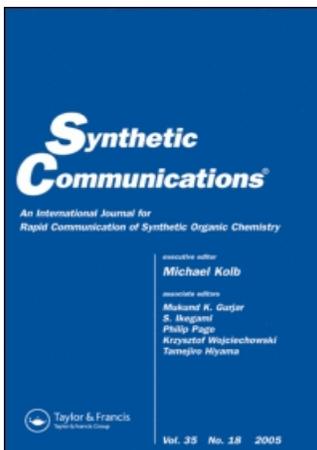


This article was downloaded by:[Universidad de Cadiz/UCA/Bibliotec CC. Salud]
On: 21 November 2007
Access Details: [subscription number 778576484]
Publisher: Taylor & Francis
Informa Ltd Registered in England and Wales Registered Number: 1072954
Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



Synthetic Communications

An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information:
<http://www.informaworld.com/smpp/title~content=t713597304>

Hemisynthesis of New Triterpene Derivatives using Oxidation by CrO_3 and NaIO_4 -(RuCl_3 , $3\text{H}_2\text{O}$)

N. Mazoir ^a; A. Auhmani ^a; M. Daoubi ^a; I. G. Collado ^b; A. Benharref ^a

^a Chemistry Laboratory of Natural Substances, University Cadi Ayyad, Faculty of Sciences Semlalia, Marrakech, Morocco

^b Department of Organic Chemistry, Faculty of Sciences, University of Cádiz, Cádiz, Spain

Online Publication Date: 01 January 2007

To cite this Article: Mazoir, N., Auhmani, A., Daoubi, M., Collado, I. G. and

Benharref, A. (2007) 'Hemisynthesis of New Triterpene Derivatives using Oxidation by CrO_3 and NaIO_4 -(RuCl_3 , $3\text{H}_2\text{O}$)', Synthetic Communications, 37:8, 1289 - 1299

To link to this article: DOI: 10.1080/00397910701226756

URL: <http://dx.doi.org/10.1080/00397910701226756>

PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: <http://www.informaworld.com/terms-and-conditions-of-access.pdf>

This article maybe used for research, teaching and private study purposes. Any substantial or systematic reproduction, re-distribution, re-selling, loan or sub-licensing, systematic supply or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

Synthetic Communications[®], 37: 1289–1299, 2007
Copyright © Taylor & Francis Group, LLC
ISSN 0039-7911 print/1532-2432 online
DOI: 10.1080/00397910701226756



Hemisynthesis of New Triterpene Derivatives using Oxidation by CrO_3 and NaIO_4 -($\text{RuCl}_3, 3\text{H}_2\text{O}$)

N. Mazoir, A. Auhmani, and M. Daoubi

Chemistry Laboratory of Natural Substances, University Cadi Ayyad,
Faculty of Sciences Semlalia, Marrakech, Morocco

I. G. Collado

Department of Organic Chemistry, Faculty of Sciences, University of
Cádiz, Cádiz, Spain

A. Benharref

Chemistry Laboratory of Natural Substances, University Cadi Ayyad,
Faculty of Sciences Semlalia, Marrakech, Morocco

Abstract: Oxidation of triterpenes resulting from *E. resinifera*, *E. officinarum*, and their derivatives, using chromic anhydride (CrO_3) and the system NaIO_4 -($\text{RuCl}_3, 3\text{H}_2\text{O}$), gives carbonyl triterpenic compounds with high chemoselectivity.

Keywords: *Euphorbia officinarum*, *Euphorbia resinifera*, hemisynthesis, latex, oxidation

The isolated triterpenes of *Euphorbia resinifera*^[1] and *Euphorbia officinarum*^[1–3] were subjected to hemisynthesis in order to prepare new carbonyl triterpenic compounds with good yield. The oxygenated triterpenic compounds exhibit good pharmacological activities. Some polyoxygenated triterpenics were proved to have the cytotoxicity against hepatoma cells in vitro.^[4] Some others, isolated from *Ganoderma lucidum*, are effective as

Received in the U.K. April 27, 2006

Address correspondence to A. Benharref, Chemistry Laboratory of Natural Substances, University Cadi Ayyad, Faculty of Sciences Semlalia, P.O. Box 2390, Marrakech 40000, Morocco. E-mail: benharref@ucam.ac.ma

cytotoxic,^[5] antiviral,^[6] and anti-inflammatory agents.^[7,8] They have been shown to inhibit farnesyl-protein transferase^[9] and also cucurbitacin picfelta-raegenin I.^[10]

To prepare a similar compound, we have used the oxidation of isolated triterpenes resulting from Moroccan cactoid euphorbium and their derivatives with chromic anhydride^[11] and catalytic oxidation using ruthenium trichloride^[12] in the presence of sodium periodate.

Thus, we were interested in the oxygenated triterpenic compounds in positions 3, 7, 11, and 24 because the access to triterpenic ketones in positions 3, 7, and 11 can be carried out by oxidation with chromic anhydride. On the other hand, the synthesis of carbonyl triterpenic derivatives in position 24 can be carried out using catalytic oxidation with the system $\text{NaIO}_4\text{-(RuCl}_3, 3\text{H}_2\text{O)}$, like an organic oxidant.

Oxidation with the system $\text{NaIO}_4\text{-(RuCl}_3, 3\text{H}_2\text{O)}$ of eupho lanosta-8,24-dien-3 β -ol (**1**), a major triterpene isolated from *Euphorbia resinifera* latex, followed by esterification and then acetylation reaction, led to the title compound (3S,5S,10S,13S,14S,17S)3 β -acetyl-25,26,27-trisnorlanost-8-en-24-oate (**2**) in 75% yield (Scheme 1).

The compound **2** was characterized more precisely in ¹H NMR by a doublet (of doublet) ($J_1 = 12$ Hz, $J_2 = 4$ Hz) at 4.44 ppm, due to the resonance of H-3. The methyl of ester group was observed as a singlet at 3.58 ppm. ¹³C NMR spectrum exhibits 30 signals. Those observed at 81.07, 171.18, and 174.87 ppm were assigned respectively to C3 and CO of acetyl group and C24.

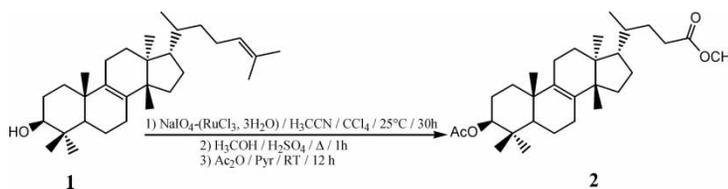
The relative stereochemistry of the title compound **2** was assigned to a known chiral center and confirmed by its single X-ray structure (Fig. 1).^[12]

Treatment of 8 α ,9 α -epoxy-4 α ,14 α -dimethyl-5 α -cholestan-3 β -ol (**3**), a triterpene derivative from *Euphorbia officinarum* latex, with 3 equiv. of chromic anhydride yielded compound **4** in 85% yield (Scheme 2).

Structure elucidation of carbonyl compound **4** was based on spectral data including ¹H NMR, ¹³C NMR, and mass spectrometry. ¹³C NMR spectrum exhibits a signal at 212.40 ppm due to the resonance of C3.

The stereochemistry has been confirmed by single-crystal X-ray diffraction (Fig. 2).^[13]

Acylation^[14] of 4 α -14 α -dimethyl-5 α -cholest-8-en-3 β -ol **5**, a major triterpene isolated from *Euphorbia officinarum* latex, followed by oxidation with 3 equiv. of CrO_3 during 12 h, gave two functionalized triterpenes **6** and **7**



Scheme 1.

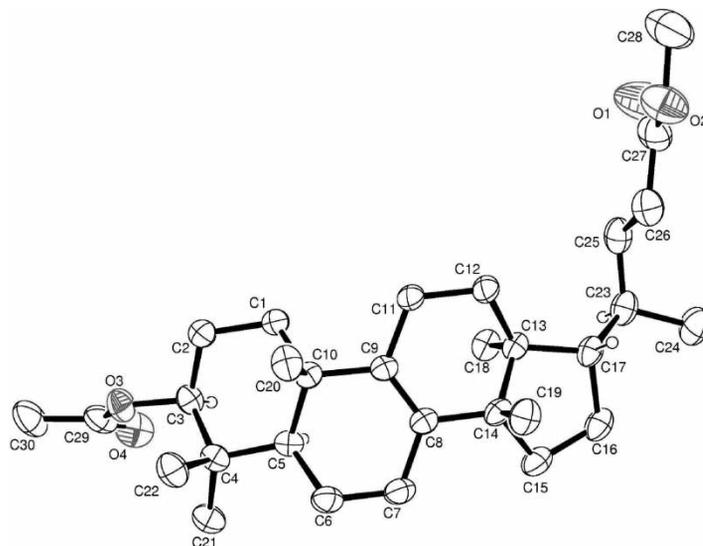
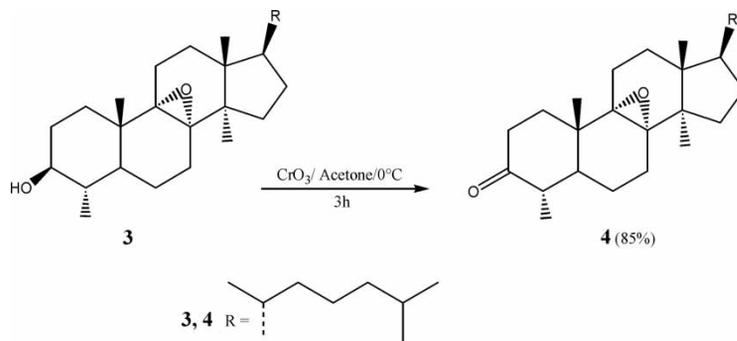


Figure 1. ORTEP drawing of **2**.

(Scheme 3). ^1H NMR spectrum of minor product **6** showed more precisely a multiplet at 4.39 ppm assigned to the H-3 proton. In ^{13}C NMR, a carbonyl group at C7 would have resonated at 197.50 ppm. The structure of the major product **7** was elucidated from ^1H NMR, ^{13}C NMR, and mass spectroscopic data. Thus, its molecular formula $\text{C}_{31}\text{H}_{48}\text{O}_4$ was determined from molecular ion $m/z = 584$ in its mass spectrum. ^{13}C NMR indicated the presence of 31 carbons, which include two carbonyl groups at 201.02 and 202.50 ppm, due to the resonance of C7 and C11 respectively.

The stereochemistry of compound **7** has been confirmed by single-crystal X-ray diffraction (Fig. 2).^[15]



Scheme 2.

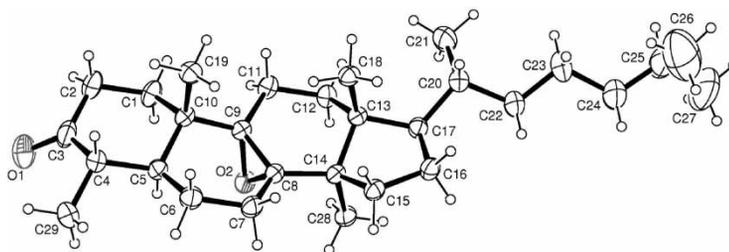


Figure 2. ORTEP drawing of **4**.

Treatment with tosyl chloride followed by an oxidation condition similar to that before gave triterpenic compounds **8** and **9** (Scheme 3).^[16]

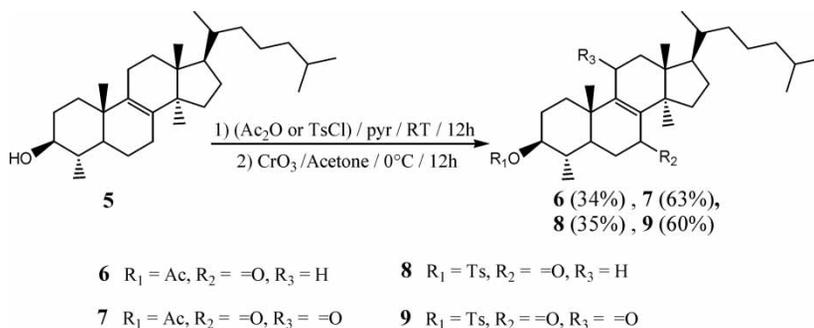
¹³C NMR spectrum revealed that **8** has one carbonyl group at C7, whereas compound **9** has two carbonyl groups at C7 and C11. The structure and relative stereochemistry of the title compound **9** were established and confirmed by single-crystal X-ray diffraction (Fig. 3).^[17]

Tosylation of 4 α -14 α -dimethyl-5 α -ergost-8-en-3 β -ol **10**, a major triterpene isolated from *Euphorbia officinarum* latex, followed by catalytic oxidation similar to that before, gave compound **11** with a good yield (75%) (Scheme 4).

Structure of **11** was elucidated from ¹H and ¹³C NMR. Thus the multiplet at 4.09 ppm was assigned to H-3 proton. In ¹³C NMR spectrum, carbonyl group at C24 was observed at 215.50 ppm.

Oxidation of compound **11** by 3 equiv. with chromic anhydride leads to preparation of two carbonyl compounds, **12** and **13** (Scheme 5).

¹³C NMR spectrum of **12** showed more precisely two signals at 198.50 and 215.45 ppm, assigned respectively to C7 and C24, whereas the carbonyl groups at C7, C11, and C24 resonated respectively at 200.68, 202.35, and 214.54 ppm for compound **13**.



Scheme 3.

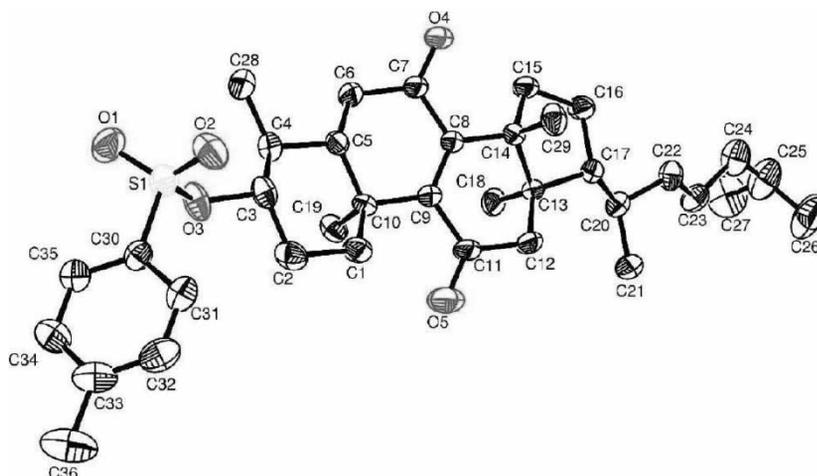


Figure 3. ORTEP drawing of **9**.

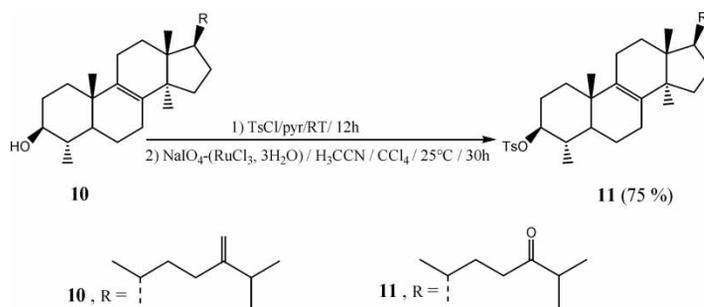
The structure of compound **13** was performed on the basis of X-ray single-crystallography analysis (Fig. 4).

In summary, we have synthesized the novel carbonyl compounds **2**, **4**, **6**, **7**, **8**, **9**, **11**, **12**, and **13** with a good yield via an oxidative route.

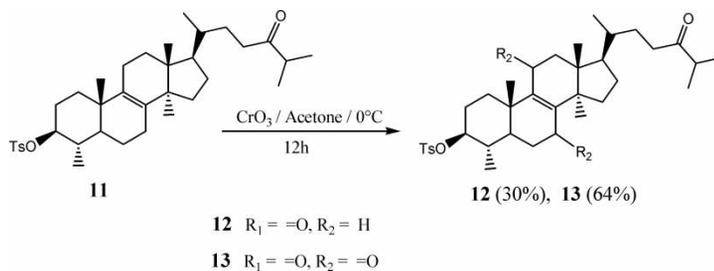
The ruthenium-catalyzed oxidation was proved to be effective and chemoselective.

EXPERIMENTAL

The ^1H and ^{13}C NMR spectrum were recorded on AMX2 Brüker 500-Hz (^1H 500 MHz, ^{13}C 125 MHz) using TMS as an internal standard and CDCl_3 as the solvent. The melting points were measured in capillaries on a Buchi 510 apparatus. The chemical shifts are given in ppm. The multiplicity of



Scheme 4.

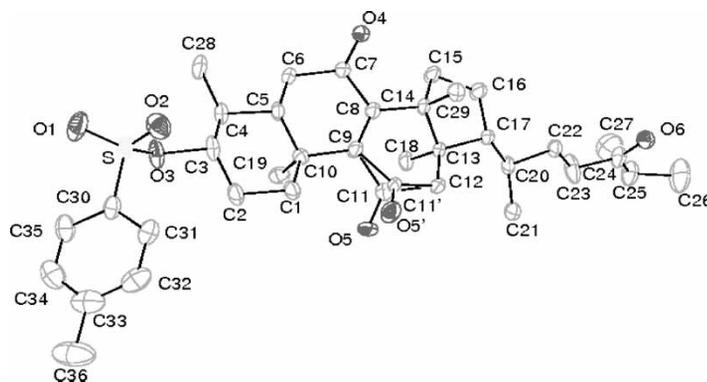


Scheme 5.

the signals observed is indicated by the letters: singlet (s), doublet (d), triplet (t), quadruplet (q), doublet and doublet (dd), and triplet dedoublet (td). Mass spectra were obtained with an Autospect Instrument 70-ev spectrometer. Column chromatography was carried out on silica gel (Merk Art. 15111, 7741); eluent: hexane–ethyl acetate. The X-ray diffraction measurements were carried out on an automated diffractometer, Nonius CCD, with monochromated Mo $K\alpha$ ($\lambda = 0.71073$) radiation.

General Procedure of Oxidation using NaIO_4 -($\text{RuCl}_3, 3\text{H}_2\text{O}$)

The sodium periodate was prepared in situ with a equimolar quantity of soda NaOH (0.5 g; 12.50 mmol) and periodic acid H_5IO_6 (2.85 g; 12.50 mmol). The mixture was stirred at 0°C . After 15 min, 5 ml of CCl_4 , 5 ml of H_3CCN , and 32.70 mg (0.12 mmol) of ruthenium trichloride were added. The mixture was stirred during 15 mn, then 1.33 g (3.12 mmol) of **1** was added. The reaction was left under agitation at 25°C for 30 h, then 20 ml of distilled water was added, and the reaction mixture was extracted with 40 ml of dichloromethane, dried over sodium sulphate, and reduced in

Figure 4. ORTEP drawing of **13**.

vacuum to afford a black solid. The latter was filtered on a silica-gel column to eliminate RuO₄. The organic layer is recovered and evaporated under reduced pressure. The residue was purified on a silica-gel column using hexane/EtOAc (90:10) as an eluent.

General Procedure of Oxidation with CrO₃

To a solution of 1.00 g (2.34 mmol) of **3** in 20 ml of acetone, 0.70 g (7.04 mmol) of chromic anhydride was added. The mixture was maintained at 0°C for 3 h (12 h for allylic oxidation), washed with 20 ml of cold water, and extracted with ethyl acetate. The organic layer was dried over Na₂SO₄ and concentrated under reduced pressure. The residue was purified on a silica-gel column using hexane/EtOAc (95:5) as an eluent.

Data

(3S,5S,10S,13S,14S,17S)3β-Acetyl-25,26,27-trisnorlanost-8-en-24-oate (2): mp = 176–177°C (methanol), yield: 75%. ¹H NMR (500 MHz, CDCl₃) δ (ppm): 4.43 (H-3, dd, *J*₁ = 12 Hz, *J*₂ = 4 Hz); 3.64 (COOCH₃), 1.98 (OCOCH₃), 0.75 (H-18), 1.00 (H-19, s), 0.95 (H-21, d, *J* = 6.2 Hz), 0.96 (H-25, s), 0.97 (H-26, s), 0.90 (H-27, s). ¹³C NMR (125 MHz, CDCl₃) δ (ppm): 35.28 (C-1), 35.84 (C-2), 81.32 (C-3), 51.8 (C-4), 51.43 (C-5), 31.10 (C-6), 30.70 (C-7), 133.9 (C-8), 134.3 (C-9), 49.8 (C-10), 28.43 (C-11), 28.37 (C-12), 44.48 (C-13), 38.24 (C-14), 27.89 (C-15), 24.80 (C-16), 50.39 (C-17), 15.85 (C-18), 20.57 (C-19), 31.43 (C-20), 18.99 (C-21), 31.11 (C-22), 37.52 (C-23), 175.09 (C-24), 24.62 (C-25), 21.88 (C-26), 16.99 (C-27), 20.57 (COOCH₃), 21.69 (OCOCH₃).

8α,9α-Epoxy-4α,14α-dimethyl-5α,cholestan-3-one (4): mp = 128–129°C (hexane), yield: 85%. ¹H NMR (500 MHz, CDCl₃) δ (ppm): 0.73 (H-18, s), 0.83 (H-19, s), 0.82 (H-21, d, *J* = 6 Hz), 0.77 (H-26, d, *J* = 2 Hz), 0.80 (H-27, *J* = 2 Hz), 1.25 (H-28, s), 0.87 (H-29, d, *J* = 6.2 Hz). ¹³C NMR (125 MHz, CDCl₃) δ (ppm): 36.3 (C-1), 36.4 (C-2), 212.4 (C-3), 49.2 (C-4), 45.4 (C-5), 22.7 (C-6), 22.0 (C-7), 69.6 (C-8), 68.3 (C-9), 36.4 (C-10), 19.4 (C-11), 26.5 (C-12), 43.9 (C-13), 43.3 (C-14), 30.9 (C-15), 29.3 (C-16), 48.6 (C-17), 15.9 (C-18), 15.5 (C-19), 36.4 (C-20), 19.6 (C-21), 36.2 (C-22), 24.1 (C-23), 39.5 (C-24), 28.1 (C-25), 21.5 (C-26), 21.8 (C-27), 16.5 (C-28), 24.5 (C-29).

3β-Acetoxy-4α,14α-dimethyl-5α-cholest-8-en-7-one (6): mp = 135–136°C (hexane); yield: 34%. ¹H NMR (500 MHz, CDCl₃) δ (ppm): 4.39 (H-3, ddd, *J*₁ = 11 Hz, *J*₂ = 11 Hz, *J*₃ = 3 Hz), 0.68 (H-18, s), 1.02 (H-26, d, *J* = 2 Hz), 1.03 (H-27, d, *J* = 2 Hz), 0.96 (H-21, d, *J* = 6.4 Hz), 1.2 (H-19, s), 0.73 (H-28, s), 0.86 (H-29, d, *J* = 6.7 Hz), 2.05 (COOCH₃, s). ¹³C NMR (125 MHz, CDCl₃) δ (ppm): 33.5 (C-1), 28.5 (C-2), 76.70 (C-3), 36.6 (C-4),

46.2 (C-5), 39.1 (C-6), 197.5 (C-7), 139.7 (C-8), 164.4 (C-9), 38.7 (C-10), 24.5 (C-11), 30.1 (C-12), 44.9 (C-13), 47.80 (C-14), 30.9 (C-15), 30.60 (C-16), 51.4 (C-17), 15.40 (C-18), 18.1 (C-19), 36.3 (C-20), 18.60 (C-21), 36.4 (C-22), 24.0 (C-23), 39.4 (C-24), 27.8 (C-25), 22.7 (C-26), 22.5 (C-27), 25.4 (C-28), 15.0 (C-29), 170.7 (COOCH₃). Low resolution: MS (m/z): 470.2 (10%), 283.2 (100%), 411.2 (50%), 117.2 (20%). High resolution: 470.3425 (calc. 470.3464).

3 β -Acetoxy-4 α ,14 α -dimethyl-5 α -cholest-8-ene-7,11-dione (7): mp = 117–119°C (hexane), yield: 63%. ¹H NMR (500 MHz, CDCl₃) δ (ppm): 4.40 (H-3, ddd, $J_1 = 11$ Hz, $J_2 = 11$ Hz, $J_3 = 3$ Hz), 0.75 (H-18, s), 0.79 (H-26, d, $J = 2$ Hz), 0.83 (H-27, d, $J = 2$ Hz), 0.84 (H-21, d, $J = 6.2$ Hz), 1.24 (H-19, s), 1.14 (H-28, s), 0.88 (H-29, d, $J = 6.6$ Hz), 2.04 (COOCH₃, s). ¹³C NMR (125 MHz, CDCl₃) δ (ppm): 33.6 (C-1), 31.3 (C-2), 77.2 (C-3), 35.2 (C-4), 47.1 (C-5), 39.2 (C-6), 201.0 (C-7), 151.6 (C-8), 152.1 (C-9), 38.4 (C-10), 202.5 (C-11), 51.4 (C-12), 47.4 (C-13), 47.6 (C-14), 32.1 (C-15), 27.3 (C-16), 48.9 (C-17), 16.7 (C-18), 16.2 (C-19), 36.5 (C-20), 18.5 (C-21), 34.9 (C-22), 24.1 (C-23), 39.4 (C-24), 27.7 (C-25), 21.8 (C-26), 22.1 (C-27), 26.1 (C-28), 14.7 (C-29), 170.6 (COOCH₃).

3 β -Tosyloxy-4 α ,14 α -dimethyl-5 α -cholest-8-en-7-one (8): mp = 123–124°C (methanol), yield: 35%. ¹H NMR (500 MHz, CDCl₃) δ (ppm): 4.00 (H-3, ddd, $J_1 = 11$ Hz, $J_2 = 11$ Hz, $J_3 = 3$ Hz), 0.72 (H-18, s), 0.98 (H-19, s), 0.84 (H-26, d, $J = 2.1$ Hz), 0.85 (H-27, d, $J = 2.1$ Hz), 0.86 (H-21, d, $J = 6.2$ Hz), 1.12 (H-28, s), 0.88 (H-29, d, $J = 6.6$ Hz), 7.72 (H-2', d, $J = 8.8$ Hz), 7.25 (H-3', d, $J = 8.8$ Hz), 2.44 (H-5'). ¹³C NMR (125 MHz, CDCl₃) δ (ppm): 33.4 (C-1), 26.3 (C-2), 86.6 (C-3), 34.3 (C-4), 48.1 (C-5), 39.2 (C-6), 197.5 (C-7), 140.2 (C-8), 164.2 (C-9), 38.3 (C-10), 22.7 (C-11), 28.3 (C-12), 47.1 (C-13), 47.5 (C-14), 32.3 (C-15), 25.4 (C-16), 49.4 (C-17), 17.5 (C-18), 16.4 (C-19), 36.0 (C-20), 18.5 (C-21), 34.3 (C-22), 25.4 (C-23), 39.7 (C-24), 28.3 (C-25), 21.5 (C-26), 22.5 (C-27), 18.4 (C-30), 144.9 (C-1'), 134.7 (C-2'), 130.1 (C-3'), 128.0 (C-4'), 21.50 (C-5'). Low resolution: MS (m/z): 395.3 (100%), 410.3 (43%), 424.3 (32%), 229 (22%), 582.3 (6%). High resolution: 582.3773 (calc. 582.3742).

3 β -Tosyloxy-4 α ,14 α -dimethyl-5 α -cholest-8-ene-7,11-dione (9): mp = 124–125°C (hexane), yield: 60%. ¹H NMR (500 MHz, CDCl₃) δ (ppm): 4.06 (H-3, ddd, $J_1 = 11$ Hz, $J_2 = 11$ Hz, $J_3 = 3$ Hz), 0.88 (H-18, s), 1.12 (H-19, s), 0.85 (H-26, d, $J = 2.2$ Hz), 0.86 (H-27, d, $J = 2.2$ Hz), 0.87 (H-21, d, $J = 6.4$ Hz), 1.16 (H-28, s), 0.90 (H-29, d, $J = 6.4$ Hz), 7.79 (H-2', d, $J = 8.2$ Hz), 7.31 (H-3', d, $J = 8.2$ Hz), 2.43 (H-5'). ¹³C NMR (125 MHz, CDCl₃) δ (ppm): 33.5 (C-1), 26.2 (C-2), 86.5 (C-3), 34.9 (C-4), 48.6 (C-5), 39.4 (C-6), 200.5 (C-7), 151.4 (C-8), 150.7 (C-9), 38.2 (C-10), 202.7 (C-11), 51.5 (C-12), 47.7 (C-13), 47.5 (C-14), 32.5 (C-15), 27.5 (C-16), 49.5 (C-17), 16.5 (C-18), 16.4 (C-19), 36.4 (C-20), 18.5 (C-21), 34.8 (C-22), 28.4 (C-23), 39.5 (C-24), 31.8 (C-25), 21.5 (C-26), 22.5 (C-27),

14.5 (C-30), 26.2 (C-32), 144.3 (C-1'), 134.5 (C-2'), 129.8 (C-3'), 127.5 (C-4'), 21.4 (C-5').

3 β -Tosyloxy-4 α ,14 α -dimethyl-5 α -ergost-8-en-24-one (11): mp = 145–146°C (hexane), yield: 75%. ¹H NMR (500 MHz, CDCl₃) δ (ppm): 4.09 (H-3, ddd, $J_1 = 11$ Hz, $J_2 = 11$ Hz, $J_3 = 3$ Hz), 0.86 (H-18, s), 1.54 (H-19, s), 0.77 (H-21, d, $J = 6.37$ Hz), 1.08 (H-26, d, $J = 1.52$ Hz), 1.09 (H-27, d, $J = 1.53$ Hz), 0.93 (H-28, s), 0.88 (H-29, d, $J = 6.38$ Hz), 7.79 (H-2', d, $J = 8.31$ Hz), 7.31 (H-3', d, $J = 7.9$ Hz), 2.43 (H-5'). ¹³C NMR (125 MHz, CDCl₃) δ (ppm): 33.5 (C-1), 26.2 (C-2), 88.8 (C-3), 44.5 (C-4), 49.2 (C-5), 22.7 (C-6), 22.0 (C-7), 133.4 (C-8), 135.2 (C-9), 38.2 (C-10), 20.7 (C-11), 51.5 (C-12), 47.7 (C-13), 47.5 (C-14), 32.5 (C-15), 27.5 (C-16), 49.5 (C-17), 16.5 (C-18), 16.4 (C-19), 36.4 (C-20), 18.5 (C-21), 34.8 (C-22), 28.4 (C-23), 215.5 (C-24), 31.8 (C-25), 21.5 (C-26), 22.5 (C-27), 144.6 (C-1'), 135.3 (C-2'), 129.9 (C-3'), 128.5 (C-4'), 21.5 (C-5'). Low resolution: MS (m/z): 582.3 (3%), 393.3 (42%), 395.3 (65%), 396 (25%), 407.3 (26%), 408.3 (27%), 409.3 (63%), 410.3 (70%), 424.3 (62%), 425.3 (25%), 442.3 (23%), 321.2 (22%), 343.2 (25%), 215.1 (25%), 241.2 (24%). High resolution: 582.3758 (calc. 582.3742).

3 β -Tosyloxy-4 α ,14 α -dimethyl-5 α -ergost-8-ene-7,24-dione (12): mp = 152–153°C (hexane), yield: 30%. ¹H NMR (500 MHz, CDCl₃) δ (ppm): 4.10 (H-3, ddd, $J_1 = 11$ Hz, $J_2 = 11$ Hz, $J_{33} = 3$ Hz), 0.90 (H-18, s), 1.54 (H-19, s), 0.76 (H-21, d, $J = 6.40$ Hz), 1.06 (H-26, d, $J = 2.00$ Hz), 1.08 (H-27, d, $J = 2.00$ Hz), 0.95 (H-28, s), 0.88 (H-29, d, $J = 6.40$ Hz), 7.77 (H-2', d, $J = 8.40$ Hz), 7.31 (H-3', d, $J = 8.00$ Hz), 2.42 (H₃-5'). ¹³C NMR (125 MHz, CDCl₃) δ (ppm): 33.5 (C-1), 26.2 (C-2), 88.8 (C-3), 44.5 (C-4), 49.2 (C-5), 22.7 (C-6), 198.5 (C-7), 140.2 (C-8), 164.2 (C-9), 38.2 (C-10), 20.7 (C-11), 51.4 (C-12), 47.7 (C-13), 47.5 (C-14), 32.5 (C-15), 27.4 (C-16), 49.5 (C-17), 16.4 (C-18), 16.4 (C-19), 36.4 (C-20), 18.5 (C-21), 34.8 (C-22), 28.4 (C-23), 215.4 (C-24), 31.8 (C-25), 21.5 (C-26), 22.5 (C-27), 144.6 (C-1'), 135.3 (C-2'), 129.9 (C-3'), 128.4 (C-4'), 21.4 (C-5'). Low resolution: 43.1 (22%), 91.1 (22%), 229.1 (24%), 302.2 (22%), 395 (26%), 424.3 (100%), 425.3 (31%), 596 (30%). High resolution: 596.3519 (calc. 596.3535).

3 β -Tosyloxy-4 α ,14 α -dimethyl-5 α -ergost-8-ene-7,11,24-trione (13): mp = 155–156°C (methanol), yield: 64%. ¹H NMR (500 MHz, CDCl₃) δ (ppm): 4.10 (H-3, ddd, $J_1 = 11$ Hz, $J_2 = 11$ Hz, $J_3 = 3$ Hz), 0.91 (H-18, s), 1.45 (H-19, s), 0.80 (H-21, d, $J = 6.40$ Hz), 1.06 (H-26, d, $J = 2.00$ Hz), 1.08 (H-27, d, $J = 2.00$ Hz), 0.95 (H-28, s), 0.88 (H-29, d, $J = 6.45$ Hz), 7.78 (H-2', d, $J = 8.10$ Hz), 7.33 (H-3', d, $J = 8.10$ Hz), 2.43 (H-5'). ¹³C NMR (125 MHz, CDCl₃) δ (ppm): 33.2 (C-1), 26.1 (C-2), 86.4 (C-3), 35.8 (C-4), 47.3 (C-5), 38.3 (C-6), 200.7 (C-7), 151.4 (C-8), 150.9 (C-9), 40.9 (C-10), 202 (C-11), 51.50 (C-12), 49.1 (C-13), 47.5 (C-14), 32.1 (C-15), 27.3 (C-16), 49.2 (C-17), 16.9 (C-18), 16.4 (C-19), 35.8 (C-20), 18.4 (C-21), 38.2 (C-22), 29.8 (C-23), 214.5 (C-24), 35.6 (C-25), 21.7 (C-26),

22.4 (C-27), 31.8 (C-25), 21.5 (C-26), 18.4 (C-27), 14.5 (C-28), 16.4 (C-29), 144.7 (C-1'), 134.6 (C-2'), 129.8 (C-3'), 127.8 (C-4'), 18.4 (C-5'). Low resolution: 610.3 (2%), 395.3 (20%), 410.3 (21%), 423.3 (23%), 438.3 (100%), 439.3 (58%), 257.1 (20%), 229 (25%). High resolution: 610.3312 (calc. 610.3328).

ACKNOWLEDGMENTS

This work was partially supported by the Collaborative Project CSIC–Laboratory of Natural Substances, University Cadi Ayyad, Faculty of Sciences Semlalia Marrakesh (FSSM), Marrakesh, Morocco, Ref. 2004 MA 0009.

REFERENCES

1. Benharref, A.; Lavergne, J.-P. Triterpènes issus des latex des euphorbes cactéoides marocaines *E. resinifera*, *E. echinus* et *E. officinarum*: Isolement, étude comparative par RMN ^{13}C des quatre classes tétracycliques, eupho-lanostane, élémolanostane, lanostane et nor-31 lanostane. *Bull. Soc. Chim. Fr.* **1985**, *5*, 965–972.
2. Daoubi, M.; Macias-Sanchez, A. J.; Hernandez-Galan, R.; Benharref, A.; Collado, I. G. Two novel steroids from *Euphorbia officinarum* latex. *Prod. Res.* **2004**, *18* (2), 177–181.
3. Mazoir, N.; Liazid, A.; Auhmani, A.; Daoubi, M.; Dakir, M.; Benharref, A.; Kenz, A.; Pierrot, M. ^1H and ^{13}C NMR structural study of products obtained by hemisynthesis on the triterpenes isolated from latex of *Euphorbia officinarum*. *Phys. Chem. News.* **2005**, *21*, 123–128.
4. Toth, J. O.; Luu, B.; Ourisson, G. Inhibitory effects of components from *Ganoderma lucidum* on the growth of human immunodeficiency virus (HIV) and the protease activity. *Tetrahedron Lett.* **1983**, *24*, 1081–1084.
5. Kohda, H.; Tokumoto, W.; Sakamoto, K.; Fujii, M.; Hirai, Y.; Yamasaki, K.; Komoda, Y.; Nakamura, H.; Ishibara, S.; Uchida, M. The biologically active constituents of *Ganoderma lucidum* (Fr.) Karst: Histamine release-inhibitory triterpenes. *Chem. Pharm. Bull.* **1985**, *33*, 1367–1373.
6. Lindequist, U.; Lesnau, A.; Teuscher, E.; Pilgrim, H. The antiviral action of ergosterol peroxide. *Pharmazie* **1989**, *44*, 579–580.
7. Tasaka, K.; Akaji, M.; Miyoushi, K.; Mio, M.; Makino, T. Anti-allergic constituents in the culture medium of *Ganoderma lucidum* (I): Inhibitory effect of oleic acid on histamine release. *Agents Actions.* **1988**, *23*, 153–156.
8. Tasaka, K.; Mio, M.; Izushi, K.; Akaji, M.; Makino, T. Anti-allergic constituents in the culture medium of *Ganoderma lucidum* (II): The inhibitory effect of cyclo-octasulfur on histamine release. *Agents Actions.* **1988**, *23*, 157–160.
9. Jayasurya, H.; Silverman, K. S.; Zink, D. L.; Jenkins, R. G.; Sanchez, M.; Pelaez, F.; Vilella, D.; Lingham, R. B.; Singh, S. B. Clavatic acid: A triterpenoid inhibitor of farnesyl-protein transferase from *Clavariadelphus truncates*. *J. Nat. Prod.* **1998**, *61* (12), 1568–1570.
10. Huang, T.; De Bruyne, T.; Apers, S.; Ma, Y.; Claeys, M.; Vanden, D.; Pieters, L.; Vlietinck, A. Complement-inhibiting cucurbitacin glycosides from *Picria felterrae*. *J. Nat. Prod.* **1998**, *61* (6), 757–761.

11. Dakir, M.; Auhmani, A.; Ait Itto, M. Y.; Mazoir, N.; Akssira, M.; Pierrot, M.; Benharref, A. Optimization of allylic oxidation of (1S,3R,8R)-2,2-dichloro-3,7,7,10-tetramethyltricyclo[6,4,0^{1,3}]dodec-9-ene. *Synth Commun.* **2004**, *34* (11), 2001–2008.
12. Mazoir, N.; Giorgi, M.; Auhmani, A. (3S,5S,10S,13S,14S,17S)-Methyl-3 β -acetyl-25,26,27-trisnorlanost-8-en-24-oate. *Acta Cryst.* **2005**, *E61*, o2382–o2383.
13. Mazoir, N.; Giorgi, M.; Benharref, A. (4S,5S,10S,13R,14R,17R)-8 α ,9 α -Epoxy-4 α ,14 α -dimethyl-5 α ,cholestan-3-one. *Acta Cryst.* **2005**, *E61*, o3709–o3711.
14. Mazoir, N.; Auhmani, A.; Ait Itto, M. Y.; Benharref, A. (3S)-Acetyl-24-methylen-elemo-lanosta-8,24-diene-7,11-dione. *Molbank.* **2004**, M365.
15. Daoubi, M.; Benharref, A.; Pierrot, M. 3 β -Acetoxy nor-31-lanostene-7,11-dione. *Acta Cryst.* **2001**, *E57*, o1187–o1188.
16. Mazoir, N.; Auhmani, A.; Dakir, M.; Ait Itto, M. Y.; Benharref, A. (3S)-Tosyl-24-methylen-elemo-lanosta-8,24-diene-7,11-dione. *Molbank.* **2004**, M366.
17. Auhmani, A.; Giorgi, M.; Mazoir, N. (3S,4S,5S,10S,13R,14R,17R)-4 α ,14 α -Dimethyl-3 β -tosyl-5 α -cholest-8-ene-7,11-dione. *Acta Cryst.* **2005**, *E61*, o1190–o1192.