, 32.4 mmol of a mixture of **4a** and **4b**) was dissolved on pyridine (50 mL), acetic anhydride (50 mL) and DMAP (10 mg). The reaction mixture was heated at reflux temperature for 2 h, ice water (50 mL) was then added, and the mixture was extracted with EtOAc (2 × 50 mL). The organic phase was washed with 10% $KHSO_4$ (2 × 20 mL), dried and concentrated. The residue was chromatographed to yield **5b** (11.23 g, 68.7%), **6b** (1.61 g, 9.8%) and **7b** (0.27 g, 1.7%). **5b**: m.p. 88-90°C (hexane/EtOAc), $[\alpha]_D^{25}$ +51.1° (c=0.522); analysis: found C, 69.21%, H, 8.77%, $C_{29}H_{44}O_6$ requires C, 69.02%, H, 8.79%; IR: 1735, 1242; ^{1}HNMR: 0.65 (s, 3H, H-18), 0.89 (d, J=6.4 Hz, 3H, H-21), 2.13 (s, 3H, $COCH_3$), 2.14 (s, 3H, $COCH_3$), 2.28 (m, 2H, H-23), 2.46 (d, J=10.7 Hz, 1H, H-9), 3.64 (s, 3H, CO_2CH_3), 4.68 (m, 1H, H-3), 4.88 (s, 1H, H-12). **6b**: m.p. 152-154°C (hexane/EtOAc), $[\alpha]_D^{25}$ +37.2° (c=0.452), analysis: found C, 69.25%, H, 8.58%, $C_{29}H_{44}O_7$ requires C, 69.02, H, 8.79%; IR: 1739, 1241; ^{1}HNMR: 0.80 (d, J=6.3 Hz, 3H, H-21), 1.06 (s, 3H, H-18), 1.13 (s, 3H, H-19), 2.02 (s, 3H, $COCH_3$), 2.10 (s, 3H, $COCH_3$), 2.34 (m, 2H, H-23), 3.65 (s, 3H, CO_2CH_3), 4.74 (m, 1H, H-3), 5.41 (d, J=10.8 Hz, 1H, H-11). **7b**: m.p. 105-107°C (hexane/EtOAc), $[\alpha]_D^{25}$ +126° (c=0.367), analysis; found C, 68.80%, H, 9.0% $C_{29}H_{44}O_7$ requires C, 69.02%, H, 9.79%; IR: 1740, 1706, 1239. ^{1}HNMR: 0.79 (d, J=6.4 Hz, 3H, H-21), 1.06 (s, 3H, H-18), 1.15 (s, 3H, H-19),

2.00 (s, 3H, $COCH_3$), 2.07 (s, 3H, $COCH_3$), 2.33 (m, 2H, H-23), 3.64 (s, 3H, CO_2CH_3), 4.67 (m, 1H, H-3), 4.86 (d, J=3.1 Hz, 1H, H-11).

ACKNOWLEDGMENTS

The authors thank FONDECYT (Research Grant 2980021) for financial support. L. E. thanks Dirección de Investigación, Pontificia Universidad Católica de Chile (DIPUC) for a fellowship.

REFERENCES

1. Adam, G. and Marquardt, V. *Phytochemistry* **1986**, *25*, 1787.

2. Brosa, C.; Capdevila, J.M. and Zamora I. *Tetrahedron* **1996**, *52*, 2435.

3. Pérez, R.; Pérez, C. and Coll, F. *Synth. Commun.* **1998**, *28*, 3387.

4. Iglesias, M. A.; Pérez, R.; Leliere, V.; Pérez, C. and Coll, F. *J. Chem. Res. (S)* **1991**, 1.

5. Huang, L. F. and Zhou, W.S. *J. Chem. Soc., Perkin Trans. 1* **1994**, 3579.

6. Iglesias, M.; Pérez, C. and Coll, F. *Synth. Commun.* **1999**, *29*, 1811.

7. Harfurn, J. J.; Loftus, G. C. and Marples, B. A. *Tetrahedron* **1998**, *54*, 11907.

8. See Ref. 7, compound **24**.

9. Elks, J.; Phillipps, H.; Walker, T. and Wyman, L. J. *J. Chem. Soc. C.* **1956**, 4330.

10. See reference 7, compound **19**.

11. Lethan; D.S. "*Biochemistry and Physiology of Plant Growth Substances*" F. Wightman and. G. Setterfield, Eds. Runge Press. Otawa, **1968**, pp. 19-30.

Received in the USA 8/19/99