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Superacidic Low Temperature Cyclization of Terpenylphenylsulfones

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Abstract: The superacidic cyclization of aliphatic and partially cyclized C_{10}-C_{20} terpenylphenylsulfones proceeds structure-selectively and stereospecifically, affording α- or mixtures of α- and γ-isomers of completely cyclized terpenylphenylsulfones. The configuration of the phenylsulfonylmethylene group in the cyclized products is predetermined by the configuration of the allylic double bond in the starting compounds.

As it was shown previously,[1-3] superacidic low temperature cyclization of aliphatic and partially cyclic terpenoids (alcohols, acetates, acids and their esters) is a stereospecific, structure- and chemoselective process resulting in fully cyclized terpenoids in good yields. In this paper the results of systematic and comparative cyclization studies of a number of terpenylphenylsulfones are presented, taking into account the fact that cyclic sulfones often served as valuable synthons for the preparation of naturally occurring compounds. The cyclization of aliphatic C_{10}-C_{20}- and bicyclic C_{20}-terpenylphenylsulfones was investigated. It should be mentioned that geranyl- and farnesylphenylsulfones cyclization by Lewis acids has previously been studied.[4,6-12]

The synthesis of aliphatic C_{10}-C_{20}-terpenylphenylsulfones **5a-5c** and **6a-6c** was performed starting from geraniol (**1a**), nerol (**2a**), *E,E*-farnesol (**1b**), *Z,E*-farnesol (**2b**), *E,E,E*-geranylgeraniol (**1c**) and *Z,E,E*-geranylgeraniol (**2c**) which were commercially available or were prepared by standard well known procedures (Scheme 1). On reaction with phosphorus tribromide[13] compounds **1a-1c** and **2a-2c** were converted into the corresponding bromides **3a-3c** and **4a-4c** which, without purification, were treated with sodium phenylsulfinate in DMF,[14] giving the desired phenylsulfones **5a-5c** and **6a-6c**. The synthesis of diterpenic bicyclic sulfones **9** and **10** was achieved according to the same scheme starting from Δ^7-isomanool (**7**).[15] The latter on bromination with phosphorus tribromide led to a mixture of bromides **8**, which reacted with sodium phenylsulfinate affording a mixture of sulfones **9** and **10**. This mixture was separated chromatographically into individual sulfones **9** and **10**. Sulfones **5a** and **5b** were identified on comparison of their spectral data with those reported in literature.[8,9] The

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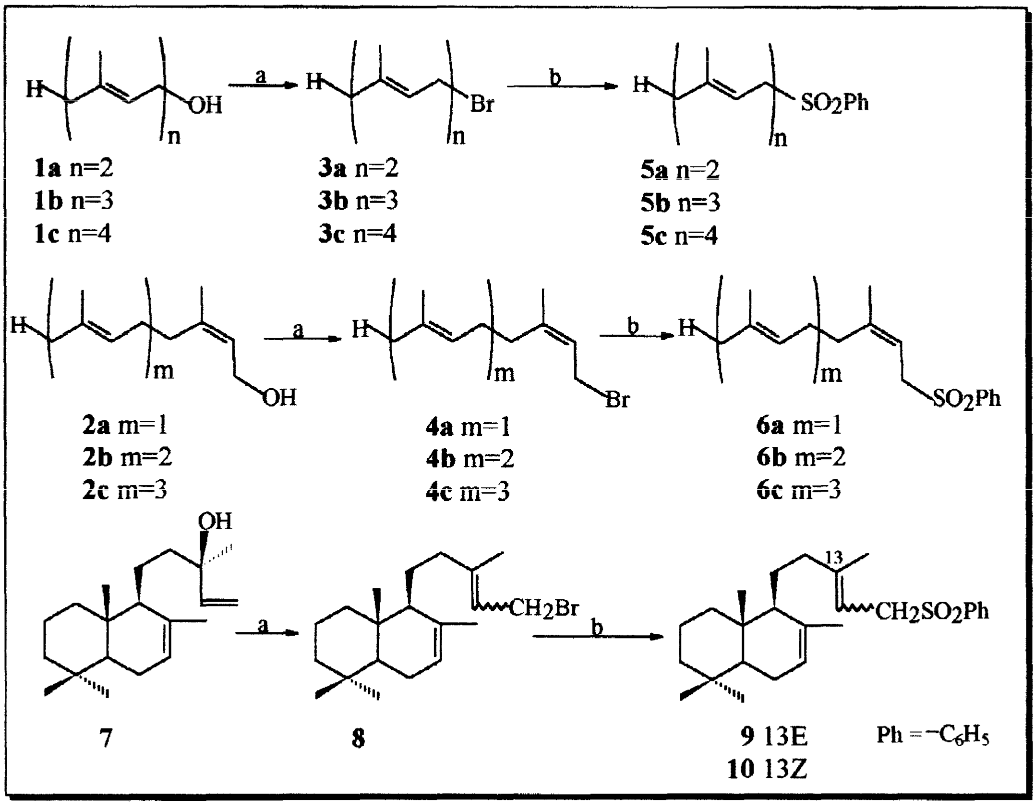
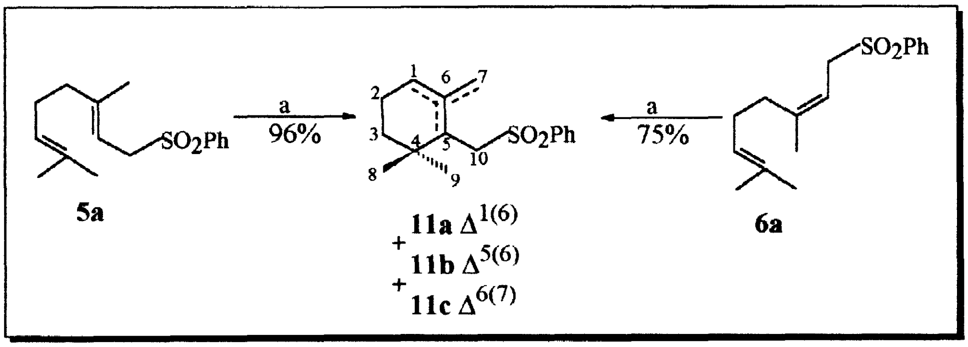
structure of compounds **5c**, **6a-6c**, **9** and **10** was established on the basis of their spectral data (IR, NMR) and elemental analysis (see experimental part).



Scheme 1. a. PBr_3, Et_2O-Py, 0°C; b. $NaSO_2Ph$, DMF, 25°C.

On cyclization of geranylphenylsulfone (**5a**) with FSO_3H (ratio substrate : cyclization agent 1:5, -78°C, 15 min) (see Table 1, entry 1) a mixture of α-, β- and γ-cyclogeranylphenylsulfones (**11a**) - (**11c**) was obtained in 96% total yield (ratio **11a**:**11b**:**11c** = 46:15:39) (Scheme 2). In such a way α-cyclogeranylphenylsulfone (**11a**) predominated in this mixture. Compounds **11a-11c** were identified by comparison of their spectral data with those reported.[5,8]



Scheme 2. a. FSO_3H (5 mol eq), *i*-$PrNO_2$, -78°C, 15 min.

Cyclization of nerylphenylsulfone (**6a**) under the same reaction conditions as for sulfone **5a** also led to a mixture of isomeric cyclogeranylphenylsulfones (**11a**)-(**11c**) in 75% total yield, but in this case the ratio of isomers is different (**11a**:**11b**:**11c** = 25:12:63), with exocyclic isomer **11c** predominating. Thus, the superacidic cyclization of geranyl- and nerylphenylsulfones (**5a**) and (**6a**) is stereospecific, but structurally only selective. An reasonable explanation of this fact could be the enhanced conformational mobility of intermediate monocyclic carbocations.

It is noteworthy that on cyclization of geranylphenylsulfone (**5a**) by both proton and Lewis acids, mixtures of only endocyclic isomers **11a** and **11b** have been obtained in high yield (87-93%),[8] and the reaction took longer time (0.5 - 32h). Cyclization of nerylphenylsulfone (**6a**) had not been studied before.

Table 1. **Cyclization of terpenylphenylsulfones by fluorosulfonic acid[a].**

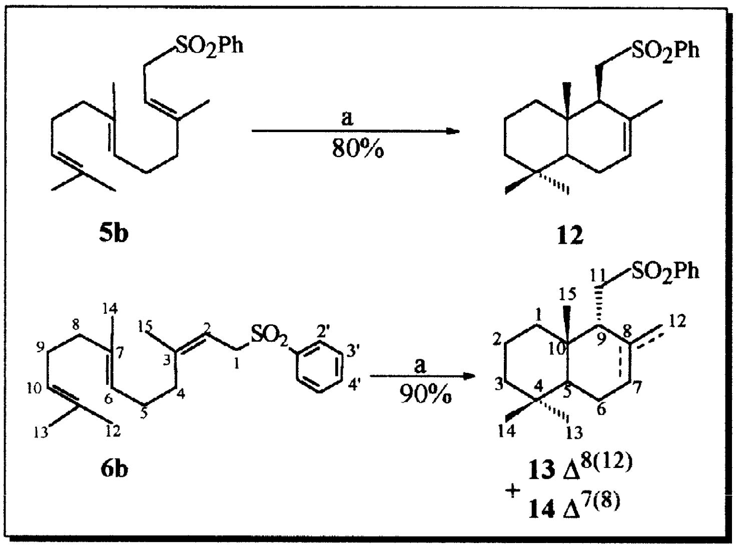
Entry	Substrate	Substrate solution mg (mmol)/*i*-PrNO$_2$ (ml)	FSO$_3$H solution mg (mmol)/*i*-PrNO$_2$ (ml)	Reaction products	Total yield (%)
1.	**5a**	390 (1.40) / 5.00	702 (7.02) / 1.50	(±)**11a** (46) (±)**11b** (15) (±)**11c** (39)	96
2.	**6a**	59 (0.21) / 0.75	106 (1.06) / 0.25	(±)**11a** (25) (±)**11b** (12) (±)**11c** (63)	75
3.	**5b**	70 (0.20) / 0.80	106 (1.06) / 0.30	(±)**12**	80
4.	**6b**	30 (0.09) / 0.30	45 (0.45) / 0.15	(±)**13** (80) (±)**14** (20)	90
5.	**5c**	34 (0.08) / 0.30	42 (0.42) / 0.15	(±)**15**	71
6.	**9**	305 (0.74) / 2.60	368 (3.68) / 0.80	(+)**15**	85
7.	**6c**	38 (0.09) / 0.30	46 (0.46) / 0.15	(±)**16** (80) (±)**17** (20)	71
8.	**10**	310 (0.75) / 2.80	375 (3.75) / 0.90	(-)**16** (80) (+)**17** (20)	82

[a] **Reaction conditions**: *i*-PrNO$_2$, -78°C, 15 min.

Superacidic cyclization of *E,E*-farnesylphenylsulfone (**5b**) (Table 1, entry 3) proceeded stereo- and structure-specifically, the drim-7-en-phenylsulfone (**12**) being the only reaction product isolated in high yield (80%) (scheme 3). Its spectral data (IR, ^{1}H NMR) were identical with those published.[9,11] Under the same reaction conditions *Z,E*-farnesylphenylsulfone (**6b**) gave in 90% total yield the mixture (4:1) of 9-*epi*-drim-

8(12)-en- and 9-*epi*-drim-7-en-phenylsulfones (**13**) and (**14**) (Table 1, entry 4) separated by chromatography on a SiO_2 column. The ^1H NMR spectrum of the minor product **14** was very similar to that of drimenylphenylsulfone (**12**). It contained the signals of three methyl groups attached to quaternary carbon atoms, one methyl group linked to an alkene carbon atom, a vinylic proton (5.32 ppm), a multiplet of allylic pseudoequatorial proton (1.96 ppm) and the doublet of doublets at 2.82 and 3.45 ppm, corresponding to the CH_2SO_2Ph group. These data, as well as the ^{13}C NMR spectrum (see experimental part), are consistent with structure **14** for minor reaction product. Therefore, the C-9 proton signal appears in the NMR spectrum of sulfone **14** in a stronger field, if compared with its epimer **12** (2.63 ppm).[11] The structure of the main reaction product **13** was also revealed on the basis of its spectral data. The only difference between ^1H NMR spectra of sulfones **13** and **14** was the presence in the former of the signals of the exocyclic double bond (broad singlets at 4.46 and 4.62 ppm) instead of the signal of only one vinylic proton in the spectrum of compound **14**. The IR and ^{13}C NMR spectra, as well as elemental analysis data, confirmed the structure of sulfone **13**. In such a way, the superacidic cyclization of *Z,E*-farnesylphenylsulfone (**6b**) is still stereospecific but structurally only selective, though to a high degree.

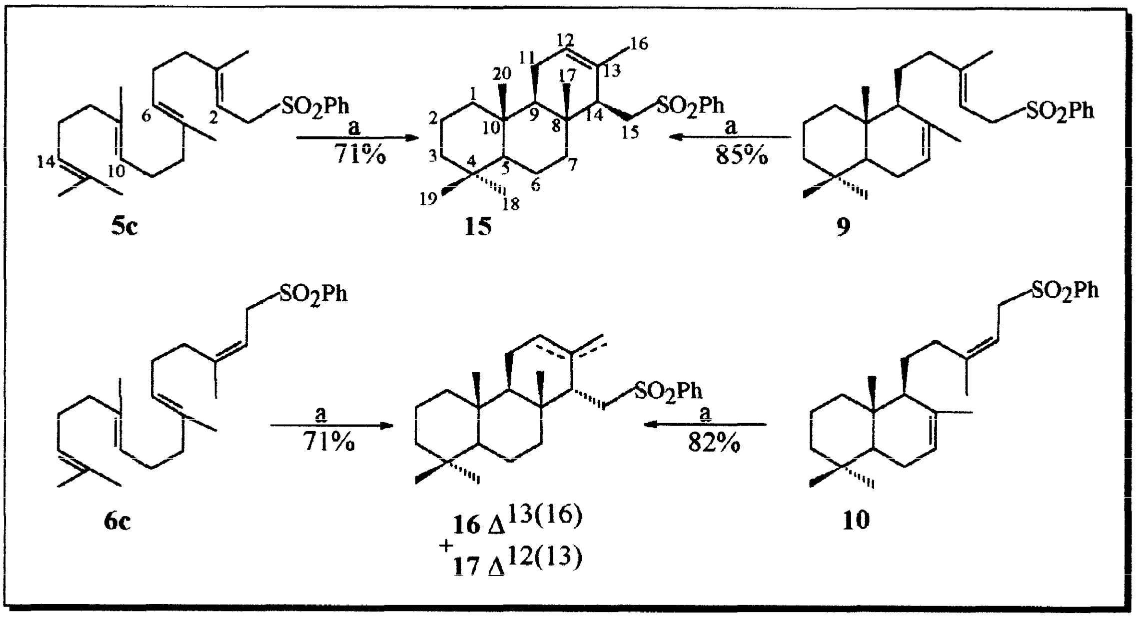
It should be mentioned that previously drimenylphenylsulfone (**12**) was obtained in good yield (77%) on tin(IV) chloride cyclization of *E,E*-farnesylphenylsulfone (**5b**).[9,11]



Scheme 3. a. FSO_3H (5 mol eq), *i*-$PrNO_2$, -78°C, 15 min.

Superacidic cyclization of diterpenic phenylsulfones **5c**, **6c**, **9** and **10** was performed under the same reaction conditions as in the case of their mono- and sesquiterpenic analogues. On all-*trans*-geranylgeranylphenylsulfone (**5c**) cyclization the only reaction product was the tricyclic isoagathanic sulfone **15** isolated in 71% yield (Table 1, entry 5, Scheme 4). Its structure assignment was done on the basis of spectral and elemental analyses data. According to the ^1H MNR spectrum, it contained four methyl groups attached to quaternary carbon atoms, another attached to a double bond, a vinylic proton, an allylic pseudoaxial proton (signal at 2.67 ppm) and a pseudoequatorial -CH_2SO_2Ph group (doublet at 3.12 ppm) (compare with the ^1H NMR spectrum of sulfone **12**). The IR and ^{13}C NMR spectral data confirmed availability of structure **15** for the investigated compound. The optically active sulfone **15** was obtained in 85% yield on superacidic cyclization of the enantiomerically pure *13E*-bicyclogeranylgeranylphenylsulfone (**9**) (Table 1, entry 6). Thus, in the cases of compounds **5c** and **9** the cyclization process is structure- and stereospecific.

The cyclization of *Z,E,E*-geranylgeranylphenylsulfone (**6c**) afforded a mixture (4:1) of the isomeric isoagathanic tricyclic sulfones **16** and **17** in 71% total yield (Table 1, entry 7). The ^1H NMR data of the minor product **17** are quite similar with those of compound **15**. The main difference was the position of C-14 proton signal: 2.67 ppm for compound **15** and 2.00 ppm for its epimer **17**, indicating that this proton is pseudoequatorial in the latter sulfone and pseudoaxial in the former one. The structure of the predominating sulfone **16** resulted from spectral (^1H, ^{13}C NMR, IR) and elemental analysis data (see experimental part). The optically active isoagathanic phenylsulfones **16** and **17** were prepared on superacidic cyclization of the enantiomerically pure *13Z*-bicyclogeranylgeranylphenylsulfone (**10**). It is noteworthy that the ratio of isomeric sulfones **16** and **17** on the cyclization of bicyclic precursor **10** is the same (4:1) as in the case of aliphatic substrate **6c**. Hence, on cyclization of *Z*-isomeric sulfones **6c** and **10**, the reaction is stereospecific, but structurally selective.



Scheme 4. a. FSO_3H (5 mol eq), *i*-$PrNO_2$, -78°C, 15 min.

In conclusion, it was shown that the regularities of superacidic cyclization of terpenylphenylsulfones differ from those observed previously[1-3] for other terpenic derivatives (alcohols, acids, esters etc.) On cyclization of terpenylphenylsulfones with *trans*-allylic double bond, the reaction products are, as well as in the case of other terpenic derivatives, the α-isomers of fully cyclized compounds with pseudoequatorial -CH_2SO_2Ph group, that is the reaction is stereo- and structure specific. Unlike this, the cyclization of terpenylphenylsulfones with *cis*-allylic double bond leads to mixtures of α- and γ-isomers of fully cyclized sulfones with pseudoaxial $-CH_2SO_2Ph$ group in which γ-isomers are predominating. The reaction is still stereospecific but structurally selective. The most probable explanation of this fact might be the anchymeric assistance of a sulfone group on the stabilization of intermediately formed carbocations which facilitates scrambling the proton from the methyl group attached to a positively charged carbon atom. Making use of molecular models supports this assumption. The monoterpenic phenylsulfones are an exception to these regularities.

Experimental

General experimental procedures. M.p. were determined on a Boetius apparatus and are uncorrected. The IR spectra were taken on a Bio-Rad FTS 7 and Specord 74 IR spectrophotometers. ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ on Bruker AM 400 and Bruker WM 300 spectrometers, chemical shifts are reported in ppm, referenced to $CHCl_3$ as internal standard (δ 7.26 for proton and δ 77.00 for carbon). Optical rotations were measured in $CHCl_3$ on a Jasco DIP 370 polarimeter, using a 10-cm microcell. Commercial Merck Si gel 60 (70-230 mesh ASTM) was used for column chromatography (CC), and Merck precoated Si gel plates were used for TLC. The chromatograms were sprayed with 0.1% $Ce(SO_4)_2$ in 2N H_2SO_4 and heated at 80°C for 5 min to detect the spots.

Synthesis of terpenylphenylsulfones (general procedure). The terpenic allylic bromides were obtained on bromination of corresponding allylic alcohols with phosphorus tribromide[13] and used in the next step without purification and characterization. Phenylsulfones were obtained on treatment of the corresponding bromides with sodium phenylsulfinate[14] and purified by CC.

Geranylphenylsulfone (5a). According to the general procedure, from 1.0 g (6.5 mmol) of geraniol (**1a**) 1.35 g (74%) of geranylphenylsulfone (**5a**) were obtained. All physical properties and spectroscopic (^1H NMR and IR) data were identical with those previously reported.[8]

Nerylphenylsulfone (6a). From 1.0 g (6.5 mmol) of nerol (**2a**) 1.2 g (66%) of nerylphenylsulfone (**6a**) were obtained: oil, IR ($CHCl_3$): ν_{max} 1134, 1307, 1586, 1654 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$, δ): 1.52 (s, 3H, CH_3-9), 1.63 (s, 3H, CH_3-8), 1.71 (bs, 3H, CH_3-10), 3.79 (d, J=8 Hz, 2H, H_2-1), 4.93 (m, 1H, H-6), 5.19 (t, J=8 Hz, 1H, H-2), 7.5-7.95 (m, 5H, Ar-H). Found (%): C, 69.13; H, 7.92; S, 11.45. $C_{16}H_{22}SO_2$ Requires (%): C, 69.02; H, 7.97; S, 11.52.

***E,E*-Farnesylphenylsulfone (5b).** From 1.2 g (4.2 mmol) of *E,E*-farnesylbromide **(4b)** 1.3 g (89%) of *E,E*-farnesylphenylsulfone **(5b)** were obtained. All physical properties and spectroscopic (^1H NMR and IR) data were identical with those reported in literatutre.[9]

***Z,E*-Farnesylphenylsulfone (6b).** From 1.0 g (4.5 mmol) of *Z,E*-farnesol **(2b)**[2] 1.3 g (83%) of *Z,E*-farnesylphenylsulfone **(6b)** were obtained: oil, IR ($CHCl_3$): ν_{max} 1147, 1307, 1653, 1707 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$, δ): 1.54 (bs, 3H, CH_3-14), 1.59 (s, 3H, CH_3-12), 1.72 (bs, 3H, CH_3-13), 1.79 (bs, 3H, CH_3-15), 3.80 (d, J=8 Hz, 2H, H_2-1), 4.80-5.10 (m, 2H, H-6 and H-10), 5.20 (m, 1H, H-2), 7.50-7.91 (m, 5H, Ar-H). Found (%): C, 72.53; H, 8.85; S, 9.01. $C_{21}H_{30}SO_2$ Requires (%):C, 72.78; H, 8.73; S, 9.25.

***E,E,E*-Geranylgeranylphenylsulfone (5c).** From 204 mg (0.67 mmol) of *E,E,E*-geranylgeraniol **(1c)** 209 mg (75%) of *E,E,E*-geranylgeranylphenylsulfone **(5c)** were obtained: oil, IR ($CHCl_3$): ν_{max} 1307, 1147, 1667, 1734 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$, δ): 1.31 (bs, 3H, CH_3-20), 1.59 (s, 9H, CH_3-16, CH_3-18 and CH_3-19), 1.68 (s, 3H, CH_3-17), 3.80 (d, J=8 Hz, 2H, H_2-1), 4.90-5.10 (m, 3H, H-6, H-10 and H-14), 5.20 (m, 1H, H-2), 7.50-7.91 (m, 5H, Ar-H). ^{13}C NMR ($CDCl_3$, δ): 56.11 (C-1, t), 110.31 (C-2, d), 138.70 (C-3, s), 39.82 (C-4, t), 26.00 (C-5, t), 123.32 (C-6, d), 134.42 (C-7, s), 39.72 (C-8, t), 26.61 (C-9, t), 124.09 (C-10, d), 135.06 (C-11, s), 39.72 (C-12, t), 26.76 (C-13, t), 124.36 (C-14, d), 131.30 (C-15, s), 17.69 (C-16, q), 25.70 (C-17, q), 16.01 (C-18, q), 16.19 (C-19, q), 17.69 (C-20, q), 146.45 (C-1', s), 128.94 (C-2', d), 128.12 (C-3', d), 130.12 (C-4', d). Found (%): C, 75.25; H, 9.16; S, 7.63. $C_{26}H_{38}SO_2$ Requires (%): C, 75.31; H, 9.24; S, 7.73.

***Z,E,E*-Geranylgeranylphenylsulfone (6c).** From 180 mg (0.59 mmol) of *Z,E,E*-geranylgeraniol **(2c)** 178 mg (73%) of *Z,E,E*-geranylgeranylphenylsulfone **(6c)** were obtained: oil, IR ($CHCl_3$): ν_{max} 1302, 1147, 1585, 1654 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$, δ): 1.54 (s, 3H, CH_3-18), 1.57 (s, 3H, CH_3-16), 1.59 (s, 3H, CH_3-19), 1.60 (s, 3H, CH_3-17), 1.73 (s, 3H, CH_3-20), 3.79 (dd, J=3.9 and 7.9 Hz, 2H, H_2-1), 4.96 (m, 1H, H-14), 5.09 (m, 2H, H-6 and H-10), 5.20 (m, 1H, H-2), 7.50-7.91 (m, 5H, Ar-H). ^{13}C NMR ($CDCl_3$, δ): 55.95 (C-1, t), 110.80 (C-2, d), 138.74 (C-3, s), 39.72 (C-4, t), 25.95 (C-5, t), 123.09 (C-6, d), 136.25 (C-7, s), 39.64 (C-8, t), 26.58 (C-9, t), 124.04 (C-10, d), 134.95 (C-11, s), 31.83 (C-12, t), 26.76 (C-13, t), 124.34 (C-14, d), 131.30 (C-15, s), 17.68 (C-16, q), 25.70 (C-17, q), 16.01 (C-18, q), 16.01 (C-19, q), 23.54 (C-20, q), 146.45 (C-1', s), 128.96 (C-2', d), 128.45 (C-3', d), 133.52 (C-4', d). Found (%): C, 75.15; H, 9.36; S, 7.44. $C_{26}H_{38}SO_2$ Requires (%): C, 75.31; H, 9.24; S, 7.73.

***13E*- and *13Z*-Bicyclogeranylgeranylphenylsulfones (9) and (10).** From 2.3 g (7.931 mmol) of Δ^7-isomanool[16] **(7)** 1.95 g (63%) of the mixture of *13E*- and *13Z*-bicyclogeranylgeranylphenylsulfones **(9)** and **(10)** were obtained. Chromatography on Si gel using a gradient elution (hexane - 10% EtOAc/hexane) gave *13Z*-isomer **10** 0.39 g, mixture of **9** and **10** 0.36 g and *13E*-isomer **9** 1.2 g.

***13E*-Bicyclogeranylgeranylphenylsulfone (9).** Colorless crystals, m.p. 82-83 °C (from hexane). $[\alpha]^{23}_D$ +25.46° (c 0.48; $CHCl_3$). IR ($CHCl_3$): ν_{max} 1320, 1147, 1590, 1653 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, δ): 0.73 (s, 3H, CH_3-20), 0.85 (s, 3H, CH_3-19), 0.87 (s, 3H, CH_3-18), 1.33 (s, 3H, CH_3-16), 1.64 (s, 3H, CH_3-17), 3.80 (d, J=8.0 Hz, 2H, H_2-15), 5.19 (bs, 1H, H-7), 5.40 (bs, 1H, H-14), 7.50-7.87 (m, 5H, Ar-H). Found (%): C, 75.56; H, 9.46; S, 7.39. $C_{26}H_{38}SO_2$ Requires (%): C, 75.31; H, 9.24; S, 7.73.

***13Z*-Bicyclogeranylgeranylphenylsulfone (10).** Oil; $[\alpha]^{23}_D$ +0.84° (c 0.57; $CHCl_3$). IR ($CHCl_3$): ν_{max} 1307, 1147 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$, δ): 0.66 (s, 3H, CH_3-20), 0.84 (s, 3H, CH_3-19), 0.86 (s, 3H, CH_3-18), 1.62 (s, 3H, CH_3-17), 1.75 (s, 3H, CH_3-16), 3.70-3.81 (m, 2H, H_2-15), 5.20 (m, 1H, H-7), 5.37 (bs, 1H, H-14), 7.52-7.88 (m, 5H, Ar-H). Found (%): C, 75.36; H, 9.26; S, 7.47. $C_{26}H_{38}SO_2$ Requires (%): C, 75.31; H, 9.24; S, 7.73.

Superacidic cyclization of terpenylphenylsulfones (general procedure). To the solution of the respective terpenylphenylsulfone in 2-nitropropane chilled to -78°C, the solution of fluorosulfonic acid in the same solvent is added on vigorous stirring. After 10 min of stirring at the same temperature, the reaction mixture is quenched by adding a 50% excess (with respect to the amount of fluorosulfonic acid used) of triethylamine in hexane (1:1). After warming up to the ambient temperature, the stirring is interrupted and the reaction mixture is worked up by diluting twice with water and extracting exhaustively with diethyl ether. The organic extracts were washed successively with a 10% sulfuric acid solution, water, saturated $NaHCO_3$ solution and water. Crude reaction products were isolated after drying over anhydrous Na_2SO_4, filtering and removal of the solvent at reduced pressure. The results obtained are listed in Table 1.

(±)-11-Phenylsulfonyl-drim-7-ene (12). (see Table 1, entry 3): m.p. 111-112°C (from hexane); IR ($CHCl_3$): ν_{max} 1320, 1145 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$, δ): 0.68 (s, 3H, CH_3-15), 0.83 (s, 3H, CH_3-13), 0.86 (s, 3H, CH_3-14), 1.70 (s, 3H, CH_3-12), 2.63 (bs, 1H, H-9), 3.12 (d, J= 4.7 Hz, 2H, H_2-11), 5.48 (bs, 1H, H-7), 7.52-7.93 (m, 5H, Ar-H). Lit.[9] m.p.111-111.5 °C.

(±)-11-Phenylsulfonyl-9-*epi*-drim-8(12)-ene (13). (see Table 1, entry 4): m.p. 137-139°C (from hexane); IR ($CHCl_3$): ν_{max} 1320, 1147 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, δ): 0.78 (s, 3H, CH_3-15), 0.84 (s, 3H, CH_3-14), 0.92 (s, 3H, CH_3-13), 1.95 (m, 1H, H-9), 2.20 (m, 2H, H_2-7), 3.18 (dd, J=8.0 and 14.5 Hz, 1H, H-11), 3.43 (dd, J=3.1 and 14.5 Hz, 1H, H-15), 4.46 (bs, 1H, H-12), 4.62 (bs, 1H, H-12), 7.52-7.89 (m, 5H, Ar-H). ^{13}C NMR ($CDCl_3$, δ): 42.36 (C-1, t), 18.87 (C-2, t), 38.40 (C-3, t), 33.17 (C-4, s), 46.64 (C-5, d), 23.18 (C-6, t), 31.28 (C-7, t), 140.06 (C-8, s), 51.11 (C-9, d), 36.52 (C-10, s), 55.33 (C-11, t), 111.97 (C-12, t), 21.88 (C-13, q), 33.30 (C-14, q), 21.64 (C-15, q), 145.77 (C-1', s), 129.02 (C-2', d), 128.31 (C-3', d), 133.42 (C-4', d). Found (%): C, 72.59; H, 8.65; S, 9.01. $C_{21}H_{30}SO_2$ Requires (%): C, 72.78; H, 8.73; S, 9.25.

(±)-11-Phenylsulfonyl-9-*epi*-drim-7-ene (14). (see Table 1, entry 4): m.p. 133-135°C (from hexane); IR ($CHCl_3$): ν_{max} 1320, 1147 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, δ): 0.82 (s, 3H, CH_3-15), 0.88 (s, 3H, CH_3-13), 0.96 (s, 3H, CH_3-14), 1.56 (d, J=1.4 Hz, 3H, CH_3-12), 1.96 (m, 1H, H-9), 2.82 (dd, J=3.3 and 14.5 Hz, 1H, H-11), 3.45 (dd, J=6.0 and 14.5 Hz, 1H, H-11), 5.32 (bs, 1H, H-7), 7.52-7.88 (m, 5H, Ar-H). ^{13}C NMR ($CDCl_3$, δ): 42.54 (C-1, t), 18.42 (C-2, t), 38.53 (C-3, t), 29.70 (C-4, s), 47.18 (C-5, d), 22.41 (C-6, t), 192.13 (C-7, d), 133.55 (C-8, s), 54.52 (C-9, d), 36.16 (C-10, s), 58.99 (C-11, t), 21.73 (C-12, q), 24.03 (C-13, q), 32.07 (C-14, q), 21.38 (C-15, q), 140.35 (C-1', s), 129.26 (C-2', d), 128.18 (C-3', d), 134.79 (C-4', d). Found (%): C, 72.54; H, 8.62; S, 9.03. $C_{21}H_{30}SO_2$ Requires (%): C, 72.78; H, 8.73; S, 9.25.

(+)-15-Phenylsulfonyl-isoagath-12-ene (15). (see Table 1, entry 6): m.p. 74-76°C (from hexane); $[\alpha]^{23}_D$ +0.84° (c 0.57; $CHCl_3$). IR ($CHCl_3$): ν_{max} 1307, 1147 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 0.65 (s, 3H, CH_3-20), 0.80 (s, 3H, CH_3-19), 0.85 (s, 6H, CH_3-17 and CH_3-18), 1.70 (s, 3H, CH_3-16), 2.67 (bs, 1H, H-14), 3.12 (d, J= 5.7 Hz, 2H, H_2-15), 5.49 (m, 1H, H-12), 7.55-7.95 (m, 5H, Ar-H). ^{13}C NMR ($CDCl_3$, δ): 39.84 (C-1, t), 18.50 (C-2, t), 41.80 (C-3, t), 33.10 (C-4, s), 55.86 (C-5, d), 18.50 (C-6, t), 41.80 (C-7, t), 39.84 (C-8, s), 54.43 (C-9, d), 39.67 (C-10, s), 22.82 (C-11, t), 124.09 (C-12, d), 133.49 (C-13, s), 54.53 (C-14, d), 55.86 (C-15, t), 21.70 (C-16, q), 15.25 (C-17, q), 21.89 (C-18, q), 33.34 (C-19, q), 14.71 (C-20, q), 140.60 (C-1', s), 129.27 (C-2', d), 128.08 (C-3', d), 131.19 (C-4', d). Found (%): C, 75.20; H, 9.21; S, 7.57. $C_{26}H_{38}SO_2$ Requires (%): C, 75.31; H, 9.24; S, 7.73.

(-)-15-Phenylsulfonyl-14-*epi*-isoagath-13(16)-ene (16). (see Table 1, entry 8): m.p. 166-167°C (from hexane); $[\alpha]^{23}_D$ -21.64° (c 1.35; $CHCl_3$). IR ($CHCl_3$): ν_{max} 1307, 1147 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, δ): 0.77 (s, 3H, CH_3-20), 0.79 (s, 3H, CH_3-19), 0.86 (s, 3H, CH_3-18), 0.91 (s, 3H, CH_3-17), 2.21 (dd, J=2.7 and 7.7 Hz, 1H, H-14), 3.16 (dd, J=7.7 and 14.6 Hz, 1H, H-15), 3.46 (dd, J=3.0 and 14.6 Hz, 1H, H-15), 4.39 (bs, 1H, H-16), 4.56 (bs, 1H, H-16), 7.52-7.90 (m, 5H, Ar-H). ^{13}C NMR ($CDCl_3$, δ): 40.15 (C-1, t), 18.55 (C-2, t), 41.94 (C-3, t), 33.30 (C-4, s), 55.54 (C-5, d), 18.55 (C-6, t), 41.94 (C-7, t), 37.58 (C-8, s), 51.21 (C-9, d), 37.14 (C-10, s), 22.85 (C-11, t), 30.83 (C-12, t), 139.94 (C-13, s), 51.38 (C-14, d), 56.80 (C-15, t), 111.45 (C-16, t), 21.58 (C-17, q), 21.89 (C-18, q), 33.40 (C-19, q), 15.96 (C-20, q), 145.64 (C-1', s), 129.00 (C-2', d), 128.30 (C-3', d), 133.40 (C-4', d). Found (%): C, 75.18; H, 9.22; S, 7.69. $C_{26}H_{38}SO_2$ Requires (%): C, 75.31; H, 9.24; S, 7.73.

(+)-15-Phenylsulfonyl-14-*epi*-isoagath-12-ene (17). (see Table 1, entry 8): m.p. 168-169°C (from hexane); $[\alpha]^{23}_D$ +81.71° (c 0.67; $CHCl_3$). IR ($CHCl_3$): ν_{max} 1307, 1147 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 0.82 (s, 3H, CH_3-20), 0.88 (s, 6H, CH_3-18 and CH_3-19), 0.94 (s, 3H, CH_3-17), 1.57 (s, 3H, CH_3-16), 2.00 (m, 1H, H-14), 2.81 (dd, J=3.2 and 15.3 Hz, 1H, H-15), 3.44 (dd, J=4.4 and 15.3 Hz, 1H, H-15), 5.28 (bs, 1H, H-12), 7.52-7.96 (m, 5H, Ar-H). ^{13}C NMR ($CDCl_3$, δ): 39.99 (C-1, t), 18.46 (C-2, t), 41.86 (C-3, t), 33.19 (C-4, s), 47.24 (C-5, d), 18.46 (C-6, t), 41.86 (C-7, t), 37.08 (C-8, s), 47.34 (C-9, d), 37.34 (C-10, s), 23.02 (C-11, t), 121.93 (C-12, d), 134.62 (C-13, s), 56.67 (C-14, d), 59.25 (C-15, t), 21.82 (C-16, q), 18.43 (C-17, q), 22.39 (C-18, q), 33.53 (C-19, q), 15.27 (C-20, q), 140.31 (C-1', s), 129.25 (C-2', d), 128.23 (C-3', d), 133.57 (C-4', d). Found (%): C, 75.21; H, 9.23; S, 7.59. $C_{26}H_{38}SO_2$ Requires (%): C, 75.31; H, 9.24; S, 7.73.

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