Novel Rearrangements of Sesquiterpenoid Panasinsane Derivatives under Acidic Conditions

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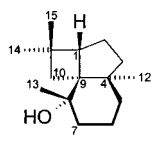
Received February 3, 2001

The sesquiterpenoid panasinsane derivatives **11** and **14**−**16** have been prepared from caryophyllene oxide (**7**). The novel rearrangement reactions of compounds **11** and **14** under TCNE-catalyzed solvolysis conditions and the reactions of compounds **15** and **16** under superacid conditions (HSO_3F/Et_2O, −63 °C) have been investigated. The ginsenol derivative **17** is obtained from compounds **11** and **14** under TCNE-catalyzed conditions. The rearrangement of compounds **15** and **16** under superacid conditions leads to the novel sesquiterpene derivatives (1*S*,4*S*,7*S*,10*S*,11*S*)-3,3,10,11-tetramethyltricyclo[5.3.1.$0^{4,10}$]undecan-1,11-yl sulfate (**19**) and (1*S*,4*S*,5*S*,8*S*)-2,2,4,8-tetramethyl tricyclo[3.3.2.$1^{4,8}$]undecan-11-one (**20**). The influence of the secondary hydroxyl group at C-5 of the panasinsane derivatives on the course of these rearrangements is discussed.

Introduction

Panasinsanol A (**1**), ginsenol (**2**), and α-neoclovene (**3**) are representatives of a group of sesquiterpenoids found in the roots of *Panax ginseng*.[1] They are derived from caryophyllene (**4**) and isocaryophyllene (**5**) through a series of cyclizations and rearrangements that interrelate each class within this group.[2]

Compounds **1**−**3** present a structural similarity to the proposed key intermediate **6**[3] in the biosynthesis[4] of the phytotoxic[5] botryane metabolites produced by *Botrytis cinerea*. In continuation of our previous studies, derivatives with the same skeleta are suitable candidates as inhibitors of the biosynthesis of the botryane metabolites. This is part of a rational approach to the control of the pathogenicity of the phytopathogenic fungus *B. cinerea*. Thus ginsenol (**2**) has been shown to inhibit the growth of *B.* cinerea.[6] The detoxification of compound **2** by the fungus has also been reported.[7] Further research requires the preparation of novel derivatives of ginsenol (**2**) and of the related panasinsane and neoclovane skeleta.



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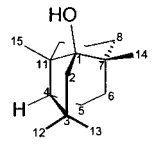

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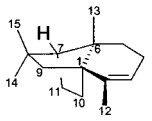

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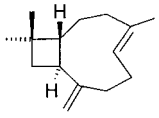

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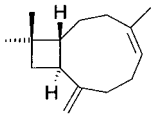

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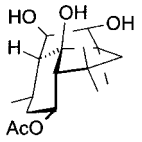

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This paper deals with the synthesis of the panasinsane derivatives **11**, **14**, **15**, and **16** and their rearrangements under TCNE-catalyzed and superacid conditions (HSO_3F/Et_2O, −63 °C). The treatment of compounds **15** and **16** under superacid conditions leads to (1*S*,4*S*,7*S*,10*S*,11*S*)-3,3,10,11-tetramethyltricyclo[5.3.1.$0^{4,10}$]undecan-1,11-yl sulfate (**19**) and (1*S*,4*S*,5*S*,8*S*)-2,2,4,8-tetramethyl tricyclo-[3.3.2.$1^{4,8}$]undecan-11-one (**20**), which possesses novel sesquiterpenoid skeleta.

Results and Discussion

Epoxides **11** and **14** and alcohols **15** and **16** were prepared from caryophyllene oxide (**7**). Treatment of compound **7**, dissolved in CH_2Cl_2, with ozone at room temperature and workup with Me_2S, gave kobusone[8] (**8**) in 52% yield. When kobusone was refluxed with KOH in MeOH for 3 h, a mixture of the hydroxy norpanasinsanone **9** (60%) and (1*S*,3*S*,5*R*,6*R*,9*R*)-6-hydroxy-6,10,-10-trimethyltricyclo[7.2.0.$0^{3,5}$]undecan-2-one[9] (**10**) (14%) were obtained (Scheme 1).

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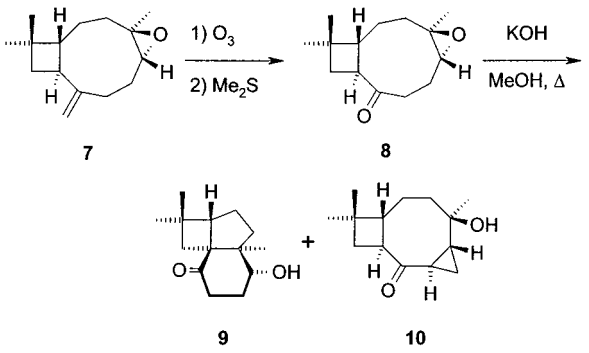
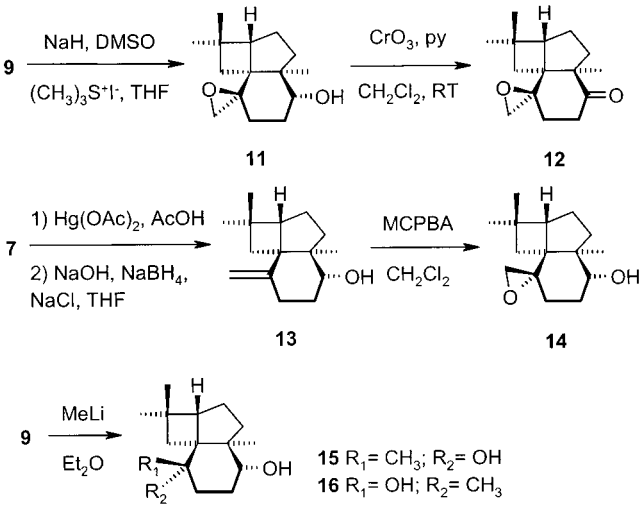
10.1021/jo0155557 CCC: $20.00
Published on Web 05/23/2001

Scheme 1



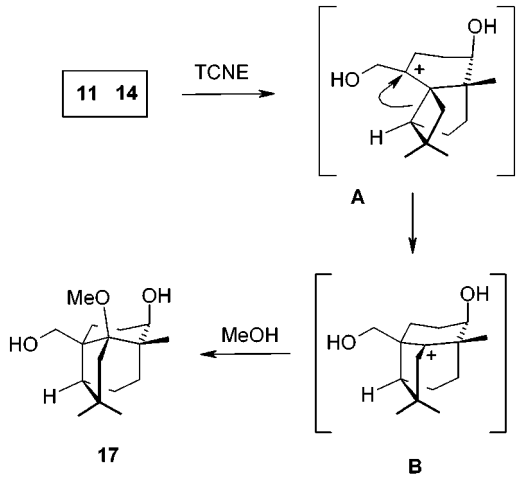
Scheme 2



The Corey−Chaykovsky reaction of ketol **9** with 2 equiv of the sulfur ylide derived from trimethylsulfonium iodide[10] furnished the epoxide **11** in 60% yield. Signals in its ^{1}H NMR spectrum at δ_H 2.48 (d, 1H, J = 4.4 Hz, H-15) and 2.60 (d, 1H, J = 4.4 Hz, H-15′) confirmed the presence of an exocyclic methylene epoxide. Confirmation of the stereochemistry of the epoxide was demonstrated by oxidation of the epoxy alcohol **11** to the crystalline epoxyketone **12** with the Collins reagent.[11] Signals in the ^{1}H NMR spectrum at δ_H 2.57 (d, 1H, J = 4.7 Hz, H-15) and 2.61 (d, 1H, J = 4.7 Hz, H-15′) confirmed the retention of the epoxide. A quaternary resonance at δ_C 213.92 (s, C-5) in the ^{13}C NMR spectrum and absorption at 1704 cm^{-1} in the IR spectrum verified the successful oxidation of the alcohol to the ketone. An X-ray[12] of this product confirmed the stereochemistry of the epoxide as shown in **12** (Scheme 2).

Epoxide **14** was prepared from panasin-8(15)-en-5α-ol (**13**), obtained by oxymercuration of caryophyllene oxide (**7**).[13] Treatment of the olefin **13** with *m*-CPBA gives exclusively compound **14** (74%) (Scheme 2). The ^{1}H NMR of this compound showed signals at δ_H 2.51 (dd, 1H, J = 3.4, 11.7 Hz), 3.08 (d, 1H, J = 4.2 Hz), and 2.58 (d, 1H, J = 4.2 Hz), which corresponded to a proton geminal to an hydroxyl group, and to the protons on an exocyclic epoxy methylene moiety. The structure and stereochemistry of the compound were confirmed by 2D COSY and NOE experiments to be consistent with the representation of the epoxide as **14**.

Scheme 3



Compound **9** was also the starting material for the preparation of alcohols **15** and **16**. Treatment of a solution of compound **9** in dry diethyl ether with 12 equiv of MeLi at room temperature for 24 h yielded two isomeric products, **15** and **16** (Scheme 2). Both of them showed absorption in the IR spectrum corresponding to a hydroxyl group (3425−7 cm^{-1}) and fragmentations in their MS corresponding to the elimination of one and two molecules of water (220 [M − 18] and 202 [M − 18 − 18], respectively). Compound **16** showed signals in its ^{1}H NMR at δ_H 3.40 (dd, 1H, J = 4.6, 11.0 Hz), 2.24 (1H, d, J = 6.6 Hz), and 1.12 (s, 3H), corresponding to H-5β, H-1β, and H-13α, respectively, while compound **15** showed signals at δ_H 3.36 (dd, 1H, J = 4.1, 12.0 Hz), 2.04 (1H, d, J = 8.0 Hz), and 1.41 (s, 3H), corresponding to H-5β, H-1β, and H-13β, respectively. The structure and stereochemistry of these products were confirmed by 2D NMR and NOE experiments. In particular, irradiation of the methyl group at δ_H 1.41 gave a NOE enhancement of 4% and 5% to the signals at δ_H 3.36 and 2.04, respectively, supporting the assigned structure for compound **15**.

The tetracyanoethylene (TCNE)-catalyzed alcoholysis of epoxides leads to ring opening[14] and selective rearrangement products.[15] Therefore, it was a reagent of choice to study the rearrangement of panasinsane derivatives (epoxides **11** and **14**) under mild conditions. The separate treatment of epoxides **11** and **14** with a catalytic amount of TCNE in methanol gave, in both cases, the same product, compound **17** (Scheme 3). Signals in the ^{1}H NMR spectrum at δ_H 3.93 (d, 1H, J = 11.6 Hz, H-15′), 3.69 (d, 1H, J = 11.6 Hz, H-15), 3.42 (dd, 1H, J = 1.8, 4.2 Hz, H-5α), and 3.40 (s, 3H, −OCH_3) revealed the presence of hydroxy methylene, hydroxy methyne, and

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(12) Atomic coordinates for compounds **12**, **17**, and **19** have been deposited with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, U.K.

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methyl ether moieties. Since compound **17** was crystalline, its structure and streochemistry were confirmed by X-ray crystallography.[12] Compound **17** possesses the same carbon skeleton as that of ginsenol (**2**). Cleavage of the epoxide in either **11** or **14** would generate a carbocation at C-8 (**A**), which Parker et al.[16] proposed as a probable intermediate in the rearrangement of caryophyllene (**4**) to neoclovene (**3**). The transposition of the 1,9-σ bond to discharge the C-8 cation leads to the formation of a ginsenane carbocation **B**, which must be sufficiently stable under these conditions not to rearrange to neoclovene but to be trapped by the solvent and to yield compound **17** (Scheme 3).

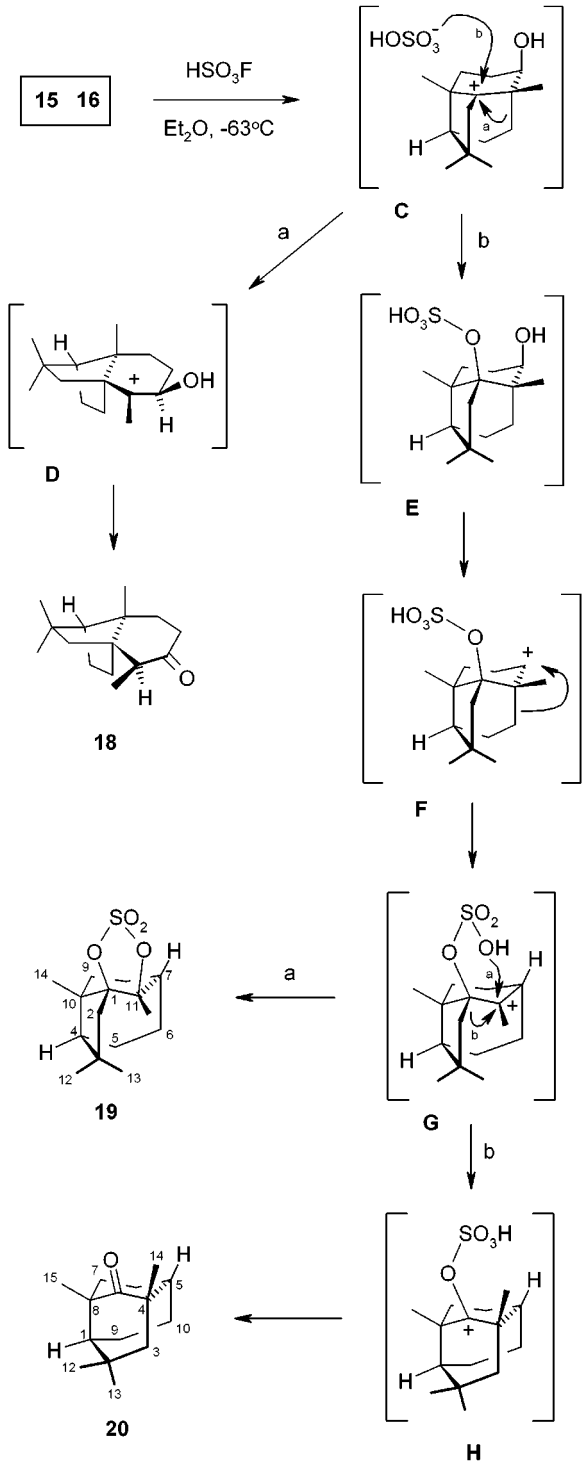
Superacids have provided valuable catalysts for more deep-seated rearrangements of sesquiterpenes.[2] The separate treatment of alcohols **15** and **16** with HSO_3F in dry Et_2O at −63 °C gave, in both cases, a mixture of three compounds, **18** (10%), **19** (6%), and **20** (5%) (Scheme 4). Product **18** showed absorption in its IR spectrum at 1710 cm^{-1} and a resonance in its ^{13}C NMR at δ_C 214.15 (s, C-3). These observations are consistent with the presence of a ketone functionality in the molecule. Study of the 1D and 2D NMR spectra and comparison with literature data[17] support the assignment of the structure of compound **18** as (1*R*,2*R*,6*S*,7*S*)-2,6,8,8-tetramethyltricyclo-[5.2.2.0^{1,6}]undecan-3-one. This compound possesses the same carbon skeleton as neoclovene (**3**).

Compound **19** possessed different spectroscopic characteristics. Absorptions in its IR spectrum at 1365 and 1112 cm^{-1}, two resonances in its ^{13}C NMR at δ_C 103.14 (s, C-1) and 97.82 (s, C-11), a molecular ion of *m*/*z* 300, together with a fragment of *m*/*z* 202 (M − 98), in its mass spectra, suggested the presence of a cyclic sulfate functionality in the molecule. Since compound **19** was crystalline,[12] its structure and stereochemistry were finally established by X-ray crystallography as (1*S*,4*S*,7*S*,10*S*,-11*S*)-3,3,10,11-tetramethyltricyclo[5.3.1.0^{4,10}]undecan-1,-11-yl sulfate. This compound has a novel sesquiterpenoid skeleton.

Compound **20** showed an absorption in its IR spectrum at 1708 cm^{-1} as well as a resonance in its ^{13}C NMR at δ_C 226.66 (s, C-11), consistent with the presence of an alicyclic ketone. 2D NMR experiments as well as NOE experiments led to an assignment of the ^1H NMR spectrum consistent with the stereochemistry shown for compound **20**, (1*S*,4*S*,5*S*,8*S*)-2,2,4,8-tetramethyltricyclo-[3.3.2.1^{4,8}]undecan-11-one. This compound also has a novel sesquiterpenoid skeleton.

The rearrangements shown for alcohols **15** and **16** can be explained by a mechanism in which evolution of ginsenane carbocation **C**, under strongly acidic and low-temperature conditions, leads, on one hand, to further rearrangement to yield compound **18**, with a neoclovane skeleton (Scheme 4). On the other hand, trapping of the tertiary carbocation by the hydrogen sulfate anion and further ionization of the secondary alcohol gives a carbocation **F**, which via a σ bond rearrangement furnishes the tertiary carbocation **G**, which undergoes two further transformations. Intramolecular attack by the sulfate

Scheme 4



moiety affords the cyclic sulfate **19**, or further rearrangement gives the carbocation **H**, which on quenching the reaction generates the ketone **20**.

To support the proposed mechanism and to clarify the role of the secondary alcohol in the previously described rearrangements, diol **16** was oxidized with PCC to yield the hydroxy ketone **21**. Treatment of this compound with HSO_3F in dry Et_2O at −63 °C gave a major product **22** and two minor products (**23** and **24**) (Scheme 5). Compound **22** showed absorption in its IR spectrum at 3371 cm^{-1}, as well as resonances in its ^{13}C NMR at δ_C 86.50 (s, C-1) and 213.10 (s, C-8), which are consistent with the presence of hydroxyl and carbonyl group in the

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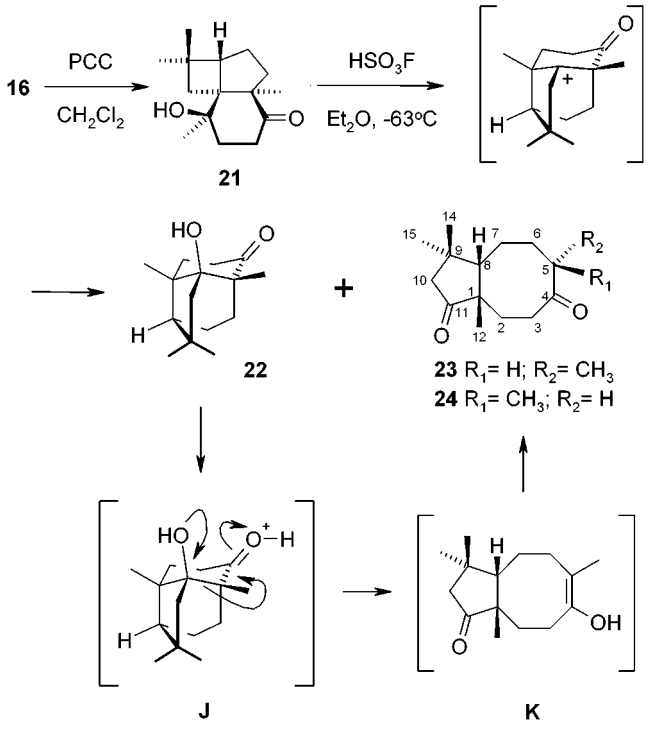
Scheme 5



molecule. Analysis of their 1D and 2D NMR spectra and comparison with previously published data[7] leads to the assignment of the structure to compound **22** as 8-oxoginsenol.

Compounds **23** and **24** showed common features in their spectra. Both showed IR absorption and resonances in their ^{13}C NMR spectra consistent with the presence of two carbonyl groups. 2D COSY, and NOE analysis led to their identification as (1*S*,5*S*,8*S*)-1,5,9,9-tetramethylbicyclo[6.3.0]undecane-4,11-dione (**23**) and (1*S*,5*R*,8*S*)-1,5,9,9-tetramethylbicyclo[6.3.0]undecane-4,11-dione (**24**). Both compounds possess a novel sesquiterpenoid skeleton.

Formation of compounds **23** and **24** can be explained via a retro-aldol reaction on 8-oxoginsenol (**22**), which would lead to an enol intermediate. The tautomeric equilibrium of this enol would lead to either of the ketones (**23** and **24**), as protonation can occur, in principle, on either face of the enol. The higher yield of ketone **23** would reflect a hindered approach for protons on the double bond of the enol. This hindrance can be attributed to a preferential conformation of enol intermediate **K**, consistent with the cis-fused nature of the bicycle **K**.

In conclusion, we have explored the reactivity of C-5, C-8 dioxygenated panasinsane derivatives, which enabled us either the selective preparation of compounds with ginsenane skeleton or the preparation of compounds with (1*S*,4*S*,5*S*,8*S*)-2,2,4,8-tetramethyltricyclo[3.3.2.1^{4,8}]undecane (**20**) and (1*S*,4*S*,7*S*,10*S*,11*S*)-3,3,10,11-tetramethyltricyclo[5.3.1.0^{4,10}]undecane (**19**) skeleta, via the successive generation and trapping of carbocations derived from alcohols at C-5 and C-8 in panasinsane derivatives. When the hydroxyl group at C-5 is transformed into a ketone (compound **21**), the genesis of compounds **19** and **20** is inhibited and 8-oxoginsenol (**22**) is formed. Nevertheless, compound **22** can suffer, under these conditions, a retro-aldol reaction, yielding diketones **23** and **24**, which also possess a novel carbon skeleton.

Experimental Section

General Methods. Melting points are uncorrected. TLC was performed on Merck Kieselgel 60 F_{254}, 0.2 mm thick. Silica gel (Merck) was used for column chromatography. Purification by HPLC was accomplished using a silica gel column (Hibar 60, 7 μm, 1 cm wide, 25 cm long).

4*β*,5*β*-Epoxy-15-norcaryophyllen-8-one (Kobusone, 8). Epoxy ketone **8** was synthesized by ozonolysis (1.15 bar of ozonized oxygen, for 45 min) of caryophyllene 4*β*,5α-oxide (**7**) (10.8 g) in anhydrous CH_2Cl_2 (30 mL) at room temperature, followed by treatment with Me_2S (3.4 mL) for 30 min. Evaporation of the solvent under reduced pressure, followed by column chromatography with increasing gradients of ethyl acetate in petroleum ether, gave 5.9 g (52%) of kobusone (**8**). The physical data for compound **8** were identical to the literature.[9a]

5α-Hydroxynorpanasinsan-8-one (9) and (1*S*,3*S*,5*R*,-6*R*,9*R*)-6-Hydroxy-6,10,10-trimethyltricyclo[7.2.0.0^{3,5}]undecan-2-one (10). A solution of KOH (8.44 g) in MeOH (18 mL) and H_2O (2 mL) was added dropwise to a solution of kobusone (**8**) (1.42 g) in MeOH (10 mL) and heated to reflux for 3 h with stirring. The mixture was then allowed to cool to room temperature, H_2O (25 mL) was added, and the solution was carefully brought to neutral pH with 2 N HCl. The mixture was extracted with diethyl ether, the combined organic layers were dried (Na_2SO_4), and the solvent was evaporated under reduced pressure. The crude reaction product was purified by column chromatography on silica gel, with increasing gradients of ethyl acetate in petroleum ether, to give **9** (941 mg) (66%) and **10** (202 mg) (14%). The physical data for compounds **9** and **10** were identical with those described in the literature.[9a,b]

8*β*,15-Epoxypanasinsan-5α-ol (11). A solution of sodium hydride (180 mg, 60% dispersion in mineral oil, washed three times with anhydrous hexane and dried in vacuo) in anhydrous dimethyl sulfoxide (DMSO) (30 mL) was stirred for 20 min at room temperature. Anhydrous tetrahydrofuran (THF) (50 L) was then added, and the solution was cooled in an ice bath. At this point, a solution of trimethyl sulfonium iodide (930 mg) in DMSO (15 mL) was added and the resulting solution was stirred for 10 min in the ice bath. Compound **9** (500 mg), dissolved in anhydrous DMSO (20 mL), was then added to this solution, and the mixture was stirred in the ice bath for 30 min. The ice bath was then removed, and the reaction was allowed to warm to room temperature and allowed to stir for 12 h. The solution was carefully poured into ice/water (200 mL) and extracted with ethyl acetate. The combined organic layers were washed with brine and dried (Na_2SO_4), and the solvent was evaporated under reduced pressure. The crude reaction product was purified by column chromatography on silica gel. Elution with ethyl acetate/petroleum ether (1:3) gave **11** (321 mg) (60%): colorless oil; $[\alpha]^{25}_D$ −37.8 (*c* 1.1 $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 3.50 (1H, dd, J = 3.9, 11.8 Hz; H-5*β*), 2.60 (1H, d, J = 4.4 Hz; H-15), 2.48 (1H, d, J = 4.4 Hz; H-15′), 1.15 (3H, s), 0.86 (3H, s), 0.80 (3H,s); IR (film) ν_{max} 3433, 919 cm^{-1}; EIMS *m*/*z* (rel intensity) 236 (20) [M$^+$], 221 (26) [M$^+$ − 15], 205 (18) [M$^+$ − 31], 41 (100); HREIMS 236.1786 [M$^+$] ($C_{15}H_{24}O_2$ requires 236.1776).

8*β*,15-Epoxypanasinsan-5-one (12). Chromium trioxide flakes (165 mg) were added cautiously in portions to anhydrous pyridine (260 mg) in anhydrous dichloromethane (20 mL) in an ice bath. When the chromium trioxide had completely dissolved, the ice bath was removed and the solution was stirred at room temperature for 20 min. 8*β*,15-Epoxypanasinsan-5α-ol (**10**) (380 mg) in anhydrous dichloromethane (20 mL) was added with cooling (ice bath). The mixture was then allowed to warm to room temperature, and it was stirred for 24 h. Then, the solvent was decanted and the solid residue was washed thoroughly with diethyl ether. The combined organic layers were washed with 1% aqueous sodium hydroxide solution, saturated aqueous copper sulfate solution, water, and brine and then dried (Na_2SO_4). The solvent was evaporated under reduced pressure. The crude reaction product was purified by column chromatography on silica gel. Elution with ethyl acetate/petroleum ether (1:19) gave **12** (279 mg) (74%).

Recrystallization from petroleum ether (60/80) gave colorless crystals suitable for single X-ray analysis: mp 99−100 °C; $[\alpha]^{25}_D$ −31.5 (*c* 1.5 $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.61 (1H, dd, J = 2.0, 4.7 Hz; H-15), 2.57 (1H, d, J = 4.7 Hz; H-15′), 1.04 (3H, s), 0.84 (3H, s), 0.72 (3H,s); IR (film) ν_{max} 1704, 900 cm^{-1}; EIMS *m/z* (rel intensity) 234 (25) [M^+], 19 (33) [M^+ − 15], 203 (13) [M^+ − 31], 151 (100). Anal. Calcd for $C_{14}H_{24}O$: C, 76.9; H, 9.5. Found: C, 76.7; H, 9.4.

Panasins-8(15)-en-5α-ol (13). Caryophyllene 4*β*,5α-oxide (**7**) (2.20 g) and mercury(II) acetate (6.40 g) were dissolved in glacial acetic acid (20 mL) and stirred at room temperature for 7 days. The acetic acid was removed in vacuo, and consecutively, tetrahydrofuran (30 mL), 3 N sodium hydroxide solution (40 mL), and sodium borohydride (500 mg) were added. The solution was stirred at room temperature for 1 h, and then the aqueous layer was saturated with sodium chloride, and after 30 min, the solution was extracted with diethyl ether. The combined organic layers were washed with brine and dried (Na_2SO_4), and the solvent was evaporated under reduced pressure. The crude reaction product was purified by column chromatography on silica gel. Elution with ethyl acetate/petroleum ether (7:93) gave **13** (398 mg) (18%). Recrystallization from acetonitrile gave **13** as white needles. The physical data for compound **13** were identical to literature.[13]

8*β*,15-Epoxypanasinsan-5α-ol (14). *m*-CPBA (295 mg) was added slowly and in portions with stirring to a solution of panasins-8(15)-en-5α-ol (**13**) (368 mg) in chloroform (100 mL), cooled in an ice bath. The reaction mixture was left to warm to room temperature, and stirring was continued for 3 h. Then, the solution was washed with saturated sodium sulfite solution, water, and brine and then dried (Na_2SO_4). The solvent was evaporated under reduced pressure, and the crude reaction product was purified by column chromatography on silica gel. Elution with ethyl acetate/petroleum ether (1:4) gave **14** (316 mg) (80%) as a colorless oil: $[\alpha]^{25}_D$ −30.2 (*c* 0.7 $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.51 (1H, dd, J = 3.4, 11.7 Hz; H-5*β*), 3.08 (1H, d, J = 4.2 Hz; H-15), 2.58 (1H, d, J = 4.2 Hz; H-15′), 2.08 (1H, dd, J = 3.1, 11.7 Hz; H-1*β*), 1.09 (3H, s), 0.90 (3H, s), 0.88 (3H,s); IR (film) ν_{max} 3433, 919 cm^{-1}; EIMS *m/z* (rel intensity) 236 (26) [M^+], 221 (29) [M^+ − 15], 205 (15) [M^+ − 31], 41 (100); HREIMS 236.1775 [M^+] ($C_{15}H_{24}O_2$ requires 236.1776).

Panasinsane-5α,8α-diol (15) and Panasinsane-5α,8*β*-diol (16). A solution of 5α-hydroxypanasinsan-8-one (**9**) (40 mg) in anhydrous diethyl ether (5 mL) was added dropwise to a solution of MeLi (1.35 mL of 1.6 M solution in diethyl ether) in anhydrous diethyl ether (2 mL). The reaction was allowed to stir at room temperature for 24 h. Then, excess MeLi was carefully quenched with water (50 mL), and the reaction was extracted with diethyl ether. The combined organic layer was washed with brine and dried (Na_2SO_4). The solvent was evaporated under reduced pressure, and the crude reaction product was purified in HPLC on silica gel. Elution with ethyl acetate/petroleum ether (7:18) gave **15** (7 mg) (18%) and **16** (14 mg) (35%).

Panasinsane-5α,8α-diol (15): mp 99−101 °C; $[\alpha]^{25}_D$ −32.8 (*c* 0.60 $CHCl_3$); ^{1}H RMN (400 MHz, $CDCl_3$) δ 3.36 (1H, dd, J = 4.1, 12.0 Hz, H-5*β*), 2.04 (1H, d, J = 8.0 Hz, H-1*β*), 1.41 (3H, s, H-13*β*), 1.16 (3H, s, H-15*β*), 0.99 (3H, s, H-12α), 0.95 (3H, s, H-14α); IR ν_{max} 3427 cm^{-1}; EIMS *m/z* (rel intensity) 220 (6) [M^+ − 18], 202 (2) [M^+ − 18 − 18], 164 (100); HREIMS 220.1829 [M^+ − 18] ($C_{15}H_{24}O$ requires 220.1827).

Panasinsane-5α,8*β*-diol (16): mp 102−104 °C; $[\alpha]^{25}_D$ −44.0 (*c* 1.75 $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.40 (1H, dd, J = 4.6, 11.0 Hz, H-5*β*), 2.24 (1H, d, J = 6.6 Hz, H-1*β*), 1.19 (3H, s, H-15*β*), 1.12 (3H, s, H-13*β*), 0.90 (3H, s, H-14α), 0.84 (3H, s, H-12α); IR ν_{max} 3425 cm^{-1}; EIMS *m/z* (rel intensity) 238 (2) [M^+], 220 (21) [M^+ − 18], 202 (6) [M^+ − 18 − 18], 43 (100); HREIMS 238.1963 [M^+] ($C_{15}H_{26}O_2$ requires 238.1932).

Rearrangement of Compound 11. 9-Methoxyginsene-8*β*,15-diol (17). Tetracyanoethylene (175 mg) was added to a solution of 8*β*,15-epoxypanasinsan-5α-ol (**11**) (630 mg) in anhydrous methanol (20 mL). The reaction mixture was stirred at room temperature for 21 days. Then, the solvent was removed in vacuo to give a dark oil, which was purified by column chromatography on silica gel. Elution with ethyl acetate/petroleum ether (7:13) yielded **11** (297 mg) and **17** (145 mg) (38%). Compound **17**: colorless plates; mp 197−199 °C; $[\alpha]^{25}_D$ +6.2 (*c* 1.4 $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.93 (1H, d, J = 11.6 Hz, H-15), 3.69 (1H, d, J = 11.6 Hz, H-15′), 3.42 (1H, dd, J = 1.8, 4.2 Hz, H-8α), 3.40 (3H, s; −OMe), 2.14 (1H, ddd, J = 8.0, 12.9, 13.9 Hz, H-10*β*), 2.12 (1H, dd, J = 0.9, 4.2 Hz, H-2*β*), 1.91 (1H, d, J = 4.2 Hz, H-2α), 1.73 (1H, t, J = 3.0 Hz, H-4*β*), 1.56 (1H, ddd, J = 2.6, 7.8, 14.5 Hz, H-5α), 1.48 (1H, ddd, J = 7.9, 11.7, 15.0 Hz, H-6α), 1.28 (3H, s), 1.16 (3H, s), 1.12 (1H, q, J = 7.8 Hz, H-6*β*), 1.08 (3H, s); IR ν_{max} 3354 cm^{-1}; EIMS *m/z* (rel intensity) 268 (8) [M^+], 253 (95) [M^+ − 15], 237 (100) [M^+ + 1 − 32], 219 (36) [M^+ + 1 − 32 − 18]; HREIMS 238.1963 [M^+ − 18] ($C_{15}H_{26}O_2$ requires 238.1932). Anal. Calcd for $C_{16}H_{28}O_3$: C, 71.6; H, 10.5. Found: C, 71.2; H, 10.7.

Rearrangement of Compound 14. 9-Methoxyginsene-8*β*,15-diol (17). Tetracyanoethylene (32 mg) was added to a solution of 8α,15-epoxypanasinsan-5α-ol (**14**) (300 mg) in anhydrous methanol (10 mL). The reaction mixture was stirred at room temperature for 2 days. Then, the solvent was removed in vacuo to give a dark oil, which was purified by column chromatography on silica gel. Elution with ethyl acetate/petroleum ether (7:18) gave **17** (73 mg) (21%).

Rearrangement of Compound 16. (1*R*,2*R*,6*S*,7*S*)-2,6,8,8-Tetramethyltricyclo[5.2.2.0^{1,6}]undecan-3-one (18), (1*S*,4*S*,-7*S*,10*S*,11*S*)-3,3,10,11-Tetramethyltricyclo[5.3.1.0^{4,10}]undecan-1,11-yl Sulfate (19), and (1*S*,4*S*,5*S*,8*S*)-2,2,4,8-Tetramethyltricyclo[3.3.2.1^{4,8}]undecan-11-one (20). Panasinsane-5α,8*β*-diol (**16**) (182 mg) was added to a solution of $HFSO_3$ (5 mL) in anhydrous diethyl ether (1 mL) at −63 °C and allowed to stir at this temperature for 1 h. Then, a mixture of acetone (5 mL) and water (1 mL) was added carefully, and the mixture was left stirring for 5 min. At this point, the reaction mixture was directly purified by column chromatography on silica gel. Elution with ethyl acetate/petroleum ether (1:49) gave **18** (18 mg) (10%), **19** (10 mg) (6%), and **20** (9 mg) (5%).

(1*R*,2*R*,6*S*,7*S*)-2,6,8,8-Tetramethyltricyclo[5.2.2.0^{1,6}]undecan-3-one (18): yellow oil; $[\alpha]^{25}_D$ −77.7 (*c* 1.80, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.53 (1H, dddd, J = 15.1, 13.2, 7.5, 0.9 Hz; H-4*β*), 2.39 (1H, qd, J = 6.6, 0.9 Hz, H-2), 2.25 (1H, ddd, J = 15.2, 5.4, 1.6 Hz, H-4α), 2.08 (1H, dddd, J = 13.4, 13.3, 5.5, 1.0 Hz, H-5α), 1.37 (3H, d, J = 1.09 Hz, H-13), 1.23 (3H, s, H-15), 1.14 (1H, d, J = 12.0 Hz, H-9α), 1.01 (3H, s, H-14), 0.88 (3H, d, J = 6.6 Hz, H-12); IR ν_{max} 1710 cm^{-1}; EIMS *m/z* (rel intensity) 220 (59) [M^+], 205(23) [M^+ − 15], 69 (100); HREIMS 220.1829 [M^+] ($C_{15}H_{24}O$ requires 238.1827).

(1*S*,4*S*,7*S*,10*S*,11*S*)-3,3,10,11-Tetramethyltricyclo[5.3.-1.0^{4,10}]undecan-1,11-yl sulfate (19): mp 108−110 °C; $[\alpha]^{25}_D$ −119.3 (*c* 0.20, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.41 (1H, d, J = 16.0 Hz, H-2*β*), 2.25 (1H, m, H-7), 2.18 (1H, d, J = 16.0 Hz, H-2α), 2.08 (1H, m, H-8*β*), 1.92 (1H, m, H-9*β*), 1.74 (3H, s, H-15), 1.33 (3H, s, H-14), 1.28 (3H, s, H-13), 1.06 (3H, s, H-12); IR ν_{max} 1365, 1112 cm^{-1}; EIMS *m/z* (rel intensity) 300 (6) [M^+], 202 (84) [M^+ − 98], 187(86) [M^+ − 98 − 15], 85 (100); HREIMS 300.1388 [M^+] ($C_{15}H_{24}O_4S$ requires 300.1395).

(1*S*,4*S*,5*S*,8*S*)-2,2,4,8-Tetramethyltricyclo[3.3.2.1^{4,8}]undecan-11-one (20): mp 54−56 °C; $[\alpha]^{25}_D$ +170.2 (*c* 1.07, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.32 (1H, ddd, J = 13.6, 9.7, 9.7 Hz, H-7*β*), 2.16 (2H, m, H-9α, H-10*β*), 2.07 (1H, d, J = 13.8 Hz, H-3*β*), 1.88 (1H, m, H-9*β*), 1.78 (1H, m, H-5), 1.60 (2H, m, H-6, H-10α), 1.52 (1H, m, H-6), 1.46 (1H, m, H-1), 1.39 (1H, ddd, J = 13.6, 10.0, 1.0 Hz, H-7α), 1.30 (1H, d, J = 13.8 Hz, H-3α), 1.09 (3H, s, H-15), 0.99 (3H, s, H-12), 0.98 (3H, s, H-14), 0.91 (3H, s, H-13); IR ν_{max} 1708 cm^{-1}; EIMS *m/z* (rel intensity) 220 (100) [M^+], 205 (16) [M^+ − 15]; HREIMS 220.1815 [M^+] ($C_{15}H_{24}O$ requires 300.1395).

8*β*-Hydroxypanasinsan-5-one (21). PCC on alumina (1.1 g) was added to a solution of compound **16** (300 mg) in CH_2Cl_2 (30 mL). The slurry was stirred for 4 h and then filtered through a pad of silica gel. The solvent was removed under reduced pressure, and the resulting oil was dissolved in diethyl ether (100 mL). The solution was washed with $NaHCO_3$ and

brine and dried (Na_2SO_4). Then, the solvent was removed under reduced pressure to give a crude product that was purified by column chromatography on silica gel, in ethyl acetate/petroleum ether (3:17), to yield **21** (276 mg) (92%): mp 90−93 °C; $[\alpha]^{25}_D$ −33.9 (*c* 0.66 $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.54 (2H, m, H-6α, H-4*β*), 2.34 (2H, m, H-6*β*, H-2α), 1.97 (1H, dd, *J* = 12.9, 2.1 Hz, H-1*β*), 1.83 (2H, m, H-7α, H-7*β*), 1.33 (3H, s, H-12), 1.20 (3H, s, H-9), 1.19 (1H, m, H-3*β*), 1.05 (3H, s, H-11), 0.94 (3H, s, H-10); IR ν_{max} 3464, 1683 cm^{-1}; EIMS *m*/*z* (rel intensity) 236(4) [M$^+$], 221(16) [M$^+$ − 15], 107 (100); HREIMS 236.1749 [M$^+$] ($C_{15}H_{24}O_2$ requires 236.1776).

Rearrangement of Compound 21. 8-Oxoginsenol (22), (1*S*,5*S*,8*S*)-1,5,9,9-Tetramethylbicyclo[6.3.0]undecane-4,-11-dione (23), (1*S*,5*R*,8*S*)-1,5,9,9-Tetramethylbicyclo[6.3.0]-undecane-4,11-dione (24). 8*β*-Hydroxypanasinsan-5-one (**21**) (238 mg) was added to a solution of $HFSO_3$ (5 mL) in anhydrous diethyl ether (1 mL) at −63 °C and allowed to stir at this temperature for 1 h. Then, a mixture of acetone (5 mL) and water (1 mL) was added carefully, and the mixture was allowed to stir for 5 min. At this point, the reaction mixture was directly purified by column chromatography on silica gel. Elution with increasing gradients of ethyl acetate in petroleum ether gave **22**[7] (60 mg) (25%), **23** (16 mg) (6%), and **24** (7 mg) (3%).

(1*S*,5*S*,8*S*)-1,5,9,9-Tetramethylbicyclo[6.3.0]undecane-4,11-dione (23): mp 74−76 °C; $[\alpha]^{25}_D$ −101.1 (*c* 1.58 $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.66 (3H, s, H-15), 2.80 (1H, m, H-5*β*), 2.64 (1H, ddd, *J* = 12.0, 11.7, 2.2 Hz, H-3*β*), 2.45 (1H, d, *J* = 15.9 Hz, H-10*β*), 2.22 (2H, m, H-2*β*, H-3α), 2.00 (1H, d, *J* = 15.9 Hz, H-10α), 1.51 (1H, m, H-2α), 1.29 (3H, s, H-12), 1.11 (3H, s, H-14), 1.03 (3H, d, *J* = 6.6 Hz, H-13), 0.95 (1H, m, H-7α); IR ν_{max} 1727 cm^{-1}; EIMS *m*/*z* (rel intensity) 236(43) [M$^+$], 221(41) [M$^+$ − 15], 110 (100); HREIMS 236.1781 [M$^+$] ($C_{15}H_{24}O_2$ requires 236.1776).

(1*S*,5*R*,8*S*)-1,5,9,9-Tetramethylbicyclo[6.3.0]undecane-4,11-dione (24): mp 42−44 °C; $[\alpha]^{25}_D$ −114.6 (*c* 0.67 $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.71 (1H, dd, *J* = 12.8, 11.2 Hz, H-3*β*), 2.54 (1H, m, H-5α), 2.42 (1H, dd, *J* = 16.1, 0.91 Hz, H-10*β*), 2.20 (2H, m, H-2*β*, H-3α), 2.01 (1H, d, *J* = 16.2 Hz, H-10α), 1.88 (2H, m, H-7*β*, H-6α), 1.76 (1H, dd, *J* = 12.8, 2.9 Hz, H-8), 1.65 (1H, m, H-2α), 1.41 (1H, m, H-6*β*), 1.20 (3H, s, H-12), 1.12 (3H, s, H-14), 1.07 (3H, d, *J* = 6.9 Hz, H-13), 1.03 (1H, m, H-7α), 0.70 (3H, s, H-15); IR ν_{max} 1737, 1704 cm^{-1}; EIMS *m*/*z* (rel intensity) 236 (16) [M$^+$], 221 (14) [M$^+$ − 15], 110 (100); HREIMS 236.1788 [M$^+$] ($C_{15}H_{24}O_2$ requires 236.1776).

Acknowledgment. This research was supported by grants from CICYT 1FD97-0668-C06-01 and European Commission FAIR-5-PL97-3351. We thank Dr. F. Lafont (University of Cordoba, Spain) for the HREIMS results. C.F.D.A. thanks the European Commission for a studentship (FAIR-5-PL97-3351). D.J.M. thanks the EPR-SC for a studentship.

Supporting Information Available: Copies of ^{1}H NMR and ^{13}C NMR spectra for compounds **15**, **16**, **18**−**21**, **23**, and **24**. Tables of ^{13}C NMR data for compounds **11**, **12**, **14**−**21**, **23**, and **24**. ORTEP drawings for compounds **12**, **17**, and **19**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO0155557