Cationic cyclization of (α-furyl)- and (β-furyl)methyl derivatives of (±)-limonene

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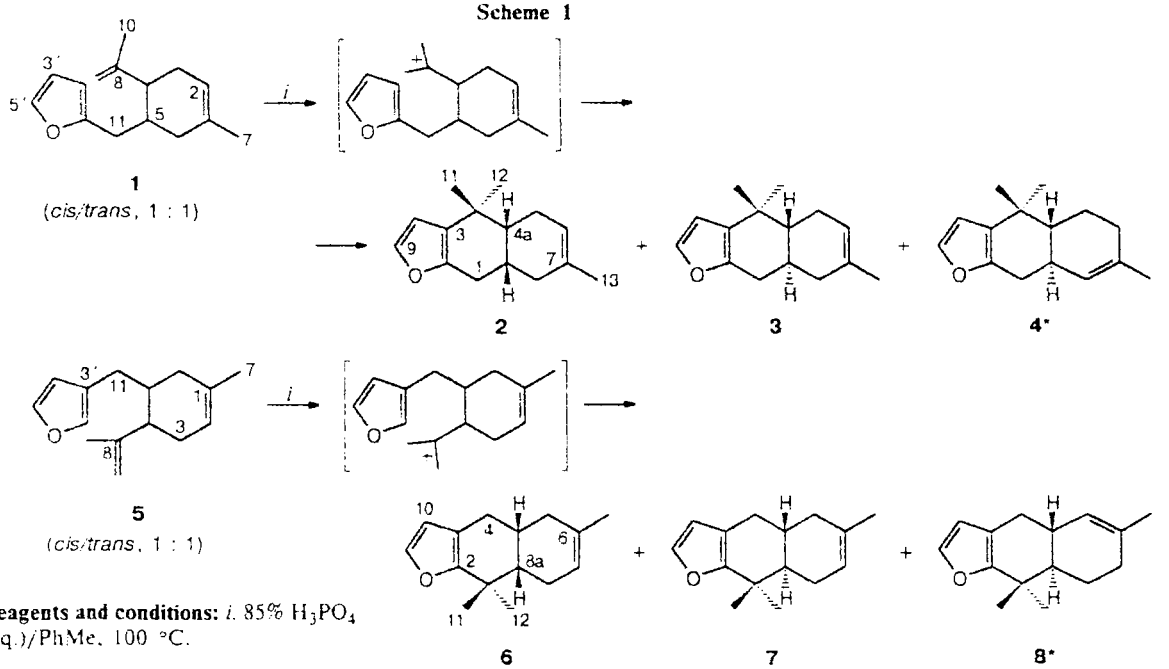
Cationic cyclization of the α- and β-furylmethyl (±)-limonene derivatives to give tricyclic furanoterpenoids, related to the metabolites of some marine organisms, was studied.

Key words: tricyclic furanoterpenoids; (±)-limonene derivatives; cationic cyclization; ^1H, ^{13}C, and 2D-NOESY NMR spectra.

In a continuation of our studies devoted to the synthesis of tricyclic furanoterpenoids,[1,2] in this work, we consider cationic cyclization (CC) of furylmethyl (±)-limonene derivatives **1** and **5** to give related structures (**2**—**4**, **6**—**8**) (Scheme 1).

Some examples of CC of type **1** and **5** compounds under the action of CF_3COOH, ZnI_2, $Tl(OCOCF_3)_4$, and $Hg(NO_3)_2$ have been reported. The yields of cyclization products in these reactions were low (<35%) (see Ref. 3). We found conditions that make it possible to increase markedly the efficiency of this process. For example, keeping a toluene solution of limonene derivatives **1** at 100 °C in the presence of 0.02 mol.equiv. of 85% H_3PO_4 (see Ref. 2) affords a mixture of bicyclic furanoterpenoids **2**—**4** in a ratio of ~4 : 1 : 3 and in a overall yield of >70%. Compounds **2** and **4** have been described in our previous study[2] and are racemic forms of a regioisomer (in the position of the multiple bond) and, correspondingly, of a stereoisomer of furodizinine, a natural metabolite of marine sponges.[3,4] Under similar

Scheme 1



Reagents and conditions: *i*. 85% H_3PO_4 (aq.)/PhMe, 100 °C.

* Obviously, compounds **4** and **8** are formed *via* the H_3PO_4-catalyzed shift of the multiple bond in the corresponding regioisomers **3** and **7** under the conditions of CC (*cf.* Ref. 2).

†Deceased.

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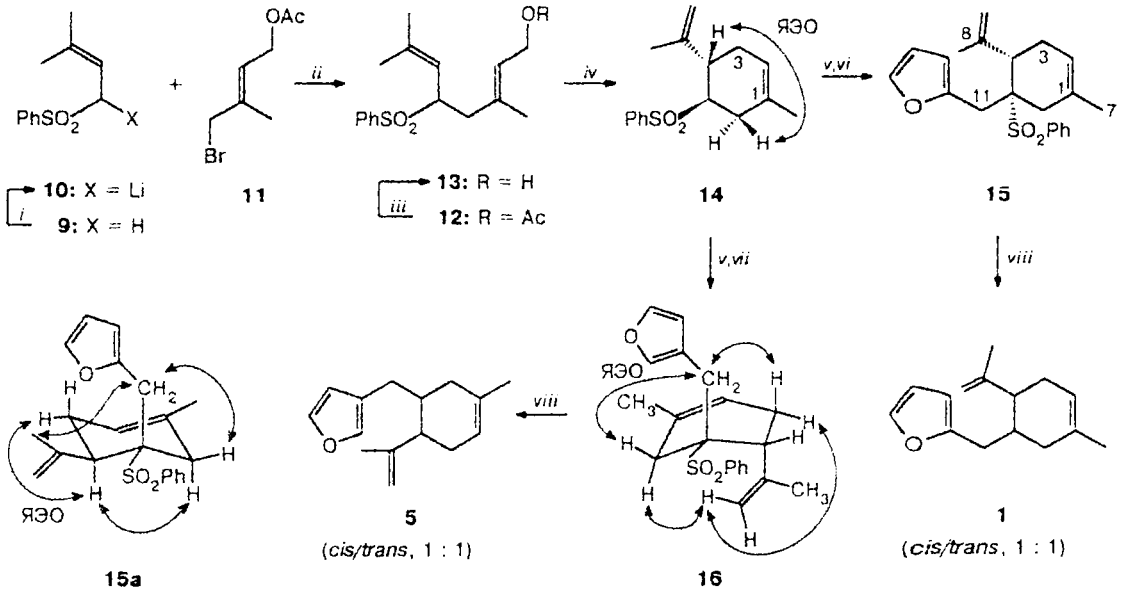
Scheme 2



Reagents and conditions: *i.* Bu^nLi/THF, −70 °C, *ii.* THF/HMPA; −20 °C, *iii.* KOH/H_2O/MeOH, 20 °C; *iv.* $F_3B \cdot OEt_2/CH_2Cl_2$, 0→20 °C; *v.* Bu^nLi/THF/HMPA, −70 °C; *vi.* (α-furyl)methyl chloride (**17**)/THF, −70 →0 °C; *vii.* (β-furyl)methyl chloride (**18**)/THF, −70→0 °C; *viii.* Li/NH_3/THF, −70 °C.

conditions, compound **5** is converted in ~70% yield into a mixture of regio- and stereoisomers (**6**—**8**) of a natural furanoterpenoid, furodizine,[3,4] formed in a ratio of ~4 : 1 : 3; compound **8** has also been synthesized in our previous work[2] by an alternative method. In both cases, the individual components of the mixtures mentioned above were quantitatively isolated by flash-chromatography on SiO_2 impregnated with 10% $AgNO_3$.

The initial (±)-limonene derivatives **1** and **5** were synthesized (Scheme 2) from the common precursor, sulfone **14**. This compound was alkylated with chlorides **17** or **18**, and then the corresponding sulfonyl derivatives **15** and **16** were desulfonylated by Li in NH_3. In its turn, sulfone **14** can be smoothly prepared by CC of diolefin **13**; the latter reaction proved to be stereospecific. Diolefin **13** results from condensation of known isobutene derivatives **9** (see Ref. 5) and **11** (see Ref. 6) followed by hydrolysis of the intermediate acetate **12**.* The 2*Z*-isomer, present in the latter compound as an impurity (~10%, according to ^1H NMR spectroscopy), apparently due to stereoisomers present in the initial bromide **11** (see Ref. 6), was separated by crystallization. In the case where crude acetate **12** is subjected to hydrolysis, the resulting mixture *E*-**13** and *Z*-**13** (~9 : 1) can be separated by chromatography on SiO_2.

It should be noted that alkylation of sulfone **14** with chlorides **17** and **18** is also highly stereoselective (the proportions of the minor *trans*-isomers in the reaction products do not exceed 10%, according to ^1H NMR spectroscopy), and the final stereochemical outcome of the above sequence of transformations resulted from the total absence of selectivity in the desulfonylation of compounds **15** and **16**; this accounts for the fact that products **1** and **5** were obtained as 1 : 1 mixtures of *cis*- and *trans*-isomers.

The structures of the previously unknown compounds **1**, **3**, **5**—**7**, and **12**—**16** were confirmed by the combination of data of spectroscopic and elemental analyses. In particular, the *trans*-configuration of the substituents in cyclohexene **14** is indicated by the magnitude of the vicinal spin-spin coupling constant $J_{HC(4)-HC(5)} = 9$ Hz in its ^1H NMR spectrum and also by the presence of the nuclear Overhauser effect (NOE, see Scheme 2), observed in the differential spectrum, for the HC(4) proton and for the HC(6) axial proton. The mutual arrangement of the substituents in sulfone **16** was determined from the data of the 2D NOESY spectrum (see Scheme 2). The configuration of this compound shown in the scheme is thermodynamically favorable as indicated by the fact that the spin-spin coupling constants calculated for it* coincide with those observed experimentally in its ^1H NMR spectrum. In fact, the value $J_{\beta\text{-}HC(3)-HC(4)} = 6.6$ Hz found experimentally is matched by the theoretical spin-spin coupling constant $J = 6.5$ Hz, and $J_{\alpha\text{-}HC(3)-HC(4)} <$

* CC of a ~ 9 : 1 mixture of *trans*-**12** and *cis*-**12** also yields sulfone **14**.

* Vicinal spin-spin coupling constants were calculated from the Karplus[7] equation with geometric parameters obtained by molecular mechanic calculations using the PCMODEL program.

2 Hz (estimated from the band broadening) is matched by a calculated value of 1.1 Hz. Similar criteria were used to prove the structure of sulfone **15**. Compounds **15** and **16** were first purified by crystallization from the impurities of *trans*-epimers that were difficult to separate by chromatography. The proportions (~10%) of these epimers in the reaction products were found by measuring the integral intensities of the additional ^{1}H NMR signals (not overlapping with the signals of protons of the major epimer) of the protons of diagnostic groups, in particular, HC(2) (δ ~ 5.3) and HC(4') (δ ~ 6.2). An epimer of sulfone **15** — **15a** — was isolated in a pure state by HPLC from the mother liquor remaining after crystallization and characterized by the data of spectral and elemental analyses. The configuration of the substituents in this compound was established from the presence of the corresponding NOE in its 2D NOESY spectrum (see Scheme 2), and the magnitudes of the $J_{HC(3)-HC(4)}$ vicinal spin-spin coupling constants confirm that its conformation with the axial orientation of the proton at C(4) is preferred. To determine the structures of new furanoterpenoids **3**, **6**, and **7**, their spectral characteristics were compared with those obtained previously for related structures.[2–4] The conclusion about the geometry of fusion of the rings in their molecules was based on the analysis of the spin-spin coupling constants of the HC(4a) and HC(8a) protons, which are 11.5 Hz for *trans*-**3** and *trans*-**7** and 2.2 Hz for *cis*-**6**.

Experimental

Melting points (not corrected) were determined using a Koffler unit. IR spectra (ν/cm^{-1}) were recorded on a Specord M-80 instrument as KBr pellets (unless otherwise stated). ^{1}H and ^{13}C NMR spectra (δ, J/Hz) of solutions in $CDCl_3$ were measured on Bruker AC-200, Bruker WM-250, and Bruker AMX-400 spectrometers, and DQF-COSY[9], NOESY,[10] and z-HMQC[11] spectra were measured on a Bruker AMX-400 instrument. Mass spectra (EI, 70 eV) were obtained on Varian MAT CH-6 and Varian MAT 311A instruments. The R_f values are given for a fixed SiO_2 layer (Silufol). HPLC was performed on a column with Silosorb 600 (10 μ, 250×24 mm) with a refractometric detector using a heptane—ethyl acetate mixture (9 : 1, v/v, 7 mL min^{-1}).

3,7-Dimethyl-5-phenylsulfonylocta-2*E*,6-dien-1-ol acetate (12). A 1.35 *M* solution of Bu^{n}Li (9.6 mL) in hexane (13 mmol) was added with intense stirring over a period of 10 min to a solution of sulfone **9** (2.52 g, 12 mmol) (see Ref. 5) in 40 mL of THF cooled to −70 °C (Ar). After 10 min, a solution of bromide **11** (2.07 g, 10 mmol) (see Ref. 6) in 10 mL of THF was added over a period of 5 min. The reaction mixture was kept for 20 min at −70 °C, warmed to 0 °C, and treated with ether and H_2O. The aqueous layer was separated and extracted with ether. The combined ethereal solutions were washed with water, dried with Na_2SO_4, and concentrated *in vacuo*. The residue (5.6 g) was chromatographed on 100 g of SiO_2. Elution with a hexane—ether mixture (7 : 3) gave 3.02 g (90%) of a mixture of *E*-**12**/*Z*-**12** (~9 : 1, according to ^{1}H NMR), whose crystallization from hexane afforded *E*-**12** as colorless needles, m.p. 51—52 °C. IR: 535, 560, 615, 695, 750, 780, 840, 970, 1030, 1090, 1150, 1230, 1305, 1370, 1450, 1735, 2860—2980. ^{1}H NMR: 1.10 and 1.62 (both br.s, 9 H, Me); 1.98 (s, 3 H, MeCO); 2.27 (dd, 1 H, HC(4), J = 14 and 11 Hz); 2.83 (br.d, 1 H, HC(4), J = 14 Hz); 3.84 (dt, 1 H, HCS, J = 11 and 3 Hz); 4.45 (d, 2 H, HCO, J = 7 Hz); 4.85 (br.d, 1 H, HC(6), J = 10.5 Hz); 5.30 (br.t, 1 H, HC(2), J = 7 Hz); 7.5—7.8 (m, 5 H, C_6H_5). Found (%): C, 64.14; H, 7.18; S, 9.42. $C_{18}H_{24}O_4S$. Calculated (%): C, 64.26; H, 7.19; S, 9.53.

3,7-Dimethyl-5-phenylsulfonylocta-2*E*,6-dien-1-ol (*E*-13) and 3,7-dimethyl-5-phenylsulfonylocta-2*Z*,6-dien-1-ol (*Z*-13). A 10% aqueous solution of KOH (7 mL) was added at 20 °C to a solution of a ~9 : 1 *E*-**12**/*Z*-**12** mixture (2.5 g, 7.43 mmol) in 30 mL of methanol. The reaction mixture was kept for 20 min and then concentrated by 3/4, and the residue was neutralized with 10% H_2SO_4 and exctracted with ether. The usual workup of the extract gave 2.1 g of a product, which was chromatographed on 150 g of SiO_2. Elution with a ether—ethyl acetate mixture (1 : 1) gave (in the order of elution) individual *Z*-**13** (0.2 g, 9%) and *E*-**13** (1.83 g, 84%).

Sulfone *Z*-**13**: colorless prisms, m.p. 110—111 °C (from ether). IR: 540, 600, 695, 720, 750, 780, 865, 900, 950, 995, 1090, 1145, 1285, 1380, 1400, 1450, 1580, 1670, 2860—3060, 3490. ^{1}H NMR: 1.04, 1.54, and 1.57 (all br.s, 9 H, Me); 2.41 (dd, 1 H, HC(4), J = 14 and 10.5 Hz); 2.74 (dd, 1 H, HC(4), J = 14 and 3 Hz); 3.78 (dt, 1 H, HCS, J = 10.5 and 3 Hz); 3.93 (dd, 1 H, HCO, J = 12 and 6.5 Hz); 4.04 (dd, 1 H, HCO, J = 12 and 7.2 Hz); 4.85 (br.d, 1 H, HC(6), J = 10.5 Hz); 5.40 (br.t, 1 H, HC(2), J = 7 Hz); 7.5—7.7 (m, 5 H, C_6H_5). Found (%): C, 65.35; H, 7.55; S, 10.79. $C_{16}H_{22}O_3S$. Calculated (%): C, 65.27; H, 7.53; S, 10.89.

Sulfone *E*-**13**: colorless prisms, m.p. 87—89 °C (from ether). IR: 530, 610, 690, 720, 750, 780, 850, 870, 915, 945, 1010, 1090, 1145, 1295, 1395, 1445, 1585, 1665, 2860—3060, 3505. ^{1}H NMR: 1.11, 1.56 and 1.61 (all br.s, 9 H, Me); 2.30 (dd, 1 H, HC(4), J = 14 and 11 Hz); 2.86 (dd, 1 H, HC(4), J = 14 and 3 Hz); 3.86 (dt, 1 H, HCS, J = 11 and 3 Hz); 4.03 and 4.09 (both dd, 2 H, HCO, J = 12 and 6.5 Hz); 4.87 (br.d, 1 H, HC(6), J = 11 Hz); 5.37 (br.t, 1 H, HC(2), J = 6.5 Hz); 7.6—7.8 (m, 5 H, C_6H_5). Found (%): C, 65.33; H, 7.50; S, 10.80. $C_{15}H_{22}O_3S$. Calculated (%): C, 65.27; H, 7.53; S, 10.89.

***trans*-4-Isopropenyl-1-methyl-5-phenylsulfonylcyclohex-1-ene (14).** $F_3B \cdot OEt_2$ (3.23 g, 22.8 mmol) was added at 0 °C (Ar) with intense stirring over a period of 10 min to a solution of alcohol *E*-**13** (2.25 g, 7.6 mmol) in 30 mL of CH_2Cl_2. The reaction mixture was warmed to 20 °C, kept for 30 min, quenched with a saturated solution of $NaHCO_3$, and extracted with ether. The usual workup of the extract gave 2.11 g of a product, which was chromatographed on 50 g of SiO_2. Elution with a hexane—ether mixture (4 : 1) gave 1.14 g (54%) of sulfone **14** as a colorless oil, R_f 0.45 (hexane—ether, 4 : 1). IR: 540, 580, 600, 650, 695, 720, 745, 800, 900, 1025, 1090, 1145, 1310, 1380, 1450, 1645, 2850—3070 (thin film). ^{1}H NMR: 1.58 and 1.62 (both br.s, 6 H, Me); 2.0—2.3 (m, 4 H, HC(3), HC(6)); 2.68 (ddd, 1 H, HC(4), J = 9.0, 7.0, and 7.0 Hz); 3.39 (dt, 1 H, HCS, J = 9.0 and 6.9 Hz); 4.78 and 4.85 (both m, 2 H, H_2C=); 5.35 (m, 1 H, HC(2)); 7.5—7.9 (m, 5 H, C_6H_5). ^{13}C NMR: 16.71, 23.04, 29.42; 30.32; 41.26; 61.93; 113.92; 120.19; 128.83; 129.09; 129.93; 133.49; 138.53; 145.36. Found (%): C, 69.23; H, 7.38; S, 11.48. $C_{16}H_{20}O_2S$. Calculated (%): C, 69.53; H, 7.29; S, 11.60.

Compound **14** (149 mg, 52%), virtually identical (^{1}H NMR) to the sample described above, was prepared from alcohol *Z*-**13** (0.3 g, 1.02 mmol) in a similar way.

The reaction involving the *E*-**12**/*Z*-**12** mixture (~9 : 1) (672 mg, 2.28 mmol) gave compound **14** (287 mg, 52%), virtually identical (^{1}H NMR) to the sample described above.

4α-Isopropenyl-1-methyl-5α-phenylsulfonyl-5β-(2′-furyl)methylcyclohex-1-ene (15) and 4β-isopropenyl-1-methyl-5α-phenylsulfonyl-5β-(2′-furyl)methylcyclohex-1-ene (15a). A 1.35 *M* solution of Bu^{n}Li in hexane (3.7 mL, 5 mmol) was added over a period of 10 min to a solution of sulfone **14** (1.32 g, 4.8 mmol) in a mixture of THF (10 mL) and HMPA (1 mL), stirred at −70 °C (Ar). After 10 min, a solution of chloride **17** (0.58 g, 5 mmol) (see Ref. 12) in THF (5 mL) was added over a period of 5 min. The reaction mixture was warmed to 0 °C over a period of 30 min and quenched with H_2O. The aqueous layer was separated and extracted with ether. The usual workup of the combined organic solutions gave 2 g of a product; the product was chromatographed on a column with 50 g of SiO_2. Elution with a hexane—ether (3 : 2) mixture gave 1.45 g (85%) of a **15/15a** mixture (~9 : 1, according to ^{1}H NMR), whose crystallization from hexane gave sulfone **15** as colorless needles, m.p. 98—100 °C. IR: 530, 570, 630, 695, 730, 745, 760, 800, 830, 910, 930, 1010, 1080, 1140, 1300, 1375, 1445, 1500, 1580, 1630, 2840—3140. ^{1}H NMR: 1.67 (br.s, 3 H, Me(7)); 1.76 (br.s, 3 H, Me(10)); 1.95 and 2.76 (both d, 2 H, HC(6), J = 17.2 Hz); 2.18 and 2.62 (both br.d, 2 H, HC(3), J = 18.4); 2.94 and 3.14 (both d, 2 H, HC(11), J = 16.5 Hz); 3.05 (dd, 1 H, HC(4), J = 7.2 and 2.3 Hz); 4.84 and 4.97 (both br.s, 2 H, HC(9)); 5.48 (br.s, 1 H, HC(2)); 6.20 (br.d, 1 H, HC(3′), J = 3.2 Hz); 6.29 (dd, 1 H, HC(4′), J = 3.2 and 1.9 Hz); 7.3 (m, 1 H, HC(5′)); 7.5—7.9 (m, 5 H, C_6H_5). ^{13}C NMR: 21.4 (Me-10); 23.3 (Me-7); 30.4 (C-3); 33.6 (C-11); 34.8 (C-6); 41.8 (C-4); 69.2 (C-5); 109.6 (C-3′); 110.3 (C-4′); 115.4 (C-9); 120.2 (C-2); 129.5 (C-1); 137.7 (C-8); 141.2 (C-5′); 150.1 (C-2′); 128.4, 130.4, 133.2, 146.5 (C arom.). Found (%): C, 70.68; H, 6.77; S, 8.88. $C_{21}H_{24}O_3S$. Calculated (%): C, 70.75; H, 6.78; S, 8.99.

Sulfone **15a** was isolated by HPLC from the mother liquor as colorless crystals, m.p. 96—98 °C (from hexane). IR: 530, 545, 570, 630, 700, 730, 755, 815, 910, 945, 1010, 1080, 1140, 1180, 1300, 1375, 1445, 1495, 1580, 1635, 2850—3140. ^{1}H NMR: 1.55 and 1.94 (both br.s, 6 H, Me-7, Me-10); 1.95 and 2.58 (both d, 2 H, HC(6), J = 16.7 Hz); 2.17 (br.d, 1 H, HC(3), J = 18.1 Hz); 2.33 (br.dd, 1 H, HC(3), J = 18.4 and 10.6); 3.02 (dd, 1 H, HC(4), J = 10.6 and 6.1 Hz); 3.22 and 3.55 (both d, 2 H, HC(11), J = 15.9 Hz); 4.96 and 4.98 (both br.s, 2 H, HC(9)); 5.28 (br.s, 1 H, HC(2)); 6.01 (br.d, 1 H, HC(3′), J = 3.2 Hz); 6.20 (dd, 1 H, HC(4′), J = 3.2 and 1.9 Hz); 7.14 (dd, 1 H, HC(5′), J = 1.9 and 0.8 Hz); 7.5—7.9 (m, 5 H, C_6H_5). ^{13}C NMR: 22.0; 23.0; 27.4; 31.1; 36.1; 44.8; 69.5; 109.5; 110.2; 115.9; 119.6; 128.1; 130.3; 130.6; 133.1; 137.1; 140.9;, 145.8; 150.1. Found (%): C, 70.70; H, 6.78; S, 8.91. $C_{21}H_{24}O_3S$. Calculated (%): C, 70.75; H, 6.78; S, 8.99.

4α-Isopropenyl-1-methyl-5α-phenylsulfonyl-5β-(3′-furyl)methylcyclohex-1-ene (16). The reaction of sulfone **14** (1.49 g, 5.4 mmol), a 1.35 *M* solution of Bu^{n}Li in hexane (4.1 mL, 5.6 mmol), and chloride **18** (0.7 g, 6 mmol) (see Ref. 13) in a mixture of THF (15 mL) and HMPA (1 mL) by a procedure similar to that described above gave 2.2 g of a product; the product was chromatographed on 50 g of SiO_2. Elution with a hexane—ether mixture (3 : 2) gave 1.59 g (83%) of compound **16** that contained the epimer as an impurity (~10%, according to ^{1}H NMR data). Crystallization from hexane afforded the individual diastereomer as colorless needles, m.p. 105—107 °C. IR: 570, 645, 740, 770, 880, 900, 1030, 1080, 1145, 1165, 1200, 1245, 1300, 1380, 1450, 1500, 1580, 1640, 2840—3140. ^{1}H NMR: 1.61 (br. s, 3 H, Me(7)); 1.77 (br.s, 3 H, Me(10)); 1.89 (d, 1 H, β-HC(6), J = 16.8 Hz); 2.06 (br.d, 1 H, α-HC(3), J = 18.2 Hz); 2.50 (m, 1 H, β-HC(3)); 2.74 (br.d, 1 H, α-HC(6), J = 17.0 Hz); 2.78 and 2.94 (both d, 2 H, HC(11), J = 15.9 Hz); 2.98 (br.d, 1 H, HC(4), J = 6.6 Hz); 4.80 and 4.97 (both br.s, 2 H, HC(9)); 5.49 (m, 1 H, HC(2)); 6.38 (br.s, H, HC(4′)); 7.25 (br.s, 1 H, HC(2′)); 7.33 (br.s, 1 H, HC(5′)); 7.5—7.9 (m, 5 H, C_6H_5). ^{13}C NMR: 21.5 (Me-7); 23.3 (Me-10); 30.4 (C-3); 30.8 (C-11); 34.9 (C-6); 41.4 (C-4); 69.3 (C-5); 112.9 (C-4′); 115.6 (C-9); 118.4 (C-3′); 120.1 (C-2); 130.0 (C-1); 138.0 (C-8); 141.96 (C-5′); 141.98 (C-2′); 128.4, 130.4, 133.2, 146.4 (C arom.). Found (%): C, 70.81; H, 6.85; S, 8.84. $C_{21}H_{24}O_3S$. Calculated (%): C, 70.75; H, 6.78; S, 8.99.

***cis*-/*trans*-4-Isopropenyl-1-methyl-5-(2′-furyl)methylcyclohex-1-ene (1).** At −70 °C (Ar), a solution of sulfone **15** (1.68 g, 4.7 mmol) in 30 mL of THF was added with intense stirring over a period of 10 min to a solution of Li (0.33 g, 47 mg.-at) in 150 mL of NH_3. The reaction mixture was kept for 20 min at −70 °C and quenched with excess NH_4Cl. Ammonia was evaporated, and the residue was treated with ether and water. The aqueous layer was separated and extracted with ether. The usual workup of the combined extracts gave 1 g of a substance; the product was chromatographed on 50 g of SiO_2. Elution with hexane gave 0.74 g (72%) of a mixture of *cis*-**1** and *trans*-**1** (~1 : 1, according to ^{1}H NMR spectrum) as a colorless oil, R_f 0.38 (hexane). Found (%): C, 83.11; H, 9.35. $C_{15}H_{20}O$. Calculated (%): C, 83.28; H, 9.32.

Chromatography of 0.2 g of this mixture on 70 g of SiO_2 impregnated with 10% $AgNO_3$ (using a 85 : 15 hexane—benzene mixture as the eluent) made it possible to isolate samples (20 mg each) of individual *cis*-**1** and *trans*-**1** in the order of elution, respectively.

***cis*-1.** IR: 600, 720, 900, 920, 1010, 1080, 1150, 1205, 1300, 1375, 1440, 1505, 1595, 1640, 2850—3070 ($CHCl_3$). ^{1}H NMR: 1.67 (br.s, 3 H, Me(7)); 1.8 and 2.1 (m, 4 H, HC(3), HC(6)); 1.82 (br.s, 3 H, Me(10)); 2.30 (m, 2 H, HC(4), HC(11)); 2.33 (m, 1 H, HC(5)); 2.44 (dd, 1 H, HC(11), J = 20.5 and 9.0 Hz); 4.77 and 4.92 (both br.s, 2 H, HC(9)); 5.45 (m, 1 H, HC(2)); 5.96 (dd, 1 H, HC(3′), J = 3.12 and 0.86); 6.29 (dd, 1 H, HC(4′), J = 3.13 and 1.88 Hz); 7.32 (dd, 1 H, HC(5′), J = 1.86 and 0.87 Hz). ^{13}C NMR: 22.79 (Me-10); 23.69 (Me-7); 25.97 (C-3); 25.69 (C-6); 33.28 (C-5); 34.43 (C-11); 42.67 (C-4); 105.58 (C-3′); 110.03 (C-4′); 110.26 (C-9); 120.02 (C-2); 131.07 (C-1); 140.80 (C-5′); 147.06 (C-8); 156.00 (C-2′).

***trans*-1.** IR: 600, 720, 900, 925, 1010, 1080, 1150, 1210, 1380, 1435, 1505, 1590, 1640, 2850—3080 ($CHCl_3$). ^{1}H NMR: 1.58 (br.s, 3 H, Me(7)); 1.65 (m, 1 H, HC(3)); 1.70 (br.s, 3 H, Me(10)); 1.9—2.2 (m, 5 H, HC(3), HC(4), HC(5), HC(6)); 2.25 (dd, 1 H, HC(11), J = 15.0 and 9.6 Hz); 2.80 (dd, 1 H, HC(11), J = 15.0 and 3.0 Hz); 4.84 (m, 2 H, HC(9)); 5.39 (m, 1 H, HC(2)); 6.01 (dd, 1 H, HC(3′), J = 3.3 and 0.9 Hz); 6.30 (dd, 1 H, HC(4′), J = 3.2 and 1.9 Hz); 7.33 (dd, 1 H, HC(5′), J = 1.9 and 0.9 Hz). ^{13}C NMR: 18.56 (Me-10); 23.38 (Me-7); 30.99 (C-6); 32.55 (C-3); 35.20 (C-5); 35.96 (C-11); 47.21 (C-4); 105.88 (C-3′); 110.03 (C-4′); 112.03 (C-9); 120.07 (C-2); 132.90 (C-1); 140.82 (C-5′); 147.84 (C-8); 155.16 (C-2′).

The reaction of **15a** (0.1 g, 0.28 mmol) and Li (20 mg, 2.9 mg-at) in NH_3 (10 mL) and THF (2 ml) carried out in a similar way gave 44 mg (72%) of a mixture of *cis*-**1** and *trans*-**1** (~1 : 1), virtually identical to the sample described above (^{1}H NMR data).

***cis*-/*trans*-4-Isopropenyl-1-methyl-5-(3′-furyl)methylcyclohex-1-ene (5).** The reaction of **15** (1.49 g, 4.18 mmol) carried out by a procedure similar to that described above for **1** gave 0.66 g (73%) of a mixture of *cis*-**5** and *trans*-**5** (~1 : 1, ^{1}H NMR data) as a colorless oil, R_f 0.36 (hexane). IR: 600, 730, 790, 880, 895, 1030, 1070, 1160, 1230, 1380, 1440, 1500,

1560, 1640, 2740—3140 (thin film). ^{1}H NMR: 1.67, 1.72, 1.80 and 1.88 (all br.s, 6 H, Me); 1.8—2.7 (m, 8 H, HC, H_2C); 4.82 and 4.98 (both.s, 2 H, HC(9) — *cis*-**5**); 4.90 (m, 2 H, HC(9) — *trans*-**5**); 5.43 and 5.51 (both m, 1 H, HC(2)); 6.28 and 6.32 (both m, 1 H, HC(4′)); 7.23 and 7.27 (both m, 1 H, HC(2′)); 7.40 (m, 1 H, HC(5′)). Found (%): C, 83.05; H, 9.54. $C_{15}H_{20}O$. Calculated (%): C, 83.28; H, 9.32.

Cyclization of limonene derivatives 1 and 5. Diolefin **1** (1.08 g, 5 mmol) was added in one portion to an emulsion of 85% H_3PO_4 (115 mg, 1 mmol) in 5 mL of PhMe stirred intensely at 100 °C (Ar). The mixture was kept for 2 h at 100 °C, then cooled to 20 °C over a period of 5 min, and diluted with ether. The ethereal extract was washed with a 5% solution of $NaHCO_3$ and water, dried with Na_2SO_4, and concentrated *in vacuo*, and the residue (1 g) was chromatographed on 20 g of SiO_2. Elution with hexane gave 0.81 g (75%) of a **2**/**3**/**4** mixture (~4 : 1 : 3, ^{1}H NMR data) as a colorless oil, R_f 0.38 (hexane).The mixture was chromatographed on 200 g of SiO_2 impregnated with 10% $AgNO_3$. Elution with a hexane—benzene mixture (85 : 15) gave (in the order of elution) compound **2** (0.4 g, 37%), **4** (0.29 g, 27%), and **3** (0.09 g, 8%).

4,4,7-Trimethyl-1,4,4aβ,5,8,8aβ-hexahydronaphtho[2,3-*b*]furan (**2**): colorless prisms, m.p. 31—33 °C (from hexane); the sample was virtually identical (^{1}H and ^{13}C NMR) to that reported previously.[2]

4,4,7-Trimethyl-1,4,4aβ,5,8,8aα-hexahydronaphtho-[2,3-*b*]furan (**3**): colorless prisms, m.p. 32—36 °C (from hexane). IR: 600, 690, 840, 900, 1050, 1140, 1200, 1250, 1330, 1370, 1385, 1450, 1470, 1510, 1630, 2820—3005 ($CHCl_3$). ^{1}H NMR: 1.00 (s, 3 H, HC(11)); 1.22 (s, 3 H, HC(12)); 1.49 (ddd, 1 H, HC(4a), J = 11.5, 11.5, 5.7 Hz); 1.68 (br.s, 3 H, HC(13)); 1.88 (m, 1 H, HC(8)); 2.02 (m, 2 H, HC(5), HC(8a)); 2.19 (m, 1 H, HC(5), J = 17.3, 5.5 Hz); 2.24 (dd, 1 H, HC(1), J = 16.5, 9.4 Hz), 2.26 (m, 1 H, HC(8)); 2.87 (dd, 1 H, HC(1), J = 16.5, 6.3 Hz); 5.46 (m, 1 H, HC(6)); 6.28 (d, 1 H, HC(10), J = 1.9 Hz); 7.22 (m, 1 H, HC(9)). ^{13}C NMR: 23.0 (C-13); 25.2 (C-5); 25.6 (C-11); 27.8 (C-12); 30.6 (C-8a); 31.0 (C-1); 33.4 (C-4); 39.3 (C-8); 43.6 (C-4a); 108.1 (C-10); 120.6 (C-6); 127.2 (C-3); 132.1 (C-7); 140.4 (C-9); 147.7 (C-2). High-resolution mass spectrum, *m/z* 216 $[M]^+$. Found: 216.15148. $C_{15}H_{20}O$. Calculated: 216.15131.

4,4,7-Trimethyl-1,4,4aβ,5,6,8aα-hexahydronaphtho-[2,3-*b*]furan (**4**): colorless prisms, m.p. 33—37 °C (from hexane); the sample was practically identical (^{1}H and ^{13}C NMR) to that described previously.[2]

The reaction of a mixture of *cis*-**5** and *trans*-**5** (~1 : 1) with 85% H_3PO_4 (58 mg, 0.5 mmol) in 2.5 mL of PhMe carried out in a similar way gave 0.6 g of a product; the product was chromatographed on 15 g of SiO_2. Elution of hexane gave 0.38 g (70%) of a mixture of isomers **6**, **7**, and **8** in a ratio of ~4 : 1 : 3 (^{1}H NMR data) as a colorless oil with R_f 0.38 (hexane). The mixture was chromatographed on 100 g of SiO_2 impregnated with 10% $AgNO_3$. Elution with a hexane—benzene mixture (85 : 15) gave (in the order of elution) compound **6** (0.19 g, 35%), **8** (0.14 g, 26%), and **7** (48 mg, 9%).

1,1,6-Trimethyl-1,4,4aβ,5,8,8aβ-hexahydronaphtho-[2,3-*b*]furan (**6**): colorless crystals, m.p. 36—39 °C (from hexane). IR: 670, 700, 890, 950, 1040, 1110, 1150, 1220, 1370, 1380, 1450, 1500, 1570, 2730—3020 ($CHCl_3$). ^{1}H NMR: 1.25 (s, 3 H, HC(11)); 1.33 (s, 3 H, HC(12)); 1.70 (br.s, 3 H, HC(13)); 1.74 (m, 1 H, HC(8a)); 1.85 (m, 2 H, HC(5), HC(8)); 2.04 (m, 1 H, HC(8)); 2.26 and 2.46 (both m, 2H, HC(4)); 2.40 (m, 1 H, HC(5)); 2.50 (m, 1 H, HC(4a)); 5.40 (m, 1 H, HC(7)), 6.15 (d, 1 H, HC(10), J =1.9 Hz); 7.26 (d, 1 H, HC(9), J =1.9 Hz). ^{13}C NMR: 23.4 (C-11); 23.6 (C-13); 23.8 (C-8); 24.3 (C-4); 29.4 (C-12); 29.8 (C-4a); 35.4 (C-1); 36.8 (C-5); 43.8 (C-8a); 110.0 (C-10); 114.2 (C-6); 120.4 (C-7); 131.2 (C-3); 140.4 (C-9); 156.2 (C-2). Found (%): C, 83.63; H, 9.42. $C_{15}H_{20}O$. Calculated (%): C, 83.28; H, 9.32. MS, *m/z* 216 $[M]^+$, 201, 145, 133, 122, 108, 105, 93, 85, 83, 78. Mol. weight 216.3

1,1,6-Trimethyl-1,4,4aβ,5,8,8aα-hexahydronaphtho-[2,3-*b*]furan (**7**): colorless crystals, m.p. 31—35 °C (from hexane). IR: 610, 700, 840, 940, 1020, 1080, 1120, 1150, 1280, 1370, 1450, 1500, 1570, 1630, 2740—3020 ($CHCl_3$). ^{1}H NMR: 1.07 (s, 3 H, HC(11)); 1.34 (s, 3 H, HC(12)); 1.60 (ddd, 1 H, HC(8a), J = 11.5, 11.5, 5.8 Hz); 1.70 (br.s, 3 H, HC(13)); 1.82 and 2.24 (m, 2 H, HC(5)); 1.91 (m, 1 H, HC(4a)); 2.04 and 2.16 (both m, 2H, HC(8)); 2.12 (dd, 1 H, HC(4), J = 16.0, 9.8); 2.67 (dd, 1 H, HC(4), J = 16.0, 5.8 Hz); 5.45 (m, 1 H, HC(7)); 6.14 (d, 1 H, HC(10), J = 1.8 Hz); 7.25 (d, 1 H, HC(9), J = 1.9 Hz). ^{13}C NMR: 23.0 (C-11); 23.3 (C-13); 24.8 (C-8); 25.5 (C-12); 30.6 (C-4); 30.8 (C-4a); 34.8 (C-1); 38.9 (C-5); 44.4 (C-8a); 109.7 (C-10); 113.4 (C-6); 120.2 (C-7); 132.3 (C-3); 140.3 (C-9); 157.7 (C-2). MS, *m/z* 216 $[M]^+$, 202, 201, 133, 122, 108, 105, 93, 85, 83, 78. $C_{15}H_{20}O$. Calculated: mol. weight 216.3.

1,1,6-Trimethyl-1,4,4aβ,7,8,8aα-hexahydronaphtho-[2,3-*b*]furan (**8**): colorless prisms, m.p. 32—35 °C (from hexane); the sample was virtually identical (^{1}H and ^{13}C NMR) to that described previously.[2]

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