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# Syntheses of 11-Hydroxylated Guaianolides

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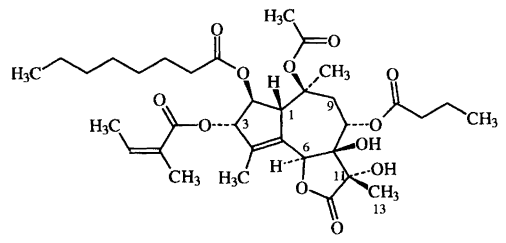
Two epimeric guaianolides, both prepared from α-santonin, were 11-hydroxylated using 2-phenylsulfonyl-3-phenyloxaziridine as a reagent. Extensive use of protecting groups enabled selective acylation of the 3- and 10-hydroxy groups.

Biological activity of sesquiterpene lactones is very often associated with the presence of an α,β-unsaturated carbonyl group in the molecule.[1–3] The α-methylene lactone group, often found in sesquiterpene lactones isolated from plant species belonging to the Asteraceae, in general provides the molecule with cytotoxic and allergenic properties.[1–4] Some examples, however, of bioactive sequiterpenes, which do not possess an α,β-unsaturated carbonyl group, or in which the biological activity does not depend on the presence of an α,β-unsaturated carbonyl group, have been reported. Examples of the latter sesquiterpene lactones are the palytoxins, which are believed to interfere with a binding site for the neurotransmitter GABA,[5] artemisinin or QHS, which is a very promising antimalarial drug,[6] and thapsigargin (**1**), which is a selective and very potent inhibitor of the microsomal $Ca^{2+}$-pumps.[7] Thapsigargin (**1**) has become a worldwide used tool for investigating the $Ca^{2+}$-homeostasis. Structure–activity relationships have revealed that the presence of the 7,11-dihydroxy part is important for the $Ca^{2+}$-pump inhibitory action of **1**.[8] This finding and the poor availability of **1**, which only can be isolated from the Mediterranean umbelliferous plant *Thapsia garganica* L.,[9] focused our interest on methods for introducing hydroxy groups in the 7 and 11 positions of guaianolides. The present paper describes a method for 11-hydroxylation of guaianolides. The key reaction is an electrophilic attack of oxygen in 2-phenylsulfonyl-3-phenyloxaziridine[10] on a lactone enolate. Selective acylation of the different hydroxy groups in the formed hydroxy guaianolide is described.



**1**

## Discussion

Isophotosantonic lactone (**4a**), in which the lactone and the cycloheptane rings are *trans*-annelated, was prepared according to literature methods by illuminating α-santonin (**2**) dissolved in a mixture of acetic acid and water (Scheme 1).[11,12] Reduction of the ketone with sodium borohydride yielded a mixture of the desired **5a** contaminated with a small amount of the tetrahydro derivative **6** (Scheme 2). The stereochemistry of the two secondary alcohols was determined from the NOESY spectra. The two alcohols, **5a** and **6**, were very difficult to separate. Addition of cerium(III) chloride[13] to the reaction mixture increased the selectivity, but decreased the yield. The two hydroxy groups of **5a** were masked as trimethylsilyl ethers (**8a**) before the 11-hydroxylation. This masking, however, only succeeded if lithium sulfide[14] was used as a catalyst. The stereochemistry of the electrophilic attack of the oxaziridine is in general directed by the steric hindrance of the two sites of the enolate.[15] In the case of the enolate

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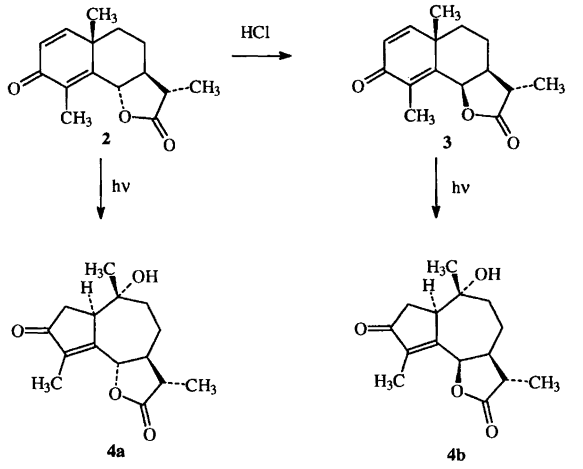
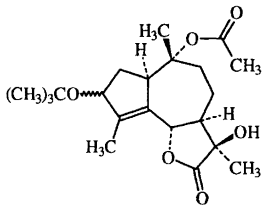
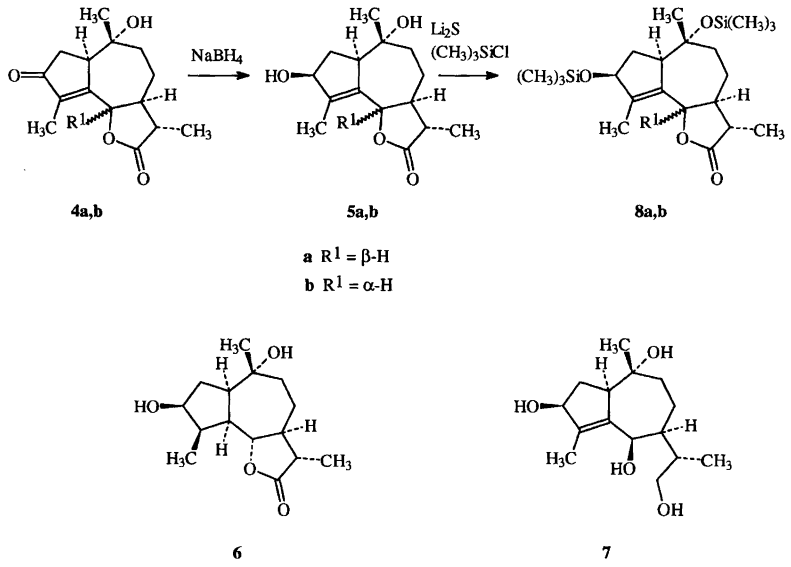



*Scheme 1.*

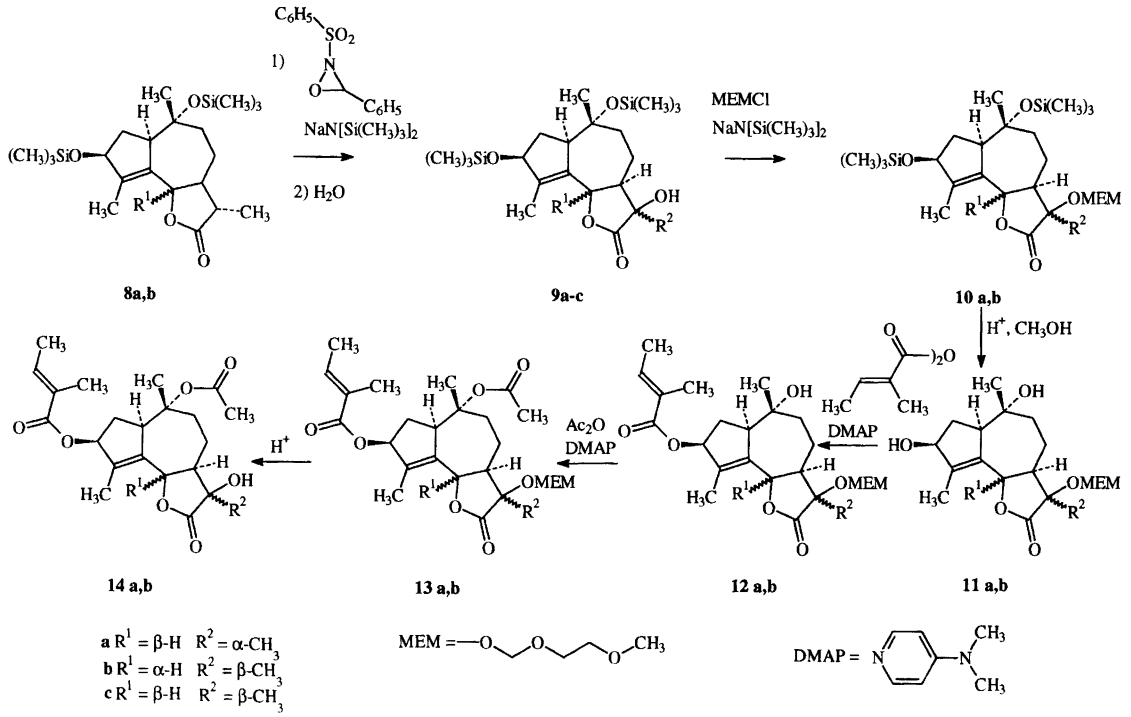
of **8a**, however, the two sites of the enolate *a priori* would be considered to be equally hindered. In spite of this the β-hydroxy derivative (**9a**) was isolated in a yield of 62% and the α-hydroxy derivative (**9c**) only in a yield of 2% (Scheme 3). The stereochemistry of the introduced hydroxy groups in **9a** and **9c** was disclosed by the presence in the NOESY spectra of a NOE between H-13 and and H-9α and between H-13 and H-6, respectively. In order to obtain an acylation pattern of **9a** similar to that of **1**, the two silyl ether groups were removed to give a triol, in which the secondary hydroxy group selectively was acylated using tiglic anhydride and 4-dimethylaminopyridine as reagents. Acetylation of this product unfortunately showed that the 11-hydroxy group was acetylated faster than the 10-hydroxy group. The failure of this attempt to convert **9a** into **14a** forced us to use protecting groups. Thus **9a** was transformed into the MEM ether **10a**,[16] which was solvolysed to give **11a**. Selective acylation of the secondary hydroxy group with tiglic anhydride afforded **12a**, which was acetylated to give **13a**. Removal of the MEM group with pyridinium toluene sulfonate in *tert*-butyl alcohol[17] yielded the target molecule **14a**. The product, however, was contaminated with the butyl ether **15**, most likely formed by an $A_{AL}1$ substitution of the tiglic ester group.[18] This side product, however, was easily avoided by running the reaction in *N*,*N*-dimethylformamide (DMF).




6-Epiisophoto-α-santonic lactone **4b**, in which the lactone and the cycloheptane rings are *cis*-annelated, was in an analogous way transformed into the *cis*-annelated thapsigargin analogue. In addition to the allylic alcohol **5b** a substantial amount of the primary alcohol **7** was formed. Reduction of lactones to primary alcohols has previously been reported.[19] As expected from sterical hindrance of the enolate of the silyl ether **8b** the 11-hydroxylation of the *cis*-annelated guaianolide exclusively afforded formation of the α-hydroxy form **9b**. Formation of the MEM ether **10b** and the following two acylations to give **13b** were performed analogously to the reactions on the *trans*-annelated guaianolides. The MEM group was removed with pyridinium toluene sulfonate in DMF.




*Scheme 2.*



*Scheme 3.*

## Experimental

*General methods.* Column chromatography separations were performed using Merck $SiO_2$ 60 (0.063–0.200 mm) or Merck $SiO_2$ (0.040–0.063 mm). Reversed-phase column chromatography was performed using Merck $SiO_2$ 60 silanised (0.063–0.200 mm). Merck $SiO_2$ 60 F254 precoated aluminium sheets were used for TLC, and the spots were visualized by UV and by spraying with an ethanolic solution containing 0.1% of vanillin, 5% of $H_2SO_4$ and 5% of glacial acetic acid. Separations by HPLC were performed using a Waters 6000A pump, a Shimadzu SPD 6A detector ($\lambda = 230$ nm) and LiChrosorp RP-18 column (5 μm, 16 × 240 mm, flow 9.0 ml $min^{-1}$). The NMR spectra were recorded on a Bruker AMX 400 or a Bruker AC 200 F spectrometer using $Me_4Si$ as an internal standard. The mass spectra (positive FAB) were obtained on a Jeol JMS-HX 110/110 A-T mass spectrometer.

*Preparation of 3β,10α-dihydroxy-1αH,6βH,11αH-guai-4-enolide (**5a**) and 3β,10α-dihydroxy-1αH,5αH,6βH,11αH-guaianolide (**6**).* To a solution of 3-keto-10α-hydroxy-1α*H*,6β*H*,11α*H*-guai-4-enolide (**4a**, 1.0 g, 3.8 mmol), prepared by photolysis of α-santonin, in methanol (25 ml) was added sodium borohydride (500 mg, 13 mmol), and the solution was stirred at 0 °C. The reaction was stopped after 10 min by addition of acetone (15 ml) and water (25 ml), and the mixture was neutralized with 4 M hydrochloric acid. The mixture was concentrated to half volume in vacuum, and the residue was saturated with NaCl and extracted with EtOAc. The EtOAc phase was dried ($MgSO_4$) and concentrated in vacuum, and the constitutents of the residue were separated by column chromatography [eluent: EtOAc–acetone (7:1)] to give **5a** (831 mg, 82%) and **6** (31 mg, 3%). An analytical sample of **5a** was recrystallized (EtOAc–petroleum ether) to give colourless crystals, m.p. 192–195 °C. Anal. for $C_{15}H_{22}O_4$, C, H. NMR data of **5a** $^1$H NMR ($CDCl_3$, 400 MHz) δ: 2.93 (br t, $J = 7.7$ Hz, 1 H, H-1), 2.49 (dt, $J = 13.8$ and 7.7 Hz, 1H, H-2α), 1.62 (m, 1 H, H-2β), 4.54 (br t, $J = 7.7$ Hz, 1 H, H-3), 4.69 (br dq, $J = 10.9$ and 2.1 Hz, 1 H, H-6), 1.89 (m, 1 H, H-7), 1.97 (m, 2 H, H-8α and H-9β), 1.38 (m, 1 H, H-8β), 1.63 (m, 1 H, H-9α), 2.21 (dq, $J = 13.9$ and 6.9 Hz, 1 H, H-11), 1.21 (d, $J = 6.9$ Hz, 3 H, H-13), 1.05 (s, 3 H, H-14), 1.89 (s, 3 H, H-15). $^{13}$C NMR ($CDCl_3$, 100 MHz) δ: 54.6 (C-1), 34.7 (C-2), 77.5 (C-3), 143.9 (C-4), 131.7 (C-5), 81.7 (C-6), 49.0 (C-7), 25.6 (C-8), 44.7 (C-9), 74.4 (C-10), 41.4 (C-11), 177.8 (C-12), 12.3 (C-13), 21.5 (C-14), 12.3 (C-15). NMR data of **6**: $^1$H NMR ($CDCl_3$, 400 MHz) δ: 2.3–2.1 (m, 1 H, H-1), 2.0–1.9 (m, 2 H, H-2α and H-4), 1.6–1.5 (m, 2 H, H-2β and H-9α), 4.06 (ddd, $J = 10.6$, 6.7 and 6.1 Hz, 1 H, H-3), 1.9–1.8 (m, 2 H, H-5 and H-8α), 4.29 (dd, $J = 10.8$ and 10.1 Hz, 1 H, H-6), 1.74 (m, 1 H, H-7), 1.33 (m, 1 H, H-8β), 2.3–2.1 (m, 2 H, H-9β and H-11), 1.12 (d, $J = 7.1$ Hz, 3 H, H-13), 1.17 (s, 3 H, H-14), 0.88 (d, $J = 7.3$ Hz, H-15). $^{13}$C NMR ($CDCl_3$, 100 MHz) δ: 50.3 (C-1, C-4, C-5, C-7, C-9 or C-11), 33.5 (C-2), 72.1 (C-3), 45.7 (C-1, C-4, C-5, C-7, C-9 or C-11), 39.7 (C-1, C-4, C-5, C-7, C-9 or C-11), 81.5 (C-6), 47.1 (C-1, C-4, C-5, C-7, C-9 or C-11), 25.4 (C-8), 41.2 (C-1, C-4, C-5,

C-7, C-9 or C-11), 73.4 (C-10), 43.6 (C-1, C-4, C-5, C-7, C-9 or C-11), 178.3 (C-12), 11.8 (C-13), 23.2 (C-14), 7.6 (C-15).

*Preparation of 3β,10α-bistrimethylsilyloxy-1αH,6βH,11αH-guai-4-enolide (***8a***).* To a solution of lithium sulfide (174 mg, 3.8 mmol) in dry acetonitrile (2 ml) was under nitrogen added distilled trimethylsilyl chloride (1 ml, 7.4 mmol). To this solution was added **5a** (53 mg, 1.2 mmol) dissolved in acetonitrile (1.5 ml), and the mixture was left under nitrogen. Trimethylsilyl chloride (0.5 ml, 3.7 mmol) and lithium sulfide (30 mg, 0.65 mmol) were added after 16 h. After an additional 16 h the mixture was concentrated under a stream of nitrogen, and to the residue was added ether (15 ml). The ether solution was washed with 2 M aqueous sodium carbonate (15 ml), water (15 ml) and brine (15 ml). The combined aqueous phases were extracted with ether, and the combined ether phases were dried ($MgSO_4$) and concentrated in vacuum. Compound **8a** (198 mg, 74%) was isolated from the residue by flash column chromatography [eluent: toluene–EtOAc (25:1)]. An analytical sample of **8a** was recrystallized (MeOH) to give colourles crystals, m.p. 92–94°C. MS: 411.2 (30%, $M+1$), 339.2 (22%, $M+1$-$C_3H_4O_2$), 321.2 (100%, $M+1$-$C_3H_9SiOH$), 231.2 (72%, $M+1$-2 × $C_3H_9SiOH$). Anal. for $C_{21}$ $H_{38}$ $O_4$ $Si_2$, C,H. $^1$H NMR ($CDCl_3$, 400 MHz) δ: 2.89 (m, 1 H, H-1), 2.28 (dt, $J$ = 13.7 and 7.7 Hz, 1H, H-2α), 1.60 (m, 1 H, H-2β), 4.42 (br t, $J$ = 7.7 Hz, 1 H, H-3), 4.65 (br dq, $J$ = 11.1 and 1.7 Hz, 1 H, H-6), 1.92–1.82 (m, 2 H, H-7 and H-8α), 1.31 (ddt, $J$ = 13.5, 11.1 and 3.4 Hz, 1 H, H-8β), 1.67 (dt, $J$ = 13.5 and 3.6 Hz, 1 H, H-9α), 1.98 (dt, $J$ = 13.5 and 3.4 Hz, 1 H, H-9β), 2.17 (dq, $J$ = 12.0 and 6.9 Hz, 1 H, H-11), 1.21 (d, $J$ = 6.9 Hz, 3 H, H-13), 1.04 (s, 3 H, H-14), 1.79 (br s, 3 H, H-15); TMS 0.13 and 0.10 (s, each 9 H) $^{13}$C NMR ($CDCl_3$, 100 MHz) δ: 55.8 (C-1), 36.1 (C-2), 144.5, (C-4), 131.0 (C-5), 82.2 (C-6), 49.3 (C-7), 25.8 (C-8), 45.2 (C-9), 78.2 (C-10), 41.6 (C-11), 178.3 (C-12), 12.5 (C-13), 22.2 (C-14), 12.5 (C-15); TMS 2.7.

*Preparation of 3β,10α-bistrimethylsilyloxy-11β-hydroxy-1αH,6βH-guai-4-enolide (***9a***) and of 3β,10α-bistrimethylsilyloxy-11α-hydroxy-1αH,6βH-guai-4-enolide (***9c***).* To a solution of sodium bis(trimethylsilyl)amide (3 mmol) in tetrahydrofuran (15 ml) a solution of **8a** (790 mg, 1.9 mmol) in tetrahydrofuran (20 ml) was added under argon at −78°C over 5 min. The mixture was stirred for 30 min at −78°C, for 30 min at room temperature and for an additional 30 min at −78°C. Over a period of 5 min a solution of 2-phenylsulfonyl-3-phenyloxaziridine (520 mg, 2.0 mmol) in dry tetrahydrofuran was added to the reaction mixture. The reaction was stopped after 15 min by addition of 12 ml of a saturated aqueous solution of ammonium chloride. The reaction mixture was concentrated to 12 ml, and the residue was extracted with ether (20 ml). The ether phase was washed with water (12 ml) and brine (20 ml), dried ($MgSO_4$) and concentrated in vacuum. Column chromatography of the residue [eluent: toluene–EtOAc (9:1)] afforded **9a** (464 mg) and a mixture of **9a** and **9c** (73 mg). Repeated chromatography of the mixture of **9a** and **9c** afforded **9a** (a total of 498 mg, 62%) and **9c** (13 mg 2%). An analytical sample of **9a** was recrystallized to give colourless crystals, m.p. 127–129°C. MS of **9a**: 427.2 (36, $M+1$), 337.1 (100, $M+1$-$C_3H_9SiOH$) Anal. for $C_{21}$ $H_{38}$ $O_5$ $Si_2$, C,H. MS of **9c**: 355.2 (42, $M+1$-$C_3H_4O_3$), 265.1 (100, $M+1$-$C_3H_4O_3$-$C_3H_9SiOH$). NMR of **9a** $^1$H NMR ($CDCl_3$, 400 MHz) δ: 2.87 (br s, 1 H, H-1), 2.29 (dt, $J$ = 14.0 and 8.0 Hz, 1H, H-2α), 1.63 (m, 1 H, H-2β), 4.43 (br t, $J$ = 6.5 Hz, 1 H, H-3), 5.07 (br dq, J = 10.8 and 6.0 Hz, 1 H, H-6), 1.82 (m, 2 H, H-7 and H-8α), 1.51 (ddt, $J$ = 14.2, 10.8 and 3.4 Hz, 1 H, H-8β), 1.63 (m, 1 H, H-9α), 2.03 (dt, $J$ = 13.2 and 2.4 Hz, 1 H, H-9β), 1.41 (s, 3 H, H-13), 1.04 (s, 3 H, H-14), 1.81 (br s, 3 H, H-15); TMS 0.15 and 0.11 (s, each 9 H) $^{13}$C NMR ($CDCl_3$, 100 MHz) δ: 55.6 (C-1), 35.9 (C-2), 77.3 (C-3) 144.6 (C-4), 130.8 (C-5), 81.2 (C-6), 50.9 (C-7), 21.6 (C-8), 44.8 (C-9), 78.7 (C-10), 73.4 (C-11), 178.2 (C-12), 20.3 (C-13), 22.0 (C-14), 12.5 (C-15); TMS 2.6. NMR of **9c** $^1$H NMR ($CDCl_3$, 400 MHz) δ: 2.92 (br s, 1 H, H-1), 2.31 (m, 1H, H-2α), 1.64 (m, 1 H, H-2β), 4.44 (br t, $J$ = 6.2 Hz, 1 H, H-3), 4.68 (br d, $J$ = 11.4 Hz, 1 H, H-6), 2.31 (m, 1 H, H-7) 1.93 (ddt, $J$ = 16.2, 4.0 and 1.0, 1 H, H-8α), 1.26 (m, 1 H, H-8β), 1.71 (dt, $J$ = 13.1 and 4.0, 1 H, H-9α), 2.02 (dt, $J$ = 13.1 and 4.0 Hz, 1 H, H-9β), 1.31 (s, 3 H, H-13), 1.02 (s, 3 H, H-14), 1.80 (br s, 3 H, H-15); TMS 0.15 and 0.11 (s, each 9 H). $^{13}$C NMR ($CDCl_3$, 100 MHz) δ: 55.1 (C-1), 35.8 (C-2), 76.6 (C-3) 145.1 (C-4), 130.9 (C-5), 79.6 (C-6), 50.7 (C-7), 21.4 (C-8), 44.6 (C-9), 77.7 (C-10), 74.7 (C-11), 179.4 (C-12), 18.2 (C-13), 22.2 (C-14), 12.3 (C-15); TMS 2.6.

*Preparation of 3β,10α-bistrimethylsilyloxy-11β-methoxyethoxymethoxy-1αH,6βH-guai-4-enolide (***10a***).* To a solution of sodium bis(trimethylsilyl)amide (0.94 mmol) in tetrahydrofuran kept under argon was at 0°C added a solution of **9a** (200 mg, 0.47 mmol) in tetrahydrofuran (3 ml). After stirring of the solution for 20 min β-methoxyethoxymethyl chloride (100 µl, 0.65 mmol) was added and the solution was left for 5 h at 0°C. The reaction was stopped by adding 0.4 M aqueous sodium carbonate (7 ml), and the mixture was concentrated to half volume in vacuum. The residue was extracted with ether (10 ml), and the organic phase was washed with water (10 ml), brine (10 ml), dried ($MgSO_4$) and concentrated in vacuum. Compound **10a** (119 mg, 49%) was isolated from the residue by column chromatography [eluent: toluene–MeOH (25:1)]. $^1$H NMR ($CDCl_3$, 400 MHz) δ: 2.86 (br t, $J$ = 6.5 Hz, 1 H, H-1), 2.29 (dt, $J$ = 14.1 and 8.0 Hz, 1H, H-2α), 1.75–1.5 (m, 3 H, H-2β, H-8β and H-9α), 4.42 (br t, $J$ = 5.9 Hz, 1 H, H-3), 5.08 (br dd, $J$ = 10.7 and 1.6 Hz, 1 H, H-6), 2.1–1–8 (m, 3 H, H-7, H-8α and H-9β), 1.40 (s, 3 H, H-13), 1.02 (s, 3 H, H-14), 1.81 (br s, 3 H, H-15); TMS 0.13 and 0.11 (s, each 9 H); MEM 4.93 (d, $J$ = 7.1 Hz, 1 H, $OCH_aO$) 4.78 (d, $J$ = 7.1, 1 H, $OCH_bO$), 3.8–3.6 (m, 2 H, $OCH_2$), 3.6–3.5 (m, 2 H,

$OCH_2$), 3.39 (s, 3 H, $CH_3$). $^{13}C$ NMR ($CDCl_3$, 100 MHz) δ: 55.1 (C-1), 35.8 (C-2), 77.6 (C-3, C-10 or C-11) 144.9 (C-4), 130.9 (C-5), 80.2 (C-6), 52.7 (C-7), 20.4 (C-8), 44.8 (C-9), 77.2 (C-10, C-3 or C-11), 78.2 (C-11, C-3 or C-10), 174.9 (C-12), 17.7 (C-13), 21.9 (C-14), 12.5 (C-15); TMS 2.5; MEM 91.0 ($OCH_2O$), 71.5 ($CH_2O$), 67.4 ($CH_2O$), 58.9 ($CH_3O$).

*Preparation of 3β,10α-dihydroxy-11β-methoxyethoxymethoxy-1αH,6βH-guai-4-enolide (***11a***).* A solution of **10a** (118 mg, 0.23 mmol) and glacial acetic acid (200 µl) in methanol (10 ml) was heated to reflux and left without heating for 1 h. The solution was concentrated in vacuum and **11a** (79 mg, 93%) was isolated from the residue by column chromatography (eluent: EtOAc). MS: 371.2 (100, $M+1$). $^1H$ NMR ($CDCl_3$, 200 MHz) δ: 2.91 (br, t, $J=6.4$ Hz, 1 H, H-1) 2.49 (dt, $J=14.0$ and 8.0 Hz, 1H, H-2α), 1.75–1.5 (m, 3 H, H-2β, H-8β and H-9β), 4.53 (br t, $J=6.6$ Hz, 1 H, H-3), 5.13 (br dd, $J=10.7$ and 1.6 Hz, 1 H, H-6), 2.1-1.8 (m, 3 H, H-7, H-8α and H-9α), 1.40 (s, H, H-13), 1.05 (s, 3 H, H-14), 1.89 (br s, 3 H, H-15); MEM 4.93 (d, $J=7.2$ Hz, 1 H, $OCH_aO$) 4.78 (d, $J=7.2$, 1 H, $OCH_bO$), 3.8–3.6 (m, 2 H, $OCH_2$), 3.6–3.5 (m, 2H, $OCH_2$), 3.41 (s, 3 H, $CH_3$). $^{13}C$ NMR ($CDCl_3$, 50 MHz) δ: 54.7 (C-1), 34.7 (C-2), 144.7 (C-4), 131.9 (C-5), 80.0 (C-6), 52.7 (C-7), 20.1 (C-8), 44.7 (C-9), 74.7 (C-10), 174.9 (C-12), 17.8 (C-13), 21.6 (C-14), 12.5 (C-15); MEM 91.1 ($OCH_2O$), 71.6 ($CH_2O$), 67.6 ($CH_2O$), 59.1 ($CH_3O$).

*Preparation of 3β-tigloyloxy-10α-hydroxy-11β-methoxyethoxymethoxy-1αH,6βH-guai-4-enolide (***12a***).* A solution of **11a** (75 mg, 0.20 mmol), 4-dimethylaminopyridine (80 mg, 0.66 mmol) and tiglic anhydride (250 µl, 1.4 mmol) in dry dichloromethane (6 ml) was left for 5 h at room temperature and concentrated in vacuum. Compound **12a** (77 mg, 84%) was isolated by column chromatography [eluent: toluene–EtOAc (1:1)]. $^1H$ NMR ($CDCl_3$, 200 MHz) δ: 2.99 (br s, 1 H, H-1), 2.58 (dt, $J=16.0$ and 7.0 Hz, 1H, H-2α), 2.1–1.6 (m, 6 H, H-2β, H-7, H-8α, H-8β, H-9α and H-9β), 5.53 (br s, 1 H, H-3), 5.13 (br dd, $J=10.6$ and 1.6 Hz, 1 H, H-6), 1.46 (s, 3 H, H-13), 1.02 (s, 3 H, H-14), 1.81 (br, s 3 H, H-15); MEM 4.95 (d, $J=7.1$ Hz, 1 H, $OCH_aO$) 4.81 (d, $J=7.1$, 1 H, $OCH_bO$), 3.8–3.6 (m, 2 H, $OCH_2$), 3.6–3.5 (m, 2 H, $OCH_2$), 3.29 (s, 3 H, $CH_3$); tigloyl: 6.87 (qq, $J=7.2$ and 1.4 Hz, 1 H, H-β), 1.84 (br d, $J=1.4$ Hz, 3 H, α-Me), 1.78 (br d, $J=7.2$ Hz, 3 H, H-γ). $^{13}C$ NMR ($CDCl_3$, 50 MHz) δ: 55.3 (C-1), 31.9 (C-2), 79.9 (C-3 or C-6), 141.7 (C-4), 134.3 (C-5), 79.6 (C-6 or C-3), 52.6 (C-7), 20.4 (C-8), 44.7 (C-9), 74.6 (C-10), 77.7 (C-11), 174.8 (C-12), 17.8 (C-13), 21.4 (C-14), 12.1 (C-15); MEM 91.1 ($OCH_2O$), 71.6 ($CH_2O$), 67.6 ($CH_2O$), 59.1 ($CH_3O$); tigloyl 167.8 (C = O), 128.7 (C-α) 137.3 (C-β), 14.4 (Me), 12.8 (Me).

*Preparation of 3β-tigloyloxy-10α-acetoxy-11β-methoxyethoxymethoxy-1αH,6βH-guai-4-enolide (***13a***).* A solution of **12a** (77 mg, 0.17 mmol), 4-dimethylaminopyridine (80 mg, 0.66 mmol) and acetic anhydride (600 µl, 5.9 mmol) in dry dichloromethane (3 ml) was left for 5 h at room temperature and concentrated in vacuum. Compound **13a** (70 mg, 83%) was isolated by column chromatography [eluent: toluene–EtOAc (5:1)]. MS: 495.1 (100, $M+1$). $^1H$ NMR ($CDCl_3$, 400 MHz) δ: 3.84 (br s, 1 H, H-1), 2.52 (dt, $J=14.9$ and 8.4 Hz, 1H, H-2α), 1.65 (m, 1 H, H-2β), 5.53 (br s, 1 H, H-3), 5.12 (br dq, $J=10.7$ and 1.4 Hz, 1 H, H-6), 2.01 (br t, $J=10.6$ Hz, 1 H, H-7), 1.88 (m, 1 H, H-8α), 1.59 (m, 1 H, H-8β), 2.41 (dt, $J=13.6$ and 4.2 Hz, 1H, H-9α), 2.19 (dt, $J=13.6$ and 3.8 Hz, 1 H, H-9β), 1.44 (s, 3 H, H-13), 1.17 (s, 3 H, H-14), 1.85 (br s, 3 H, H-15); MEM 4.93 (d, $J=7.1$ Hz, 1 H, $OCH_aO$) 4.79 (d, $J=7.1$, 1 H, $OCH_bO$), 3.75–3.6 (m, 2 H, $OCH_2$), 3.7–3.5 (m, 2 H, $OCH_2$), 3.39 (s, 3 H, $CH_3$); tigloyl: 6.87 (qq, $J=7.1$ and 1.4 Hz, 1 H, H-β), 1.85 (br d, $J=1.4$ Hz, 3 H, α-Me), 1.81 (br d, $J=7.1$ Hz, 3 H, H-γ); acetyl 1.96 (s, 3 H). $^{13}C$ NMR ($CDCl_3$, 100 MHz) δ: 51.9 (C-1), 31.9 (C-2), 79.9 (C-3), 142.0 (C-4), 133.6 (C-5), 79.3 (C-6), 52.4 (C-7), 20.0 (C-8), 37.7 (C-9), 86.5 (C-10), 77.7 (C-11), 174.7 (C-12), 17.8 (C-13), 20.0 (C-14), 12.1 (C-15); MEM 91.2 ($OCH_2O$) 71.7 ($CH_2O$), 67.6 ($CH_2O$), 59.1 ($CH_3O$); tigloyl 167.8 (C = 0), 128.7 (C-α) 137.4 (C-β), 14.4 (Me), 12.9 (Me); acetyl 170.3 (C = 0), 22.5 (C-α).

*Preparation of 3β-tigloyloxy-10α-acetoxy-11β-hydroxy-1-αH,6βH-guai-4-enolide (***14a***)* and 3-tert-*butoxy-10α-acetoxy-11β-hydroxy-1αH,6βH-guai-4-enolide (***15***).* A solution of **13a** (70 mg, 0.15 mmol) and pyridinium *p*-toluene sulfonate (350 mg,) in dry *tert*-butyl alcohol (4 ml) was refluxed under argon for 4 h and freeze-dried. A mixture (45 mg) of **14a** and **15** in a ratio of 3:1 as estimated by $^1H$ NMR spectroscopy was obtained by column chromatography [eluent: toluene–methanol (25:1)]. The two compounds were separated by HPLC [eluent: acetonitrile–water (2:3), $t_r$(**14a**) 83 min, $t_r$(**15**) 71 min] to give **14a** (9 mg) and **15** (3 mg). $^1H$ NMR of **15** ($CDCl_3$, 400 MHz) δ: 3.77 (br s, 1 H, H-1), 2.24 (dt, $J=13.8$ and 8.0 Hz, 1 H, H-2α), 1.57 (m, 1 H, H-2β), 4.33 (br t, $J=6.0$, 1 H, H-3), 5.07 (br dq, $J=10.8$ and 1.4 Hz, 1 H, H-6), 1.96 (m, 1 H, H-7), 1.86 (m, 1 H, H-8α), 1.57 (m, 1 H, H-8β), 2.47 (dt, $J=13.2$ and 4.1 Hz, 1H, H-9α), 2.11 (dt, $J=13.2$ and 3.7 Hz, 1 H, H-9β), 1.42 (s, 3 H, H-13), 1.17 (s, 3 H, H-14), 1.85 (br s, 3 H, H-15); *tert*-butyl 1.22 (s, 9 H); acetyl 2.02 (s, 3 H).

*Preparation of 3β-tigloyloxy-10α-acetoxy-11β-hydroxy-1αH,6βH-guai-4-enolide (***14a***).* A solution of **13a** (13 mg, 0.03 mmol) and pyridinium *p*-toluenesulfonate (25 mg) in dry DMF (2 ml) was heated to 95°C under argon for 1 h, added water (5 ml) and freeze dried. A mixture of **13a** and **14a** was isolated from the residue by column chromatography [eluent: toluene–methanol (25:1)]. The two compounds were separated by reversed-phase chromatography [eluent: methanol–water (2:1)] to give **14a** (5 mg, 47%). MS: 407.2 ($M+1$). MS/MS: 389.3 (100, $M+1$-$H_2O$), 347.3 (36, $M+1$-$CH_3COOH$), 315.3

(66, $M$ + 1-OH-$CH_3$-$CH_3COOH$), 265.2 (11, $M$ + 1-$CH_3COOH$-$C_4H_6CO$), 247.3 (22, $M$ + 1-$CH_3COOH$-$C_4H_7COOH$) 219.3 (12, $M$ + 1-$C_4H_7COOH$-$C_3H_4O_3$), 159.0 ($M$ + 1-$C_4H_7COOH$-$CH_3COOH$-$C_3H_4O_3$). Exact mass calc. For $C_{22}$ $H_{31}$ $O_7$: 407.2069. Found: 407.2095. $^1$H NMR ($CDCl_3$, 400 MHz) δ: 3.87 (br s, 1 H, H-1), 2.53 (dt, $J$ = 14.9 and 8.4 Hz, 1 H, H-2α), 1.63 (dt, $J$ = 14.9 and 5.2 Hz, 1 H, H-2β), 5.55 (br s, 1 H, H-3), 5.09 (br dq, $J$ = 10.6 and 1.4 Hz, 1 H, H-6), 2.00 (m, 1 H, H-7), 1.88 (m, 1 H, H-8α), 1.58 (ddt, $J$ = 13.8, 10.8 and 3.8 Hz, 1 H, H-8β), 2.44 (dt, $J$ = 13.6 and 4.1 Hz, 1H, H-9α), 2.18 (dt, $J$ = 13.6 and 3.8 Hz, 1 H, H-9β), 1.44 (s, 3 H, H-13), 1.18 (s, 3 H, H-14), 1.86 (br s, 3 H, H-15); tigloyl: 6.88 (qq, $J$ = 7.1 and 1.4 Hz, 1 H, H-β), 1.86 (br d, $J$ = 1.4 Hz, 3 H, α-Me), 1.81 (dq, $J$ = 7.1 and 1.1 Hz, 3 H, H-γ); acetyl 1.97 (s, 3 H). $^{13}$C NMR ($CDCl_3$, 100 MHz) δ: 50.6 (C-1), 32.0 (C-2), 79.9 (C-3), 142.1 (C-4), 133.4 (C-5), 79.9 (C-6), 52.7 (C-7), 20.0 (C-8), 37.6 (C-9), 86.5 (C-10), 74.2 (C-11), 177.9 (C-12), 21.7 (C-13), 19.9 (C-14), 12.1 (C-15); tigloyl 168.8 (C = O), 128.9 (C-α) 137.6 (C-β), 14.2 (Me), 12.9 (Me); acetyl 171.6 (C = O), 22.3 (C-α).

*Preparation of 3β,10α-dihydroxy-1*α*H,6*β*H,11*α*H-guai-4-enolide (***5b***) and 3β,6β,10α,12-tetrahydroxy-1*α*H-guai-4-en (***7***).* To a solution of 3-keto-10α-hydroxy-1α*H*,6α*H*,11α*H*-guai-4-enolide (**4b**, 6.5 g, 24 mmol), prepared by photolysis of 6-*epi*-α-santonin, in methanol (200 ml) was added sodium borohydride (3.0 g, 78 mmol), and the solution was stirred at 0 °C. The reaction was stopped after 20 min by addition of acetone (60 ml) and water (100 ml). The mixture was concentrated to half volume in vacuum, and the residue was saturated with NaCl and extracted with EtOAc. The EtOAc phase was dried ($MgSO_4$), concentrated in vacuum, and the constitutents of the residue were separated by column chromatography [eluent: EtOAc–acetone (7:1)] to give **5b** (1.2 g, 60%) and **7** (1.2 g, 18%). An analytical sample of **5b** was recrystallized (EtOAc–hexane) to give colourless crystals, m.p. 73–75 °C. Anal. for $C_{15}H_{22}O_4$, C,H. NMR data of **5b**: $^1$H NMR ($CDCl_3$, 400 MHz) δ: 2.63 (br t, $J$ = 6.3 Hz), 2.38 (dt, $J$ = 13.7 and 6.3 Hz, 1H, H-2α), 1.7–1.5 (m, 4 H, H-2β, H-8α, H-8β and H-9α), 4.49 (br t, $J$ = 6.3 Hz, 1 H, H-3), 5.50 (br d, $J$ = 8.0, 1 H, H-6), 2.43 (m, 1 H, H-7), 1.92 (m, 1 H, H-9β), 2.17 (p, $J$ = 7.3 Hz, 1 H, H-11), 1.28 (d, $J$ = 7.3 Hz, 3 H, H-13), 1.18 (s, 3 H, H-14), 1.81 (br s, 3 H, H-15). $^{13}$C NMR ($CDCl_3$, 200 MHz) δ: 56.4 (C-1), 35.8 (C-2), 79.0 (C-3), 140.4, (C-4), 133.7 (C-5), 79.7 (C-6), 45.7 (C-7), 27.1 (C-8), 39.9 (C-9), 73.8 (C-10), 42.6 (C-11), 179.7 (C-12), 14.3 (C-13 or C-15), 26.3 (C-14), 12.3 (C-15 or C-13). NMR data of **7**: $^1$H NMR (DMSO-$d_6$, 400 MHz) δ: 2.55 (m, 1 H, H-1), 2.13 (dt, $J$ = 13.3 and 7.7 Hz, 1H, H-2α), 1.9–1.3 (m, 6 H, H-2β, H-7, H-8α, H-9α, H-9β and H-11), 4.19 (br q, $J$ = 6.9 Hz, 1 H, H-3), 4.36 (br d, $J$ = 5.0, 1 H, H-6), 1.13 (m, 1H, H-8β), 3.29 (m, 1 H, H-12), 0.88 (d, $J$ = 7.0 Hz, 3 H, H-13), 1.03 (s, 3 H, H-14), 1.61 (s, 1 H, H-15). $^{13}$C NMR (DMSO-$d_6$, 100 MHz) δ: 55.6 (C-1), 35.5 (C-2), 76.0 (C-3), 141.1 (C-4), 139.8 (C-5), 66.9 (C-6), 43.2 (C-7), 20.3 (C-8), 46.7 (C-9), 72.9 (C-10), 41.1 (C-11), 63.6 (C-12), 14.7 (C-13 or C-15), 20.8 (C-14), 11.7 (C-15 or C-13).

*Preparation of 3β,10α-bistrimethylsilyloxy-1*α*H,6*α*H,11*α*H-guai-4-enolide (***8b***).* Compound **5b** (3.0 g, 11 mmol) was silylated as described above for preparation of **8a** using lithium sulfide (2 g, 43 mmol) and chlorotrimethylsilane (15 ml) dissolved in dry acetonitrile (20 ml) to give after flash chromatography over silica gel [eluent: toluene–EtOAc (25:1)] **8b** (3.6 g, 80%) as a viscous colourless oil, which quickly became yellowish. Owing to instability the product was quickly converted into **9b**. $^1$H NMR of **8b** ($CDCl_3$, 200 MHz) δ: 2.61 (br t, $J$ = 7.3 Hz), 2.15 (m, 1H, H-2α), 1.70 (m, 1 H, H-2β), 4.39 (br t, $J$ = 6.7 Hz, 1 H, H-3), 5.55 (br d, $J$ = 8.0 Hz, 1 H, H-6), 2.44 (m, 1 H, H-7) 1.70 (m, 2 H, H-8α and H-9α), 1.43 (m, 1 H, H-8β), 1.85 (m, 1 H, H-9β), 2.15 (m, 1 H, H-11), 1.27 (d, $J$ = 6.7 Hz, 3 H, H-13), 1.18 (s, 3 H, H-14), 1.69 (br s, 3 H, H-15); TMS 0.15 (s, 9 H) $^{13}$C NMR ($CDCl_3$, 100 MHz) δ: 56.5 (C-1), 37.1 (C-2), 78.3 (C-3), 139.1 (C-4), 132.9 (C-5), 79.9 (C-6), 45.2 (C-7), 27.2 (C-8 or C-14), 39.0 (C-9), 77.0 (C-10), 42.0 (C-11), 179.6 (C-12), 14.4 (C-13 or C-15), 27.0 (C-14 or C-8), 11.9 (C-15 or C-13); TMS 2.5.

*Preparation of 3β,10α-bistrimethylsilyloxy-11α-hydroxy-1*α*H,6*α*H-guai-4-enolide (***9b***).* Compound **8b** (2.3 g, 5.6 mmol) was hydroxylated as described above for preparation of **9a** using sodium bis(trimethylsilyl)amide (10 mmol) and 2-(phenylsulfonyl)-3-phenyloxaziridine (1.4 g, 5.4 mmol) dissolved in tetrahydrofuran (115 ml) to give **9b** (1.7 g, 71%) after column chromatography over silica gel [eluent: toluene–EtOAc (9:1)]. $^1$H NMR ($CDCl_3$, 400 MHz) δ: 2.63 (m, 1 H, H-1), 2.19 (dt, $J$ = 13.4 and 7.7 Hz, 1H, H-2α), 1.56 (ddd, $J$ = 13.4, 6.4 and 4.8 Hz, 1 H, H-2β), 4.35 (br t, $J$ = 6.0 Hz, 1 H, H-3), 5.65 (br d, $J$ = 7.2 Hz, 1 H, H-6), 2.63 (m, 1 H, H-7), 1.62 (m, 1 H, H-8α), 1.46 (m, 1 H, H-8β), 1.68 (m, 1 H, H-9α), 1.95 (ddd, $J$ = 14.4, 5.3 and 4.1 Hz, 1 H, H-9β), 1.37 (s, 3 H, H-13), 1.17 (s, 3 H, H-14), 1.75 (br s, 3 H, H-15); TMS 0.16 and 0.13 (s, each 9 H) $^{13}$C NMR ($CDCl_3$, 100 MHz) δ:57.3 (C-1 or C-7), 36.5 (C-2), 78.5 (C-3) 142.1 (C-4), 131.9 (C-5), 79.5 (C-6), 48.4 (C-7 or C-1), 21.5 (C-8), 41.3 (C-9), 77.2 (C-10), 76.0 (C-11), 178.7 (C-12), 21.0 (C-13), 24.9 (C-14), 12.8 (C-15); TMS 2.5.

*Preparation of 3β,10α-bistrimethylsilyloxy-11α-methoxyethoxymethoxy-1*α*H,6*α*H-guai-4-enolide (***10b***).* Compound **9b** was methoxyethoxylated as described above for preparation of compound **10a** using **9b** (740 mg, 1.74 mmol), sodium bis(trimethylsilyl)amide (3.5 mmol) and β-methoxyethoxymethyl chloride (400 µl, 3.2 mmol) dissolved in tetrahydrofuran (6 ml). A mixture of starting material (**9b**) and **10b** (800 mg) in the ratio 1:11 was obtained by column chromatography [eluent: toluene–MeOH (25:1)]. $^1$H NMR ($CDCl_3$, 400 MHz) δ: 2.63 (m, 1 H, H-1), 2.18

(dt, $J$ = 14.0 and 8.2 Hz, 1H, H-2α), 1.75–1.55 (m, 3 H, H-2β, H-8α and H-9α), 4.35 (br s, 1 H, H-3), 5.59 (br d, $J$ = 4.9 Hz, 1 H, H-6), 2.61 (m, 1 H, H-7), 1.31 (m, 1 H, H-8β), 1.96 (ddd, $J$ = 13.8, 5.9 and 2.9, 1 H, H-9β), 1.37 (s, 3 H, H-13), 1.14 (s, 3 H, H-14), 17.8 (br s, 3 H, H-15); TMS 0.15 and 0.11 (s, each 9 H); MEM 4.93 (d, $J$ = 7.1 Hz, 1 H, $OCH_aO$) 4.85 (d, $J$ = 7.1, 1 H, $OCH_bO$), 3.8–3.6 (m, 2 H, $OCH_2$), 3.6–3.5 (m, 2 H, $OCH_2$), 3.39 (s, 3 H, $CH_3$). $^{13}C$ NMR ($CDCl_3$, 100 MHz) δ: 57.6 (C-1), 36.1 (C-2), 78.7 (C-3 or C-6) 144.4 (C-4), 131.6 (C-5), 78.5 (C-6 or C-3), 49.3 (C-7), 21.2 (C-8), 43.4 (C-9), 77.5 (C-10), 80.9 (C-11), 175.6 (C-12), 17.0 (C-13), 23.5 (C-14), 13.2 (C-15); TMS 2.7; MEM 91.2 ($OCH_2O$), 71.6 ($CH_2O$), 67.7 ($CH_2O$), 59.1 ($CH_3O$).

*Preparation of 3β,10α-dihydroxy-11α-methoxyethoxymethoxy-1αH,6αH-guai-4-enolide (***11b***).* Compound **10b** (800 mg, 1.60 mmol) was desilylated as described above for preparation of compound **11a** by treatment with glacial acetic acid (1 ml) in MeOH (8 ml) to give **11b** (480 mg, 83%) after column chromatography (eluent: EtOAc). MS: 371.2 (95, $M$ + 1), 353.1 (100, $M$ + 1-$H_2O$). $^1H$ NMR ($CDCl_3$, 200 MHz) δ: 2.69 (br s, 1 H, H-1) 2.36 (dt, $J$ = 14.6 and 8.4 Hz, 1H, H-2α), 1.75 (dt, $J$ = 14.6 and 3.8 Hz, 1 H, H-2β), 4.44 (br d, $J$ = 5.9 Hz, 1 H, H-3), 5.62 (br d, $J$ = 4.9 Hz, 1 H, H-6), 2.57 (ddd, $J$ = 12.8, 4.9 and 3.0, 1 H, H-7), 1.62 (m, 2 H, H-8α and H-9α), 1.23 (m, 1 H, H-8β), 1.95 (m, 1 H, H-9β), 1.38 (s, 3 H, H-13), 1.10 (s, 3 H, H-14), 1.86 (br s, 3 H, H-15); MEM 4.90 (d, $J$ = 7.4 Hz, 1 H, $OCH_aO$) 4.83 (d, $J$ = 7.4, 1 H, $OCH_bO$), 3.75–3.65 (m, 2 H, $OCH_2$), 3.6–3.5 (m, 2 H, $OCH_2$), 3.35 (s, 3 H, $CH_3$). $^{13}C$ NMR ($CDCl_3$, 100 MHz) δ: 56.8 (C-1), 34.8 (C-2) 78.8 (C-3 or C-6) 145.2 (C-4), 132.5 (C-5), 78.2 (C-6 or C-3), 49.8 (C-7), 21.0 (C-8), 43.2 (C-9), 73.8 (C-10), 81.1 (C-11), 175.4 (C-12), 16.7 (C-13), 22.7 (C-14), 13.4 (C-15); MEM 91.3 ($OCH_2O$), 71.6 ($CH_2O$), 67.7 ($CH_2O$), 59.0 ($CH_3O$).

*Preparation of 3β-tigloyloxy-10α-hydroxy-11α-methoxyethoxymethoxy-1αH-6αH-guai-4-enolide (***12b***).* Compound **11b** (420 mg, 1.1 mmol), 4-dimethylaminopyridine (250 mg, 2.0 mmol) and tiglic anhydride (800 µl, 4.4 mmol) was dissolved in dry dichloromethane (15 ml) and left for 5 h. Compound **12b** (417 mg, 81%) was isolated by column chromatography [eluent: toluene–EtOAc (1:1)] of the residue obtained by concentration of the reaction mixture in vacuum. $^1H$ NMR ($CDCl_3$, 400 MHz) δ: 2.77 (br d, 1 H, H-1), 2.45 (dt, $J$ = 15.6 and 8.7 Hz, 1 H, H-2α), 1.92 (dt, $J$ = 15.6 and 2.5 Hz, 1 H, H-2β), 5.49 (br d, $J$ = 8.7 Hz, 1 H, H-3), 5.64 (br s, 1 H, H-6), 2.56 (ddd, $J$ = 12.7, 4.6 and 2.7, 1 H, H-7), 1.65 (m, 2 H, H-8α and H-9α), 1.27 (m, 1 H, H-8β), 2.00 (m, 1 H, H-9β), 1.41 (s, 3 H, H-13), 1.00 (s, 3 H, H-14), 1.85 (br, s, 3 H, H-15); MEM 4.92 (d, $J$ = 7.4 Hz, 1 H, $OCH_aO$) 4.87 (d, $J$ = 7.4, 1 H, $OCH_bO$), 3.8–3.5 (m, 2 H, $OCH_2$), 3.6–3.5 (m, 2 H, $OCH_2$), 3.37 (s, 3 H, $CH_3$); tigloyl: 6.85 (qq, $J$ = 7.2 and 1.4 Hz, 1 H, H-β), 1.84 (br d, $J$ = 1.4 Hz, 3 H, α-Me), 1.79 (br d, $J$ = 7.2 Hz, 3 H, H-γ). $^{13}C$ NMR ($CDCl_3$, 100 MHz) δ: 57.2 (C-1), 32.1 (C-2), 80.9 (C-3) 142.1 (C-4), 135.0 (C-5), 78.2 (C-6), 50.6 (C-7), 21.0 (C-8), 43.9 (C-9), 74.4 (C-10), 81.0 (C-11), 175.1 (C-12), 16.5 (C-13), 21.9 (C-14), 12.1 (C-15); MEM 91.2 ($OCH_2O$), 71.6 ($CH_2O$), 67.7 ($CH_2O$), 59.1 ($CH_3O$); tigloyl 168.0 (C = O), 128.7 (C-α) 137.5 (C-β), 14.4 (Me), 12.1 (Me).

*Preparation of 3β-tigloyloxy-10α-acetoxy-11α-methoxyethoxymethoxy-1αH,6αH-guai-4-enolide (***13b***).* Compound **12b** (380 mg, 0.84 mmol), 4-dimethylaminopyridine (250 mg, 2.1 mmol) and acetic anhydride (1 ml) was dissolved in dichloromethane (15 ml) and left for 5 h. The residue after concentration of the reaction mixture in vacuum was purified by column chromatography [eluent: toluene–EtOAc (2:1)] to give **13b** (410 mg, 98%). MS: 495.1 ($M$ + 1). $^1H$ NMR ($CDCl_3$, 400 MHz) δ: 3.58 (br s, 1 H, H-1), 2.44 (br t, $J$ = 15.6 and 8.7 Hz, 1H, H-2α), 1.82 (m, 1 H, H-2β), 5.49 (br d, $J$ = 8.7 Hz, 1 H, H-3), 5.63 (br s, 1 H, H-6), 2.56 (ddd, $J$ = 13.2, 4.3 and 2.7, 1 H, H-7), 1.62 (m, 2 H, H-8α), 1.24 (m, 1 H, H-8β), 2.25 (m, 1 H, H-9α) 2.34 (ddd, $J$ = 13.7, 6.8 and 2.5 Hz, 1 H, H-9β), 1.41 (s, 3 H, H-13), 1.28 (s, 3 H, H-14), 1.86 (br s, 3 H, H-15); MEM 4.92 (d, $J$ = 7.4 Hz, 1 H, $OCH_aO$) 4.87 (d, $J$ = 7.4, 1 H, $OCH_bO$), 3.8–3.65 (m, 2 H, $OCH_2$), 3.6–3.5 (m, 2 H, $OCH_2$), 3.37 (s, 3 H, $CH_3$); tigloyl: 6.85 (qq, $J$ = 7.1 and 1.4 Hz, 1 H, H-β), 1.83 (br d, $J$ = 1.4, 3 H, α-Me), 1.80 (br d, $J$ = 7.1 Hz, 3 H, H-γ); acetyl 1.96 (s, 3 H). $^{13}C$ NMR ($CDCl_3$, 100 MHz) δ: 53.8 (C-1), 31.9 (C-2), 80.9 (C-3) 143.3 (C-4), 134.2 (C-5), 77.7 (C-6), 50.8 (C-7), 20.6 (C-8), 37.6 (C-9), 86.1 (C-10), 81.2 (C-11), 175.0 (C-12), 16.3 (C-13), 19.7 (C-14), 12.1 (C-15); MEM 91.2 ($OCH_2O$), 71.6 ($CH_2O$), 67.8 ($CH_2O$), 59.1 ($CH_3O$); tigloyl 167.8 (C = O), 128.6 (C-α) 137.6 (C-β), 14.4 (Me), 12.9 (Me); acetyl 170.3 (C = O), 22.6 (C-α).

*Preparation of 3β-tigloyloxy-10α-acetoxy-11α-hydroxy-1αH,6αH-guai-4-enolide (***14b***).* Compound **13b** (100 mg, 0.20 mmol) was demasked as described above for preparation of **14a** using pyridinium *p*-toluene sulfonate (500 mg) in DMF (5 ml) to give **14b** (42 mg, 51%) after column chromatography [eluent: toluene–MeOH (25:1)]. MS: 407.2 (32, $M$ + 1), 347 (33, $M$ + 1-$CH_3COOH$), 247.1 (100, $M$ + 1-$CH_3COOH$-$C_4H_7COOH$). $^1H$ NMR ($CDCl_3$, 400 MHz) δ: 3.25 (br d, $J$ = 9.0 Hz, 1 H, H-1), 2.44 (dt, $J$ = 15.5 and 8.7 Hz, 1 H, H-2α), 1.70 (m, 2 H, H-2β and H-8α), 5.49 (br d, $J$ = 8.2 Hz, 1 H, H-3), 5.61 (br d, $J$ = 4.2 Hz, 1 H, H-6), 2.49 (ddd, $J$ = 12.6, 5.1 and 3.3, 1 H, H-7), 1.28 (m, 1H, H-8β), 2.25 (dt, $J$ = 13.6 and 2.1 Hz, 1 H, H-9α), 2.36 (ddd, $J$ = 13.6, 6.8 and 2.2 Hz, 1 H, H-9β), 1.43 (s, 3 H, H-13), 1.31 (s, 3 H, H-14), 1.85 (br s, 3 H, H-15); tigloyl: 6.85 (qq, $J$ = 7.1 and 1.4 Hz, 1 H, H-β), 1.85 (br d, $J$ = 1.4 Hz, 3 H, α-Me), 1.80 (br d, $J$ = 7.1 Hz, 3 H, H-γ); acetyl 1.96 (s, 3 H). $^{13}C$ NMR ($CDCl_3$, 100 MHz) δ: 54.0 (C-1), 32.0 (C-2), 81.1 (C-3) 142.8 (C-4), 134.2 (C-5), 78.3 (C-6), 50.3 (C-7), 20.8 (C-8), 37.1 (C-9), 86.1 (C-10), 76.6 (C-11), 177.1 (C-12), 20.4 (C-13), 19.9 (C-14), 12.1 (C-15); tigloyl 168.8 (C = O),

128.9 (C-α) 137.6 (C-β), 14.2 (Me), 12.9 (Me); acetyl 171.6 (C = O), 22.3 (C-α).

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