MOLECULAR REARRANGEMENTS OF HIGHLY FUNCTIONALIZED TERPENES. AN UNIQUE REACTIVITY OF BICYCLIC FRAMEWORK AND POLIENIC CHAIN INHIBITION UNDER SUPERACIDIC TREATMENT

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Abstract. Synthesis of polyfunctional triterpene derivative [8(27),13*E*,17*E*,21*E*]-15-phenylsulfonyl-16-oxo-bicyclofarnesylfarnesol benzyl ether (**8**) from commercially available monoterpene geraniol and diterpene manool has been accomplished in 73% yield and its chemical transformation in superacid medium has been investigated. An unexpected rearrangement of **8** occurred, which involved methyl migration in the bicyclic fragment and total inhibition of the lateral polienic chain. A new bicyclic triterpene product [5(10),13*E*,17*E*,21*E*]-15-phenylsulfonyl-16-oxo-30(10→9)-abeo-bicyclofarnesylfarnesol benzyl ether (**9**), with rearranged new carbon skeleton has been obtained. Its bicyclic moiety is analogous to this of a natural triterpene neopolypodatetraene.

Keywords: triterpenes, synthesis, superacid, isomerization.

Introduction

Triterpenes is a group of terpenes with a high structural diversity, which includes natural products with more than 100 types of skeleton [1–3]. Reviews related to biological activities of triterpenes appear regularly and are focused on their anti-inflammatory [4], antitumor [5], anti-HIV [6,7] and insecticidal [8] activities, and also their use in treatment of metabolic and vascular diseases [9].

Results and discussions

The aim of the present work is development of the method for synthesis of bicyclic polyfunctional triterpenes with a new carbon skeletons and study of their conversion in superacid medium.

Synthesis of the bicyclic triterpenoids containing two structural blocks, fragment A (monoterpene - aliphatic) and fragment B (diterpene - bicyclic) has been drawn, in order to achieve the proposed goal.

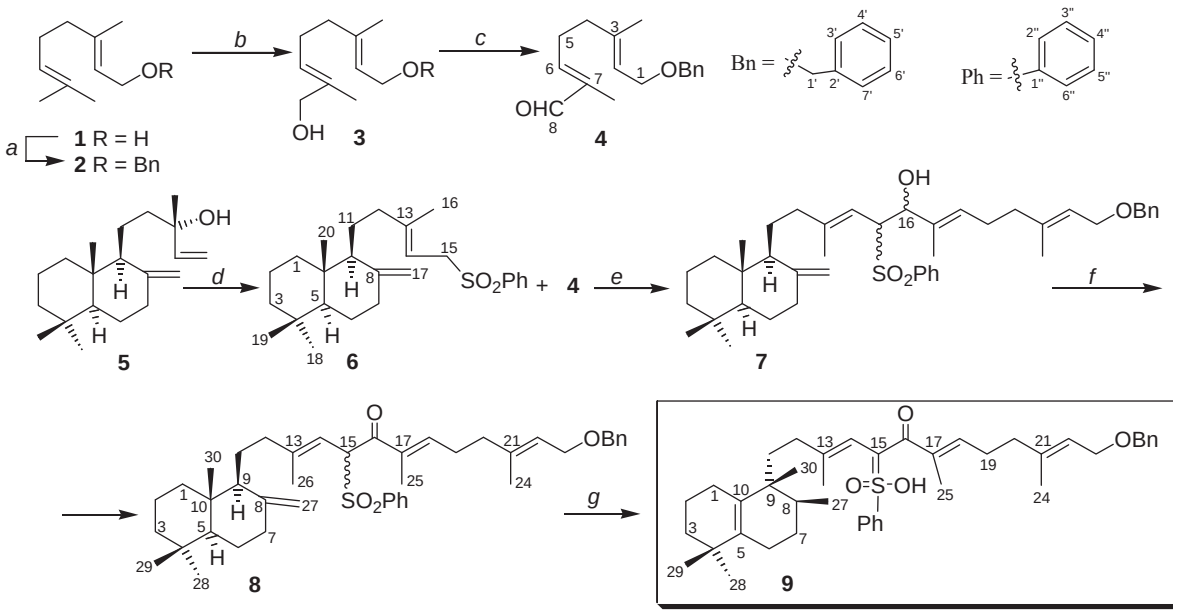
Fragment A has been obtained from commercially available monoterpene – geraniol (**1**) in three steps (Scheme 1). Treatment of geraniol (**1**) with benzyl chloride in dichloromethane and sodium hydride led to the corresponding benzyl ether. Its spectral data and physico-chemical constants are in accordance with the reported ones [10]. Compound **2** has been subjected to oxidation with selenium dioxide in ethanol furnishing the α,ω-bifunctionalized derivative **3** in a modest 45% yield. Finally, the monoterpene alcohol **3** has been oxidized with pyridinium chlorochromate (PCC) into the corresponding aldehyde **4** [11] (fragment A) in a 72% yield, its overall yield is ~32%.

Synthesis of fragment B has been achieved starting from commercially available manool (**5**). It was transformed into new diterpenic phenylsulfone **6** in a two-step sequence, according to the reported method [12]. It should be mentioned that from reaction product by column chromatography also the 13*Z*- izomer of diterpenyl-phenylsulfone **6** was obtained in ~20% yield.

The *n*-BuLi-assisted coupling reaction of aldehyde **4** (fragment A) and diterpenylphenylsulfone **6** (fragment B) in tetrahydrofuran gave bicyclic triterpene compound **7** in a 62% yield. Compound **7** was subjected to Swern oxidation giving the [8(27),13*E*,17*E*,21*E*]-15-phenylsulfonyl-16-oxo-bicyclofarnesylfarnesol benzyl ether (**8**) in acceptable yield (73%). It should be mentioned that an alternative oxidation of compound **7** with PCC in dichloromethane, led to a complex mixture of compounds where the content of target compound **8** does not exceed ~30%.

The structures of coupling reaction **7** and oxidation reaction **8** products have been established on the basis of their spectral data (see Experimental part).

Since the molecule of bicyclic triterpene derivative **8** is characterized by more than one double bond that is prone to chemical transformation in acid medium, the behavior of compound **8** in superacid medium at low temperature has been further explored [13-16]. Thus, following a previous elaboration, [8(27),13*E*,17*E*,21*E*]-15-phenylsulfonyl-16-oxo-bicyclofarnesylfarnesol benzyl ether (**8**) has been treated with fluorosulfonic acid in 2-nitropropane at -78°C [12,17].



Scheme 1

Reagents and conditions. (*a*) NaH, BnCl, TBAI, CH_2Cl_2, r.t., 12 h, 92%; (*b*) SeO_2, EtOH, reflux, 3h, 45%; (*c*) PCC, CH_2Cl_2, r.t., 1.5h, 70%; (*d*) 1) PBr_3/Et_2O; 2) $NaSO_2Ph$/DMF, overall for two steps 74%; (*e*) *n*-BuLi/THF, 66%; (*f*) $(COCl)_2$/DMSO, CH_2Cl_2, -60°C, Et_3N, 73%; (*g*) FSO_3H, *i*-$PrNO_2$, -78°C, 20 min, 62%.

The product [5(10),13*E*,17*E*,21*E*]-15-phenylsulfonyl-16-oxo-30(10→9)-abeo-bicyclofarnesylfarnesol benzyl ether (**9**) has been isolated in a 62% yield, its structure being assigned by IR and NMR spectroscopic data. The IR spectrum exhibited absorption bands at 1145, 1385, 1451, 1668, 1793, 2286, 2993 and 3362 cm^{-1}, suggesting the presence of carbonyl-, phenylsulfonyl- and olefinic groups. NMR characteristics of compound **9** have been obtained on the basis of its 1D (^1H, ^{13}C, DEPT-13°) and 2D homo- ($^1H/^1H$ COSY-45°) and heteronuclear ($^1H/^{13}C$ HSQC and $^1H/^{13}C$ HMBC) correlation spectra (Fig. 1). The ^1H NMR spectrum (Table 1) displayed singlets of geminal dimethyl at δ_H 0.99, 1.01, (each 3H, H-28, H-29), signal of one tertiary and one secondary methyl groups at δ_H 0.86 (6H, H-30, H-27) that appears as a multiplet due to overlapping, low-field singlets of three methyls attached to double bonds at δ_H 1.49, 1.66, 1.80 (each 3H, H-26, H-24, H-25), downfield signals of ether methylens at δ_H 4.00 (*d*, *J* = 6.6 Hz, H-23) and δ_H 4.50 (s, H-1') and deshielded signals of three sp^2 methines: δ_H 5.44 (*tq*, *J* = 6.6; 1.1 Hz, H-22), 5.74 (*br. s*., H-14), 6.96 (*tq*, *J* = 7.2; 1.2 Hz, H-18).

The ^1H NMR spectrum of compound **9** also contains the signals of two phenyl groups: one belonging to benzyl moiety, for which strong signal overlapping has been noted, at δ_H 7.26-7.35 (*m*, 4H, H-3'-7') and another one, identifying phenylsulfone fragment at δ_H 7.50 (*bt*, *J* = 8.0 Hz, H- 3", 5" and 8.09 (*dm*, *J* = 8.0 Hz, H- 2", 6"). The clear substructures H-18 - H-19 -H-20; H-14 -H-26; H-22 -H-23 - H-24 -H-20 and, in contrast to the precursor **8**- H-2"- H-3", H-4", H-5"- are evident in $^1H/^1H$ COSY spectrum, the accurate description of all methylene protons being difficult because of severe signal overlapping (see: Table 1). The ^{13}C NMR data exhibited thirty nine carbon signals, which were assigned by a DEPT experiment as seven methyls, eleven sp^3 methylenes, one sp^3 and nine sp^2 methines, two sp^3 and ten sp^2 quaternary carbons. The presence of α,β-unsaturated carbonyl moiety has been corroborated in the molecules of precursor **8**, by the ^1H and ^{13}C NMR data [δ_C 190.3 (C-16), 132.4 (C-17), 147.0 (C-18); δ_H 1.80 (s, 3H, H-25)]. The rearranged carbon framework of **9** becomes obvious while examining its HMBC spectrum. Thus, the observed correlations from both H-6 and H-1 to two sp^2 hybridized (C-5, δ_C 137.8 and C-10, δ_C 131.7) instead of two sp^3 (C-5, δ_C 51.9 and C-10, δ_C 40.4) in the former compound **8** were indicative on $\Delta^{5,10}$ localization, which was supported also by the correlations of H_3-29/C-5, H_3-28/C-5. The logical migration of methyl H_3-30 from C-10 to C-9 position has been ascertained by H_3-30/C-10, H_3-30/C-9 and H_3-30/C-11 cross-peaks in the HMBC spectrum, while the evident substitution of two olefinic carbons (C-8, δ_C 148.5 and C-27, δ_C 106.2) in the precursor **8** by the corresponding sp^3 atoms in **9** (C-8, δ_C 33.6 and C-27, δ_C 16.1) has been proved by long-range correlations H_3-27/C-6, H_3-27/C-7 and H_3-27/C-9.

Table 1.

^{1}H (400.13 MHz) and ^{13}C NMR (100.61 MHz) data of compound 9 in $CDCl_3$ (δ in ppm).

Position	Compound 9		
	δ ^{1}H	m, *J* (Hz)	δ ^{13}C [a,b]
1	1.73, 1.98	m[c]	25.9 CH_2
2	1.49-1.65	m[c]	20.0 CH_2
3	1.37, 1.48	m[c]	40.0 CH_2
4	--	--	34.6 qC
5	--	--	137.8 qC
6	1.96	m[c]	25.2 CH_2
7	1.43	m[c]	34.2 CH_2
8	1.60	m[c]	33.6 qC
9	--	--	40.6 qC
10	--	--	131.7 qC
11	1.34, 1.48	m[c]	27.2 CH_2
12	1.70, 2.00	m[c]	35.9 CH_2
13	--	--	150.8 qC
14	5.74	br. s.	119.4 qC
15	--	--	not detected
16	--	--	190.3 qC
17	--	--	132.4 qC
18	6.96	tq (7.2; 1.2)	147.0 CH
19	2.40	m	27.7 CH_2
20	2.10	m	37.8 CH_2
21	--	--	138.5 qC
22	5.44	tq (6.6; 1.1)	122.0 CH
23	4.00	d (6.6)	66.5CH_2
24	1.66	s	16.5 CH_3
25	1.80	s	12.4 CH_3
26	1.49	s	18.4 CH_3
27	0.86	m[c]	16.1 CH_3
28	0.99	s	29.2 CH_3
29	1.01	s	27.7 CH_3
30	0.86	m[c]	21.2 CH_3
1’	4.50	s	72.3 CH_2
2’	--	--	138.4 qC
4’, 6’	7.30	m[c]	127.8 CH
3’, 7’	7.30	m[c]	128.4 CH
5’	7.30	m[c]	128.4 CH
1’’	--	--	136.5 qC
2’’, 6’’	8.09	dm (8.0)	132.5 CH
3’’, 5’’	7.50	br.t. (8.0)	128.2 CH
4’’	7.64	dm (7.5)	134.0 CH

[a] – degree of protonation found by DEPT sequence,
[b] –HMBC experiments (*J* = 8 Hz),
[c] – signal overlapping.

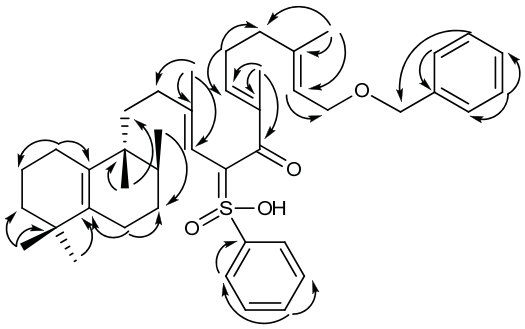
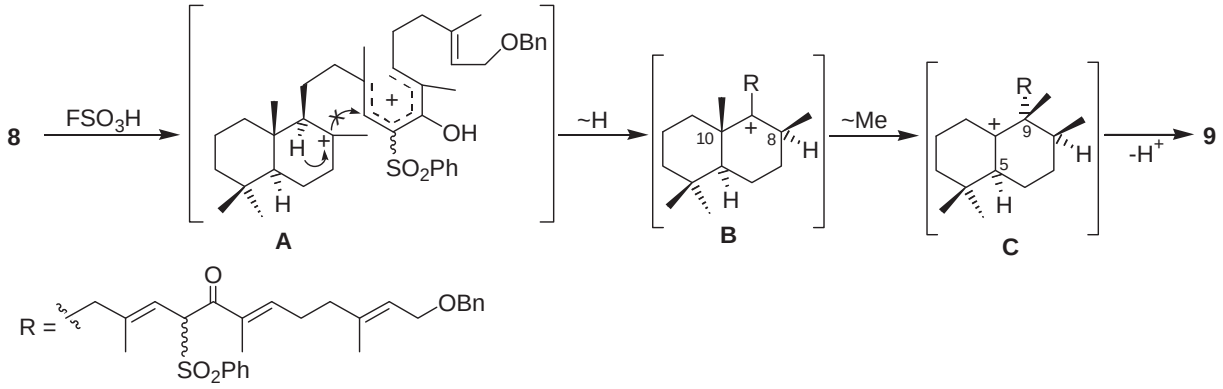


Figure 1. Selected HMBC correlations for compound 9.

The rearranged triterpene derivative **9** has been thereby obtained as a result of selective reactivity of the bicyclic part under superacidic treatment. Its plausible formation from compound **8** is depicted in Scheme 2. Due to the presence of oxygenated groups in side chain at C-16 and C-17 that can be easily protonated the bication A, which blocks the carbocyclisation in acid medium, is formed. In such a manner only the migration of proton from C-9 to C-8 takes place, producing the carbocation B. The latter is subjected to ulterior conversion into the carbocation C, as a result of methyl group migration from C-10 to C-9. While „quenching" the carbocation C the separation of proton at C-5 occurs and the final product **9** is obtained.



Scheme 2. Superacid-promoted molecular isomerization of compound 8.

It should be noted that the polyfunctional triterpene derivative **9** can be considered a congener of natural triterpenoid neopolypodatetraene (**10**), especially on considering the similarity in the bicyclic fragment (Figure 2). The latter has been isolated from a squalene hopene cyclase mutant of the prokaryotic bacterium *Alicyclobacillus acidocaldarius* F365A [18].

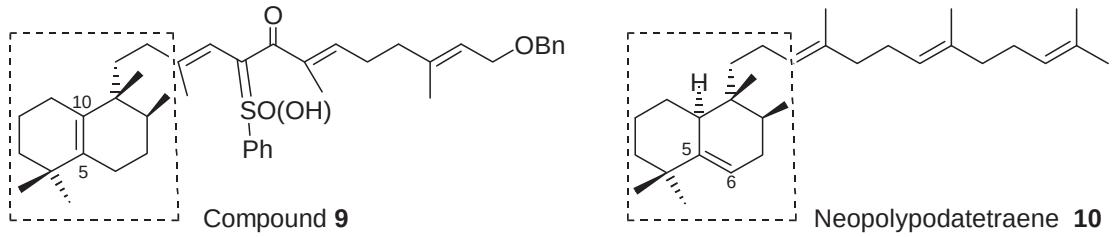


Figure 2.

Conclusions

Synthesis of polyfunctional triterpene derivative [8(27),13*E*,17*E*,21*E*]-15-phenylsulfonyl-16-oxo-bicyclofarnesylfarnesol benzyl ether has been achieved and its chemical transformation in superacid medium has been

studied. Mentioned bicyclic triterpene product with rearranged carbon framework, which is a structural analogous of the natural triterpene neopolypodatetraene, has been obtained for the first time.

Experimental

General. Melting points (mp) were determined on a Boetius hot stage. IR Spectra were recorded on a Spectrum-100 FT-IR spectrophotometer (Perkin-Elmer), with the universal ATR sampling accessory (υ in cm^{-1}). ^{1}H- and ^{13}C-NMR spectra were recorded in $CDCl_3$ on Bruker 400 Avance III spectrometer (400.13 and 100.61 MHz); chemical shift are given in ppm and are referenced to measured in chloroform ($CHCl_3$) as internal standard (δ = 7.26 ppm for proton and δ = 77.0 for carbon). Optical rotations were measures in chloroform on a Jasco DIP 370 polarimeter, using 5 cm cell. Commercial Merck Si gel 60 (70–230 mesh ASTM) was used for flash chromatography, and Merck pre-coated SiO_2 plates were used for TLC. The chromatograms were sprayed with 0.1% solution of cerium (IV) sulfate in 2*N* sulfuric acid and heated at 80°C for 5 min to detect the spots. GC/MS analysis were recorded on Agilent 7890A chromatograph, equipped with quadrupole MS detector MSD 5975C and HP-5 ms capillary column (30 m/0.25 mm). Treatment of reaction mixtures in organic solvents included the extraction by Et_2O, washing of the extract with H_2O up to neutral reaction, drying over anhydrous Na_2SO_4, and solvent removal *in vacuum*.

Geraniol benzyl ether (2). Geraniol (**1**) (12 g, 77.9 mmol) in dry THF (103 mL) was treated with 60% NaH (3.68 g), benzyl chloride (10.61 mL, 92.2 mmol) and tetrabutylammonium iodide (2.88 g, 7.79 mmol). The reaction mixture was stirred for 12 h at room temperature. Then, 10% aqueous solution of H_2SO_4 (20 mL) was added. Usual work up gave a crude reaction product (25 g), which was purified by flash chromatography using 1% ethyl acetate/light petroleum ether mixture to yield 17.52 g (92%) of the geraniol benzyl ether (**2**), as a pale yellow oil. IR liquid film (ν, cm^{-1}): 735, 1069, 1101, 1270, 1377, 1453, 1496, 1670, 1726, 2924. ^{1}H NMR (400 MHz, δ_H): 1.62 (*s*, 3H, H-9), 1.66 (*s*, 3H, H-10), 1.69 (*d*, *J* = 0.9 Hz, 3H, H-8), 2.06 (*m*, 2H, H-4), 2.12 (*m*, 2H, H-5), 4.04 (*dd*, *J* = 6.8, 0.3 Hz, 2H, H-1), 4.51 (*s*, 2H, H-1'), 5.12 (*m*, 1H, H-6), 5.42 (*m*, 1H, H-2), 7.34 (m, 5H, Ar-H). ^{13}C NMR (100 MHz, δ_C): 16.4 (*q*, C-10), 17.6 (*q*, C-9), 25.6 (*q*, C-8), 26.4 (*t*, C-5), 39.6 (*t*, C-4), 66.6 (*t*, C-1), 71.9 (*t*, C-1'), 138.6 (*d*, C-2), 124.0 (*d*, C-6), 127.5 (*d*, C-5'), 127.8 (*d*, C-3', 7'), 128.3 (*d*, C-4', 6'), 131.6 (*s*, C-7), 138.6 (*s*, C-2'), 140.3 (*s*, C-3). All physical properties and spectroscopic data were identical with those reported in literature [10].

8-Hydroxygeraniol benzyl ether (3). A suspension of selenium dioxide (1.45 g, 13.08 mmol) in ethanol (9 mL) was added to a solution of geranylbenzyl ether (**2**) (6.38 g, 26.15 mmol) in ethanol (89 mL). The mixture was refluxed for 3 h, cooled to 0°C, treated with $NaBH_4$ (500 mg, 13.08 mmol) and stirred at the same temperature for 2 h. After, the reaction was quenched with a 10% soln. of H_2SO_4 (10 mL), and the mixture was worked up as usual. The crude product (7.5 g) was submitted to flash chromatography on silica gel (200 g) with increasing gradient of ethyl acetate in light petroleum ether to give starting ether (**2**) (3.14 g, 49%) and 8-hydroxygeraniol benzyl ether (**3**) (3.05 g, 45%), as colorless viscous oil. IR liquid film (ν, cm^{-1}): 697, 736, 1067, 1453, 1639, 3429. ^{1}H NMR (400 MHz, δ_H): 1.65 (s, 3H, H-10), 1.66 (*s*, 3H, H-9), 2.08 (*t*, *J* = 7.3 Hz, 2H, H-4), 2.17 (*q*, *J* = 7.3 Hz, 2H, H-5), 3.97 (*s*, 2H, H-8), 4.02 (*d*, *J* = 6.8 Hz, 2H, H-1), 4.50 (*s*, 2H, H-1'), 5.39 (*m*, 2H, H-2 and H-6), 7.31 (*m*, 5H, Ar-H). ^{13}C NMR (100 MHz, δ_C): 13.6 (*q*, C-9), 16.4 (*q*, C-10), 25.8 (*t*, C-5), 39.1 (*t*, C-4), 66.5 (*t*, C-1), 68.9 (*t*, C-8), 72.1 (*t*, C-1'), 121.1 (*d*, C-2), 125.5 (*d*, C-6), 127.5 (*d*, C-5'), 127.8 (*d*, C-3', 7'), 128.3 (*d*, C-4', 6'), 135.1 (*s*, C-3), 139.9 (*s*, C-7). All physical properties and spectroscopic data were identical with those reported in literature [10].

8-Oxo-geraniol benzyl ether (4). Hydroxyether (**3**) (1.41 g, 5.42 mmol) was dissolved in dry CH_2Cl_2 (83 mL) and PCC (1.75 g, 8.13 mmol) was added. After stirring the reaction mixture at room temperature for 1.5 h, it was diluted with diethyl ether (60 mL) and passed through a short silica gel pad. The crude product (1.9 g) was subjected to flash chromatography. Elution with 4% ethyl acetate/light petroleum ether mixture gave 980 mg (70%) of unsaturated aldehyde (**4**), as a pale yellow oil. IR liquid film (ν, cm^{-1}): 697, 736, 1069, 1116, 1381, 1453, 1686, 2857, 2975. ^{1}H NMR (400 MHz, δ_H): 1.69 (*s*, 3H, H-10), 1.76 (*d*, *J* = 0.8 Hz, 3H, H-9), 2.23 (*t*, *J* = 7.6 Hz, 2H, H-4), 2.5 (*q*, *J* = 7.6 Hz, 2H, H-5), 4.06 (*d*, *J* = 6.7 Hz, 2H, H-1), 4.51 (*s*, 2H, H-1'), 5.46 (apparent *tq*, *J* = 6.7, 1.2 Hz, 1 H, H-2), 6.47 (*td*, *J* = 7.6, 1.3 Hz, 1H, H-6), 7.31 (*m*, 5H, Ar-H), 9.39 (*s*, 1H, H-8). ^{13}C NMR (100 MHz, δ_C): 9.0 (*q*, C-9), 16.2 (*q*, C-10), 26.9 (*t*, C-5), 37.6 (*t*, C-4), 66.3 (*t*, C-1), 72.0 (*t*, C-1'), 121.9 (*d*, C-2), 127.4 (*d*, C-5'), 127.5 (*d*, C-3', 7'), 128.2 (*d*, C-4', 6'), 138.2 (*s*, C-2'), 138.3 (*s*, C-3), 139.3 (*s*, C-7), 153.5 (*d*, C-6), 194.8 (*d*, C-8). All physical properties and spectroscopic data were identical with those reported in literature [11].

Synthesis of 8(17),13E-bicyclogeranylgeranylphenylsulfone (6). A solution of phosphorus tribromide (1.54 g, 5.69 mmol) in dry ether (5.0 mL) was added dropwise to a stirred solution of manool (**5**) (1.20 g, 4.14 mmol) in dry ether (10 mL) with cooling on an ice bath. The mixture was stirred for 2 h at room temperature and treated with saturated $NaHCO_3$ solution. The ether layer was separated, washed with brine, dried, and concentrated *in vacuo*. The resulting

bromide (1.25 g, 86%) was added to a solution of the sodium salt of benzenesulfonic acid (0.90 g, 5.45 mmol) in dry DMF (10 mL). The mixture was stirred at room temperature under argon in the dark for 3 h, treated with NaCl solution, and extracted with ether. The extract was worked up as usual to afford a liquid product that was chromatographed on silica gel (42 g) with gradient elution by petroleum ether: AcOEt to elute 13*E*-bicyclogeranylgeranylphenylsulfone (**6**) (1.09 g, overall for two steps ~74%), as colorless crystals, m.p. 87-88°C (from hexane), $[\alpha]_D^{25}$ +32.2° (*c* 1.45, $CHCl_3$). IR liquid film (ν, cm^{-1}): 730, 1149, 1306, 1447, 1587, 1642, 2927. ^{1}H NMR (400 MHz, δ_H): 0.65 (*s*, 3H, H-20), 0.79 (*s*, 3H, H-19), 0.86 (*s*, 3H, H-18), 1.29 (*s*, 3H, H-16), 3.80 (*d*, *J* = 8 Hz, 2H, H-15), 4.42 (*d*, *J* = 1.2 Hz, 1H, H_b-17), 4.80 (*d*, *J* = 1.4 Hz, 1H, H_a-17), 5.14 (*td*, *J* = 8.0, 1.3 Hz, 1H, H-14), 7.68 (*m*, 5H, Ph-H). ^{13}C NMR (100 MHz, δ_C): 14.5 (*q*, C-20), 16.2 (*q*, C-16), 19.4 (*t*, C-2), 21.7 (*q*, C-19), 21.8 (*t*, C-11), 24.4 (*t*, C-6), 33.6 (*s*, C-4), 33.6 (*q*, C-18), 38.3 (*t*, C-7), 38.6 (*t*, C-12), 39.1 (*t,* C-1), 39.7 (*s*, C-10), 42.1 (*t*, C-3), 55.5 (*d*, C-5), 56.1 (*t*, C-15), 56.3 (*d*, C-9), 106.2 (*t*, C-17), 110.0 (*d*, C-14), 128.6 (*d*, C-3'', 5''), 128.9 (*d*, C-2'', 6''), 133.4 (*d*, C-4''), 138.8 (*s*, C-1'') 147.2 (*s*, C-13), 148.5 (*s*, C-8). Found (%): C, 75.42; H, 9.31. $C_{26}H_{38}SO_2$. Calculated (%): C, 75.31; H, 9.24.

[8(27),13E,17E,21E]-15-phenylsulfonyl-16-hydroxy-bicyclofarnesylfarnesol benzyl ether (7). Compound **6** (529 mg, 1.28 mmol, 1.2 eq.) was co-evaporated with benzene, dried under high vacuum, and then dissolved in anhydrous THF (4.6 mL) and cooled to −78 °C. Then *n*-BuLi (1.7 M, 0.75 mL, 1.28 mmol, 1.2 equiv) was added drop-wise to the 8(17),13*E*-bicyclogeranylgeranylphenylsulfone (**6**) solution over 2 min. under argon atmosphere. The resulting bright yellow solution was stirred at −78°C for 30 min and gradually warmed to -40°C over 1 h and then cooled to -78°C. Aldehyde **4** (279 mg, 1.07 mmol, 1 equiv) was dried under high vacuum, dissolved in THF (4.6 mL), cooled to −78 °C, and added drop-wise to the sulfone anion solution using a syringe. After 30 min of stirring at −78°C, the reaction mixture was gradually heated to -40°C and sat. aq. NH_4Cl (4 mL) was added followed by usual workup. The residue (900 mg) was purified by silica gel flash column chromatography (10% ethyl acetate/light petroleum ether mixture) affording compound **7** (472 mg, 66%), as a clear yellow oil. IR liquid film (ν, cm^{-1}): 730, 1144, 1230, 1446, 2191, 2290, 2947. ^{1}H NMR (400 MHz, δ_H): 0.64 (*s*, 3H, H-30), 0.79 (*s*, 3H, H-29), 0.86 (*s*, 3H, H-28), 1.11 (*s*, 3H, H-26), 1.49 (*s*, 3H, H-25), 1.61 (*s*, 3H, H-24), 3.95 (*m*, 1H, H-15), 4.00 (*d*, *J* = 6.7 Hz, 2H, H-23), 4.37 (*d*, *J* = 0.8 Hz, 1H, H_b-27), 4.49 (*s*, 2H, H-1'), 4.61 (*d*, *J* = 9.7 Hz, 1H, H-16), 4.67 (*m*, 1H, H-14), 4.80 (*d*, *J* = 0.9 Hz, 1H, H_a-27), 5.37 (*t*, *J* = 6.7 Hz, 1H, H-22), 5.42 (*t*, *J* = 6.8 Hz, 1H, H-18), 7.31 (*m*, 5H, Ar-H), 7.68 (*m*, 5H, Ph-H). ^{13}C NMR (100 MHz, δ_C): 10.6 (*q*, C-25), 14.5 (*q*, C-30), 16.1 (*q*, C-26), 16.5 (*q*, C-24), 19.4 (*t*, C-2), 21.7 (*q*, C-29), 24.4 (*t*, C-6), 26.0 (*t*, C-11), 29.7 (*t*, C-19), 33.3 (*s*, C-4), 33.6 (*q*, C-28), 38.3 (*t*, C-7), 38.8 (*t*, C-12), 38.9 (*t*, C-20), 39.2 (*t*, C-1), 39.8(*s*, C-10), 42.2 (*t*, C-3), 55.6 (*d*, C-5), 56.5 (*d*, C-9), 66.6 (*t*, C-23), 68.6 (*d*, C-15), 72.1 (*t*, C-1'), 76.5 (*d*, C-16), 106.2 (*t*, C-27), 114.0 (*d*, C-14), 121.3 (*d*, C-22), 127.5 (*d*, C-5'), 127. 8 (*d*, C-3', 7'), 128.3 (*d*, C-4', 6'), 128.8 (*d*, C-3'', 5''), 129.4 (*d*, C-2'', 6''), 130.2 (*d*, C-18), 133.4 (*s*, C-17), 133.8 (*d*, C- 4''), 137.7 (*s*, C-1''), 138.6 (*s*, C-2'), 139.6 (*s*, C-21), 145.3 (*d*, C-13), 148.5 (*s*, C-8). Found (%): C, 76.53; H, 8.89. $C_{43}H_{60}SO_4$. Calculated (%): C, 76.74; H, 8.99.

[8(27),13E,17E,21E]-15-phenylsulfonyl-16-oxo-bicyclofarnesylfarnesol benzyl ether (8). A solution of DMSO (0.085 mL, 1.21 mmol) in CH_2Cl_2 (1.8 mL) was added dropwise to a stirred solution of oxalyl chloride (0.07 mL, 0.61 mmol) in CH_2Cl_2 (1.8 mL) cooled to –60 °C. After 5 min of stirring at this temperature, a solution of compound (**7**) (185 mg, 0.275 mmol) in CH_2Cl_2 (1.8 mL) was added dropwise. After 30 min of stirring (–60°C) triethylamine (0.5 mL, 3.03 mmol) was added to the reaction mixture, and after another 15 min the cooling bath was removed and water (3 mL) was added at room temperature. After separation of the phases, the aqueous phase was extracted with CH_2Cl_2 (3×10 mL) and the combined organic phase was subsequently washed with a 20% H_2SO_4, a sat. $NaHCO_3$ solution, brine to neutral pH. Drying with Na_2SO_4 and subsequent evaporation of the solvent gave a crude reaction product, which was submitted to flash chromatography (8% ethyl acetate/light petroleum ether) to give polar ketone **8** (134 mg, 0.2 mmol, 73%), as a pale yellow oil. IR liquid film (ν, cm^{-1}): 745, 1144, 1309, 1394, 1449, 1665, 1791, 2289, 2986, 3365. ^{1}H NMR (400 MHz, δ_H): 0.82 (*s*, 3H, H-29), 0.87 (*s*, 3H, H-28), 0.92 (*s*, 3H, H-30), 1.65 (*s*, 3H, H-26), 1.68 (*s*, 3H, H-24), 1.82 (s, 3H, H-25), 4.04 (*d, J* = 6.6 Hz, 2H, H-23), 4.42 (*d, J* = 0.9 Hz, 1H, H_b-27), 4.51 (s, 2H, H-1'), 4.82 (*d*, *J* = 1.0 Hz, 1H, H_a-27), 5.15 (*d*, *J* = 3.0 Hz, 1H, H-14), 5.46 (*t*, *J* = 6.6 Hz, 1H, H-22), 5.63 (*d*, *J* = 3.0 Hz, 1H, H-15), 6.69 (*m*, 1H, H-18), 7.31 (*m*, 5H, Ar-H), 7.65 (*m*, 5H, Ph-H). ^{13}C NMR (100 MHz, δ_C): 11.8 (*q*, C-25), 16.4 (*q*, C-24), 17.1 (*q*, C-26), 26.3 (*t*, C-11), 19.3 (*t*, C-2), 20.1 (*q*, C-30), 21.7 (*q*, C-29), 24.4 (*t*, C-6), 27.6 (*t*, C-19), 33.25 (*s*, C-4), 33.28 (*q*, C-28), 37.9 (*t*, C-20), 38.3 (*t*, C-7), 39.0 (*t*, C-1), 40.39 (*t*, C-12), 40.41 (*s*, C-10), 41.8 (*t*, C-3), 51.9 (*d*, C-5), 56.3 (*d*, C-9), 66.5 (*t*, C-23), 68.7 (*d*, C-15), 72.3 (*t*, C-1'), 106.2 (*t*, C-27), 113.5 (*d*, C-14), 122.2 (*d*, C-22), 127.5 (*d*, C-5'), 127.8 (*d*, C-3', 7'), 128.3 (*d*, C-4', 6'), 128.5 (*d*, C-3'', 5''), 130.0 (*d*, C-2'', 6''), 133.7 (*d*, C- 4''), 137.4 (*s*, C-1''), 137.8 (*s*, C-17), 138.4 (*s*, C-2'), 138.6 (*s*, C-21), 145.0 (*d*, C-18), 147.1 (*s*, C-13), 148.5 (*s*, C-8), 192.2 (*s*, C-16). Found (%): C, 76.83; H, 8.82. $C_{43}H_{58}SO_4$. Calculated (%): C, 76.97; H, 8.71.

[5(10),13E,17E,21E]-15-phenylsulfonyl-16-oxo-30(10→9)-abeo-bicyclofarnesylfarnesol benzyl ether (9). Compound **8** (40 mg, 0.06 mmol) was dissolved in 2-nitropropane (0.7 mL) and a solution of FSO_3H (0.017 mL, 0.3 mmol, 5 equiv.) in 2-nitropropane (0.2 mL) was added under argon to the resulting solution at –78°C. After 20 min of stirring,

the reaction mixture was quenched with a solution of triethylamine (0.5 mL) in light petroleum ether (0.5 mL), then reaction mixture was wormed to room temperature, diluted with brine (10 mL). After usual work-up the crude reaction product (42 mg), was submitted to flash chromatography (1% ethyl acetate/benzene) to give compound **9** (25 mg, 62%). IR liquid film (ν, cm^{-1}): 740, 1145, 1312, 1385, 1451, 1668, 1793, 2286, 2993, 3362. ^{1}H NMR (see: Table 1). ^{13}C NMR (see: Table 1). Found (%): C, 77.12; H, 8.91. $C_{43}H_{58}SO_4$. Calculated (%): C, 76.97; H, 8.71.

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