88. Synthesis of the Bretonins, Polyolefinic Esterified Glyceryl Ethers of an Unidentified Sponge from the North-Brittany Sea: Absolute Configuration and Novel Structure Assignment

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(18.III.91)

The absolute configurations of acetylated bretonin A (= *(+)-(R)-1-[(acetoxy)methyl]-2-{[(4E,6E,8E)-dodeca-4,6,8-trienyl]oxy}ethyl 4-acetoxybenzoate;* (−)-**1b**) and isobretonin A (= *(+)-(S)-3-{[(4E,6E,8E)-dodeca-4,6,8-trienyl]oxy}-2-hydroxypropyl 4-hydroxybenzoate;* (+)-**2**), previously isolated from an undetermined sponge of the North Brittany sea, were established by comparison with synthetic (+)-**1b** and (+)-**2**, obtained from the condensation of commerical (−)-(*R*)-2,2-dimethyl-1,3-dioxolan-4-yl *p*-toluenesulfonate ((−)-(*R*)-**15**) with a mixture of (4*E*,6*E*,8*E*)- (**14e**) and (4*E*,6*Z*,8*E*)-dodeca-4,6,8-trien-1-ol (**14z**). This also allowed confirming the structure and configuration of bretonin B (= *(S)-2-{[(4E,6Z,8E)-dodeca-4,6,8-trienyl]oxy}-1-(hydroxymethyl)ethyl 4-hydroxybenzoate;* **3**) which was also isolated from the same sponge, albeit in a too small amount for a complete study. As concerns the glyceryl ethers precursors of the bretonins, co-occurrence of the usual (*S*)-configuration (from **1a**) with the unusual (*R*)-configuration (from (+)-**2**) poses intriguing biogenetic problems.

1. Introduction. – Recently, the ethers of glycerol have raised much interest under several respects. It is in fact amazing that long-chain, saturated alkyl ethers of glycerol have widespread occurrence in marine invertebrates and vertebrates while they do not occur on either land or freshwater [1a] [2]. It is also known that monoolefinic analogues occur in marine sponges and in certain seaweeds [1a], while isoprenic ethers of glycerol replace in the Archaebacteria the ordinary lipids of the other kingdoms [1a] [2]. Moreover, certain marine long-chain acetylenic enol ethers, called raspailynes [1], are unique organic molecules, insofar as they react with triplet oxygen, under mild conditions compatible with life, with cleavage of the enol ether C=C bond [1b][1]). Whenever checked, these glyceryl ethers proved to have the (*S*)-configuration. As an unique example from mammals, although of bacterial origin, polyolefinic enol ethers of glycerol – called fecapentaenes – may be abnormally present in human feces and act as most potent mutagenic agents [4].

Recently, another structural variant has been found in an unidentified sponge belonging to the class Demospongiae of Brittany waters. These compounds, called bretonins and available in very minute amounts, are glycerol derivatives etherified at a primary alcoholic function by a 4,6,8-trienic C_{12} chain and esterified at either the secondary alcohol function, such as with bretonin A (**1a**), or the other primary alcoholic function, by 4-hydroxybenzoic acid, such as with isobretonin A ((+)-**2**) [5][2]).

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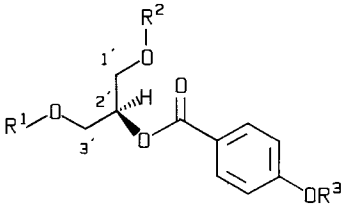
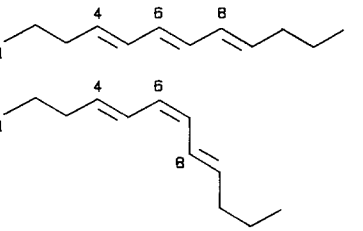
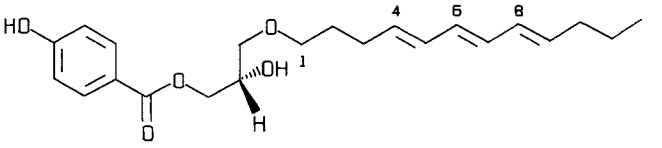
[1]) Curiously, this feature has not been mentioned while reporting about closely related compounds of another marine sponge [3].

[2]) Except for retrieval purposes (see *Exper. Part*), we use an arbitrary numbering in describing the bretonins.



bretonin A **1a** $R^1=R^3=H$,
bretonin A diacetate (–)-**1b** $R^1=R^3=Ac$,
bretonin B **3** $R^1=R^3=H$,



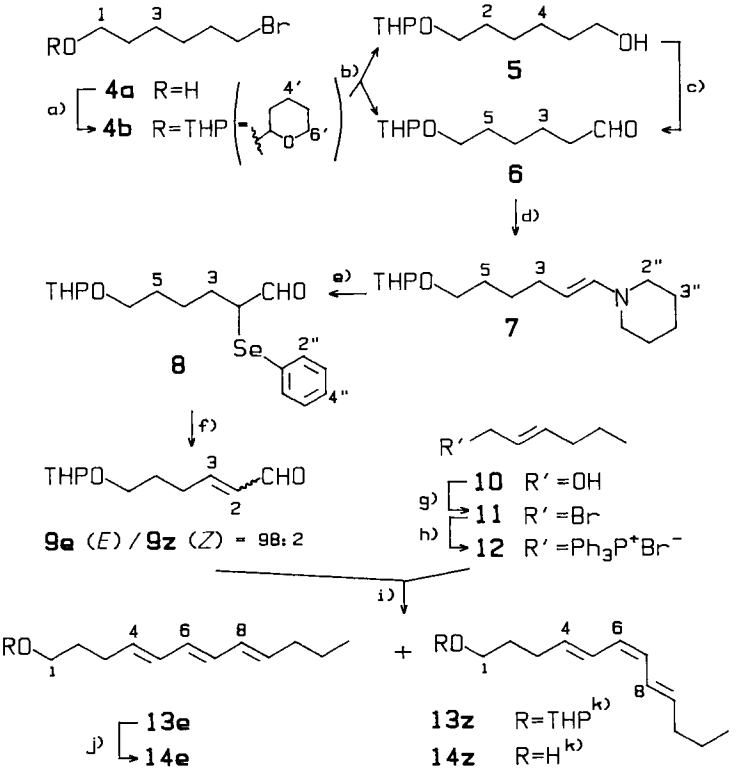


isobretonin A (+)-**2**

While the polyolefinic chain is (all-*E*)-configurated in the above cases [5], the same sponge also contains in trace amounts another glyceryl ether, which ^{1}H-NMR spectra preliminarily indicated to possess a (6*Z*)-side chain. Being unable to obtain ^{13}C-NMR data because of the extreme scarcity of material – which could not be provided in larger amount for this unidentified sponge – this glyceryl ether, called bretonin B, was not reported. This problem is now solved by synthesis which, in order to meet also the interest in the biogenesis of glyceryl ethers [6], has been planned so as to give both (6*Z*)- (such as bretonin B, **3**), and (6*E*)-bretonins, relying on chromatographic separations.

2. Results and Discussion. – Our plan of synthesis had thus to account for the twofold aspect of the problem, *i.e.* confirming the structure for a rare new (6*Z*)-bretonin and assigning the absolute configuration to those previously described. To this end, we considered to combine an easily available C_3 chiral builing block – thereby establishing the C(2′) configuration – with a mixture of the (all-*E*)- and isomeric (6*Z*)-C_{12} linear polyolefinic carbon reactant. Our expectation from the known chemistry of monoacylated 1,2-diols in acidic or alkaline media [7] was also to obtain a partial aroyl transfer from the primary position to the less easily aroylated secondary position. This would afford bretonin- and isobretonin-type glyceryl esters at the same time without recourse to more elaborated specific synthetic routes. On the basis of our experience with the natural mixtures of the bretonins, separation of the synthetic isomeric bretonins was expected to be easily achieved by HPLC.

Scheme 1



a) Dihydropyran, Py·TsOH, CH_2Cl_2, r.t., 2 h. b) DMSO, $NaHCO_3$, 150°, 15 min. c) PDC, CH_2Cl_2, r.t., overnight. d) Piperidine, 4-Å molecular sieves, PhH, reflux, 3 h. e) PhSeCl, THF, −110°, H_2O, r.t., 3 h. f) $NaIO_4$, MeOH/H_2O/THF 2:1:1, r.t., 3 h. g) $(PhO)_3P$, Br_2, Py, Et_2O, r.t., overnight. h) Ph_3P, PhH, reflux, 5 h. i) η-BuLi, THF, −5°; r.t., 1 h; reflux 1 h. j) *Amberlyst-15*, MeOH, 40°, 2 h. k) **e** and **z** in 45:55 mixtures.

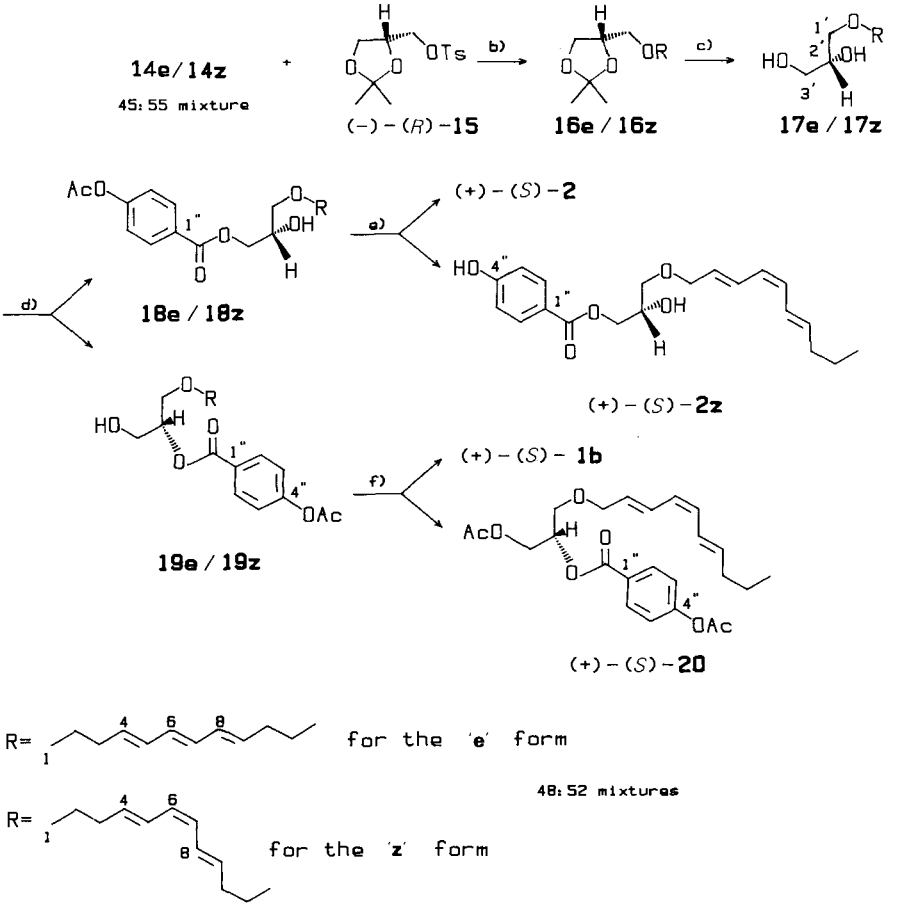
This plan was realized as follows. Commercial 6-bromohexanol (**4a**; *Scheme 1*) was protected as tetrahydropyran-2-yl (THP) ether [8] (**4b**) which, on oxidation with $(CH_3)_2SO/NaHCO_3$ at 150° [9], gave a 5:1 mixture of the desired aldehyde **6** and undesired alcohol **5**. The latter could be oxidized to the former with pyridinium dichromate [10], however, thus obtaining **6** in overall 80% yield. Aldehyde **6** was then converted into enamine **7**, which was then treated with PhSeCl[3]) [11] to obtain the α-(phenylseleno)aldehyde **8**, from which the (*E*)-α,β-unsaturated aldehyde **9e** was obtained with high stereoselectivity and fair yield (72% from **6**).

Triphenylphosphonium bromide **12** (prepared in overall 80% yield from commercial (*E*)-hex-2-en-1-ol (**10**) and $(PhO)_3P/Br_2$ [12a] followed by the addition of Ph_3P [12b]) was treated with BuLi to form a ylide which was added to **9e** [13] obtaining, after purification

[3]) The alternative treatment of aldehyde **6** with LDA/PhSeCl proved inferior in terms of the yield of **9e**, which, moreover, was accompanied by a complex mixture of products.

by flash chromatography (FC), a 45:55 mixture[4]) of the (all-*E*)- and (*E*,*Z*,*E*)-THP ethers **13e** and **13z**, respectively, in overall 45% yield from commercial **4a**. Deprotection of the **13e**/**13z** mixture over acidic *Amberlyst-15* in MeOH [14] gave a 45:55 mixture of the dodecatrienols **14e**/**14z**[5]).

Scheme 2[a])



a) An arbitrary C-atom numbering is used for all the compounds. b) NaH, THF, 0°, reflux 1 h; 0°, (−)-**15**, reflux 4 h. c) *Dowex 50W*; MeOH/H_2O 50:1; 50°, 1 h. d) 1) 4-Acetoxybenzoyl chloride, pyridine, r.t., overnight; 2) FC. e) 1) 4-(Dimethylamino)pyridine, r.t., overnight; 2) reversed-phase HPLC. f) 1) Ac_2O, pyridine, r.t., overnight; 2) HPLC.

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[4]) The FC procedure did not alter the **13e**/**13z** ratio, which proved by NMR spectroscopy to be the same either in this reaction mixture after *ca.* 12 h at r.t. or after reflux in THF for *ca.* 1 h.

[5]) The **13e**/**13z** and **14e**/**14z** mixtures proved to be air- and daylight-sensitive, being in any case more stable in dilute solution than when solvent-free or in concentrate solutions. Degradation of these mixture gave origin to polar products which could be detected by TLC/UV but which were not further investigated. Therefore, the **14e**/**14z** mixture, after filtration over basic Al_2O_3 in order to suppress any residual acidity from the *Amberlyst-15* resin, was rapidly used in dilute solution under N_2 and in the dark as indicated in *Scheme 2*.

In the next step, the chirality was introduced *via* the stereochemically-stable [15] *p*-toluenesulfonate (−)-(*R*)-**15** (*Scheme 2*) which was treated with the alcoholates of **14e**/**14z**, generated with NaH in THF [16], to give a 48:52 mixture of the acetonides **16e**/**16z**. These were then deprotected on a *Dowex* resin (H^+ form) [17] to give a 48:52 mixture of glyceryl ethers **17e**/**17z** in 50% yield from the **14e**/**14z** mixture.

Although 4-hydroxybenzoyl chloride can not be obtained from 4-hydroxybenzoic acid and $SOCl_2$ [18], the known resistance of the aroyloxy function to hydrolysis [19] gave good prospects that the easily obtained 4-acetoxybenzoyl chloride could be used and then the Ac group removed. Following this line, reaction of the above **17e**/**17z** mixture with 1 mol-equiv. of 4-acetoxybenzoyl chloride in pyridine gave the two regioisomeric couples of (*E*/*Z*)-isomers **18e**/**18z** and **19e**/**19z** which could be separated by FC[6]).

Following our expectations, the (*E*/*Z*)-mixtures of **18** and **19** must have resulted from acyl transfer, which, therefore, can not have involved the chiral center. This made substrates of both the isobretonin and bretonin type simultaneously available, and easily separable by FC without the need of selectively protecting the primary alcohol function [20] or to recur to troublesome reversed mono-esterification procedures [21].

According to our plan, the phenolic function was freed by the treatment of the above **18e**/**18z** mixture with 4-(dimethylamino)pyridine[7]) to give isobretonin A ((+)-(*S*)-**2**), identical with a sample isolated from a sponge of Brittany waters [5], and its unnatural (6*Z*)-isomer (+)-(*S*)-**2z**, which were separated by reversed-phase HPLC.

No polarimetric data were reported for bretonin A (**1a**) [5], since the optical rotation was too small at all wavelengths to be taken with confidence; therefore, the **19e**/**19z** mixture was subjected to acetyltion followed by HPLC separation to give (+)-(*S*)-**1b** (enantiomeric with a sample obtained by acetylation of bretonin A from the same sponge above) and (*S*)-**20**. The latter proved to be the acetate of bretonin B (= (*S*)-2-{[(4*E*,6*Z*,8*E*)-dodeca-4,6,8-trienyl]oxyl}-1-(hydroxymethyl)ethyl 4-hydroxybenzoate; **3**)[8]) which was also isolated from the same sponge above, albeit in too small amount to record ^{13}C-NMR and polarimetric data.

The comparison of polarimetric data for (−)-**1b**, previously obtained by acetylation of natural bretonin A (**1a**) [5], with (+)-**1b** obtained by synthesis, shows that (−)-**1b** has the (*R*)-configuration; therefore, bretonin A (**1a**) must be assigned the (*S*)-configuration. This is further supported by the observation that the CD spectrum of (+)-**1b** is in specular relationship with that of (−)-**1b** (*Exper. Part*).

The above observations rule out a biogenetic route to isobretonin A ((+)-**2**) from bretonin A (**1a**) *via* esterification of the primary or secondary alcohol function, respectively, of a hypothetical common 3-[(dodecatrienyl)oxy]propane-1,2-diol precursor. Moreover, a biogenetic route to (+)-**2** from **1a** *via* aroyl transfer could have not affected

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[6]) The presence of the couples **18e**/**18z** and **19e**/**19z** was already noticed by ^{1}H-NMR of the crude mixture, which also allowed us establishing that there is no appreciable aroyl transfer on silica gel.

[7]) We have also proven that, on reaction of the above **17e**/**17z** mixture with 4-acetoxybenzoyl chloride in pyridine in the presence of a catalytic amount of 4-(dimethylamino)pyridine, the monoaroylated product with free phenol function is obtained directly and with shorter (4 h) reaction times, albeit together with a more complex mixture of products.

[8]) An indication of the presence of (6*Z*)-isomers was already obtained from a ^{1}H-NMR pattern for the triene system of the mixture **13e**/**13z** of the type reported for bretonin B (**3**; *Exper. Part*).

the chiral center [7] and would have, therefore, led to the same absolute configuration, contrary to our observation[9]).

The hypothesis of biogenetic origin of **1a** and (+)-**2** from glyceryl ethers of opposite configuration is also not palatable. Therefore, the alternative hypothesis may be considered of an epoxide intermediate formed by intramolecular displacement of the carboxylate by the OH group at C(3'), followed by epoxide opening at C(3') by the carboxylate.

We thank Mr. *A. Sterni* for recording the mass spectra and the M.P.I. (Progetti di interesse Nazionale) and the C.N.R., Roma, for financial support.

Experimental Part

General. $SOCl_2$ and $(CH_3)_2SO$ were distilled just before use, while the following solvents were distilled over the specified reagents: THF and Et_2O ($LiAlH_4$), benzene (Na, and collected over flame-dried 4-Å molecular sieves), CH_2Cl_2 (CaH_2), pyridine (BaO). Commercial BuLi (*Aldrich*) was standardized by acid-base titration [22]. Reactions were carried out in flame-dried glassware under N_2. All evaporations were at reduced pressure at r.t. Flash chromatography (FC): *Merck Si-60*, 15–25 μm. HPLC: *Merck-LiChrosorb Si-60.* Reversed-phase HPLC: *Merck-LiChrosorb RP-18.* All HPLC columns were 25 × 1 cm with 5 ml min^{-1} solvent flux. Polarimetric data: *JASCO-DP-181* polarimeter. UV: *Perkin-Elmer Lambda 3* spectrophotometer (λ_{max} in nm, ε $mol^{-1}\cdot l\cdot cm^{-1}$). IR: *Perkin-Elmer-337* spectrometer (ν_{max} in cm^{-1}). CD: *Jasco J-710* spectropolarimeter (λ_{max} in nm, ε in $mol^{-1}\cdot l\cdot cm^{-1}$). NMR: *Varian-XL-300*; δ[ppm] relative to internal Me_4Si (= 0 ppm) and J in Hz; ^{1}H-NMR at 229.94 MHz and ^{13}C-NMR at 75.43 MHz; solvent $CDCl_3$, freshly eluted from a Al_2O_3 column; multiplicities from DEPT [23]. Proton assignments for compound **3**; from ^{1}H,H-COSY [24]. EI-MS (*m/z*, %): home-built quadrupole mass spectrometer based on the *ELFS-4-162-8 Extranuclear* quadrupole [25].

1. *6-Bromo-1-[(3,4,5,6-tetrahydro-2*H*-pyran-2-yl)oxy]hexane* (**4b**). A soln. of *6-bromohexan-1-ol* (**4a**; *Aldrich;* 1.38 g, 7.6 mmol) in CH_2Cl_2 (10 ml) was added of DHP (3,4-dihydro-2*H*-pyran; 0.67 g, 7.96 mmol) and Py·TsOH (0.58 g, 2.3 mmol) and stirred for 3 h at r.t. The solvent was then evaporated, and the mixture was added of H_2O (10 ml) and extracted with Et_2O (3 × 30 ml). The combined org. phase was dried (Na_2SO_4) and evaporated to give crude **4b** (1.91 g, 95%) as a colorless oil. ^{1}H-NMR[10]): 4.55 (*m*, H–C(2')); 3.90–3.40 (series of *m*, 2 H–C(1), 2 H–C(6')); 3.39 (*t*, J = 6.9, 2 H–C(6)); 1.85 (*quint.*, J = 6.9, 2 H–C(5)); 1.80–1.35 (series of *m*, 2 H–C(2), 2 H–C(3), 2 H–C(4), 2 H–C(3'), 2 H–C(4'), 2 H–C(5')). ^{13}C-NMR[10]): 98.89 (*d*, C(2')); 67.39 (*t*, C(1)); 62.38 (*t*, C(6')); 33.89, 32.72, 30.74, 29.54, 27.99, 25.45 (two coincident signals), 19.69 (8*t*, 8 CH_2). MS: 266/264 (1,1, M^+), 265/263 (6,6, $[M-1]^+$), 165/163 (4,4, $[M-OTHP]^+$), 164/162 (3,3), 123/121 (2,2), 109/107 (3,3), 101 (6), 85 (100), 83 (8), 67 (11), 55 (37), 41 (31).

2. *6-[(3,4,5,6-Tetrahydro-2*H*-pyran-2-yl)oxy]hexanal* (**6**). A mixture of **4b** (1.82 g, 6.9 mmol), $(CH_3)_2SO$ (40 ml), and $NaHCO_3$ (4.62 g) was stirred for 15 min at 150° with evolution of white fumes. The mixture was then cooled to r.t., added of H_2O (20 ml) and extracted with Et_2O (3 × 30 ml). The combined org. phase was washed with H_2O, dried (Na_2SO_4) and evaporated. The residue was subjected to FC (hexane/Et_2O 7:3) to give **6** (0.99 g, 72%) and **5** (0.20 g, 14%). The latter was stirred overnight in CH_2Cl_2 at r.t. white pyridinium dichromate [10] to give **6** (81%).

*Data of 6-[(3,4,5,6-Tetrahydro-2*H*-pyran-2-yl)oxy]hexan-1-ol* (**5**). Colorless oil. IR (neat): 3420*m* (br.), 2942*s*, 2868*s*, 1240*s*, 1140*s*, 1122*s*, 1032*s*. ^{1}H-NMR[10]): 4.52 (*m*, H–C(2')); 3.90–3.30 (series of *m*, 2 H–C(1), 2 H–C(6')); 3.57 (*t*, J = 6.6, 2 H–C(6)); 2.01 (br. *s*, OH), 1.90–1.30 (series of *m*, 2 H–C(2), 2 H–C(3), 2 H–C(4), 2 H–C(5), 2 H–C(3'), 2 H–C(4'), 2 H–C(5')). ^{13}C-NMR[10]): 98.81 (*d*, C(2')); 67.44 (*t*, C(1)); 62.70 (*t*, C(6)); 62.33 (*t*, C(6')); 32.62, 30.68, 29.60, 25.95, 25.49, 25.39, 19.64 (7*t*, 7 CH_2). MS: 201 (1, $[M-1]^+$), 117 (4), 115 (3), 101 (44, $[M-OTHP]^+$), 99 (4), 85 (100), 83 (19), 67 (17), 57 (16), 55 (63), 41 (40).

Data of **6.** Colorless oil. IR (neat): 2940*vs*, 2852*vs*, 2815*m*, 2720*m*, 1728*s* (C=O), 1124*vs*, 1080*s*, 1038*s*. ^{1}H-NMR[10]): 9.72 (*t*, J = 1.8, CHO); 4.52 (*m*, H–C(2')); 3.85–3.40 (series of *m*, 2 H–C(6), 2 H–C(6')); 2.40 (*td*,

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[9]) No isomerization of either (+)-**2** or the **19z**/**19z** mixture was observed in the presence of silica gel; this rules out aroyl transfers during the isolation of the bretonins [5].

[10]) NMR Assignments according to the arbitrary C-atom numbering indicated in formulae and *Schemes*.

J = 7.2, 1.8, 2 H–C(2)); 1.90–1.40 (series of *m*, 2 H–C(3), 2 H–C(4), 2 H–C(5), 2 H–C(3'), 2 H–C(4'), 2 H–C(5')). ^{13}C-NMR[10]): 202.63 (*d*, CHO); 98.82 (*d*, C(2')); 67.16 (*t*, C(6)); 62.30 (*t*, C(6')); 43.74 (*t*, C(2)); 30.65, 29.39, 25.79, 25.36, 21.81, 19.60 (6*t*, 6 CH_2). MS: 199 (1, $[M-1]^+$), 156 (1), 115 (3), 101 (54), 99 (47, $[M-OTHP]^+$), 98 (10), 86 (11), 85 (100), 84 (20), 67 (20), 57 (36), 55 (76), 41 (69).

3. *Perhydro-1-{6-[(3,4,5,6-tetrahydro-2*H*-pyran-2-yl)oxy]hex-1-enyl}pyridine* (**7**). In a *Dean-Stark* apparatus with flame-dried 4-Å molecular sieves (1.8 g), **6** (0.80 g, 4.0 mmol), benzene (5 ml), and piperidine (0.42 ml, 4.2 mmol) were stirred under reflux for 3 h. The mixture was then evaporated to give **7** (1.06 g, 100%) as a colorless oil. IR (neat): 2940*s*, 2868*m*, 1680*m* (C=C), 1137*m*, 1121*m*, 1078*m*, 1035*m*. ^{1}H-NMR[10]): 5.80 (*dt*, J = 13.8, 1.2, H–C(1)); 4.55 (*m*, H–C(2')); 4.36 (*dt*, J = 13.8, 6.9, H–C(2)); 3.90–3.30 (series of *m*, 2 H–C(6), 2 H–C(6')); 2.71 (*m*, 2 H–C(2''), 2 H–C(6'')); 1.96 (*qd*, J = 7.2, 1.2, 2 H–C(3)); 1.90–1.35 (series of *m*, 2 H–C(4), 2 H–C(5), 2 H–C(3'), 2 H–C(4'), 2 H–C(5'), 2 H–C(3''), 2 H–C(4''), 2 H–C(5'')). ^{13}C-NMR[10]): 140.43 (*d*, C(1)); 101.08 (*d*, C(2)); 98.75 (*d*, C(2')); 67.60 (*t*, C(6)); 62.25 (*t*, C(6')); 50.11 (2*t*, C(2''), C(6'')); 30.75, 30.39, 29.15, 27.93, 25.48, 25.42 (2 coincident signals), 24.35, 19.64 (9*t*, 9 CH_2). MS: 267 (1, $M^{+\cdot}$), 183 (5), 182 (32), 124 (44), 101 (25), 98 (30), 85 (100), 84 (24), 67 (14), 57 (15), 55 (33), 41 (20).

4. *2-(Phenylseleno)-6-[(3,4,5,6-tetrahydro-2*H*-pyran-2-yl)oxy]hexanol* (**8**). Crude **7** (0.99 g, 3.7 mmol) in dry THF (6 ml) was added dropwise during 10 min to a stirred soln. of PhSeCl (0.84 g, 4.4 mmol) in THF (4 ml) at −110°. The mixture was then brought to −80°, added of H_2O (5 ml) and Et_2O (30 ml), stirred at r.t. for 3 h, and finally extracted with Et_2O (3 × 20 ml). The combined org. phase was washed first with aq. $NaHCO_3$, then with H_2O, and dried (Na_2SO_4) and evaporated. The residue was subjected to FC (hexane/Et_2O 9:1) to give pure **8** (0.98 g, 74%) as a pale-yellow oil. IR (neat): 3040*w*, 2945*s*, 2870*s*, 1710*s* (C=O), 1122*m*, 1035*m*, 743*m*, 694*m*. ^{1}H-NMR[10]): 9.39 (*d*, J = 3.6, CHO); 7.51–7.26 (series of *m*, Ph); 4.55 (*m*, H–C(2')); 3.90–3.30 (series of *m*, 2 H–C(6), 2 H–C(6')); 3.60 (*td*, J = 6.9, 3.6, H–C(2)); 2.40–1.40 (series of *m*, 2 H–C(3), 2 H–C(4), 2 H–C(5), 2 H–C(3'), 2 H–C(4'), 2 H–C(5')). ^{13}C-NMR[10]): 192.90 (*d*, CHO); 135.9 (2*d*, C(2''), C(6'')); 129.26 (2*d*, C(3''), C(5'')); 128.87 (*d*, C(4'')); 125.81 (*s*, C(1'')); 98.88 (*d*, C(2')); 67.08 (*t*, C(6)); 62.37 (*t*, C(6')); 52.83 (*d*, C(2)); 30.72, 29.33, 27.44, 25.44, 24.79, 19.66 (6*t*, 6 CH_2). MS: 272/270 (46, 24), 255/253 (6, 3, $[M-OTHP]^+$), 158/156 (32, 18), 157/155 (26, 16), 115 (7), 101 (8), 97 (11), 85 (100), 77 (20), 55 (23), 41 (20).

5. *(2*E*)-6-[(3,4,5,6-Tetrahydro-2*H*-pyran-2-yl)oxy]hex-2-enal* (**9e**) *and Its (2*Z*)-Isomer* **9z**. To **8** (0.96 g, 2.7 mmol) in MeOH/H_2O/THF 2:1:1 (100 ml) was added $NaIO_4$ (1.16 g, 5.4 mmol), and the resulting mixture was vigorously stirred at r.t. for 3 h and then evaporated, and the residue was extracted with Et_2O (3 × 20 ml). The combined org. phase was washed first with aq. $NaHCO_3$, then with H_2O, and dried (Na_2SO_4) and evaporated to give a 98:2 mixture **9e**/**9z** (0.524 g) as a colorless oil. FC (hexane/Et_2O) of this mixture gave **9e**/**9z** 95:5 in the first eluate.

Data of the 95:5 Mixture **9e**/**9z**. IR (neat): 2950*s*, 2876*s*, 2820*w*, 2740*w*, 1688*s* (C=O), 1640*m* (C=C), 1443*m*, 1356*m*, 1138*s*, 1027*s*, 978*m*. ^{1}H-NMR[10])[11]): 9.49 [10.07, J = 8.1] (*d*, J = 7.8, CHO); 6.88 [6.63, J = 11.1, 7.8] (*dt*, J = 15.6, 6.9, H–C(3)); 6.13 [5.95, *dd*, J = 11.1, 8.1] (*ddt*, J = 15.6, 7.8, 1.8, H–C(2)); 4.55 (*m*, H–C(2')); 3.85–3.35 (series of *m*, 2 H–C(6), 2 H–C(6')); 2.25–2.20 (series of *m*, 2 H–C(4), 2 H–C(5)); 1.90–1.50 (series of *m*, 2 H–C(3'), 2 H–C(4'), 2 H–C(5')). ^{13}C-NMR[10]): 194.07 [190.65] (*d*, CHO); 158.37 [152.60] (*d*, C(2)); 133.05 [130.47] (*d*, C(3)); 98.95 (*d*, C(2')); 66.43 (*t*, C(6)); 62.39 (*t*, C(6')); 30.64, 29.62, 27.97, 25.43, 19.66 (5*t*, 5 CH_2). MS: 198 (3, $M^{+\cdot}$), 197 (5, $[M-1]^+$), 113 (4), 101 (17), 97 (23, $[M-OTHP]^+$), 85 (100), 69 (12), 67 (23), 55 (41), 41 (32).

6. *(*E*)-1-Bromohex-2-ene* (**11**). In a two-necked flask, to a stirred soln. of $(PhO)_3P$ (2.6 ml, 9.9 mmol) in dry Et_2O (10 ml) at 0° was added Br_2 (0.5 ml, 9.7 mmol) dropwise with stirring. After 2 h, the mixture was cooled to −10°, (*E*)-hex-2-en-1-ol (*Aldrich*; 1 ml, 8.1 mmol) in dry pyridine (0.85 ml, 10.5 mmol) was added, and the mixture stirred at r.t. overnight. The mixture was filtered and evaporated, and the filter was washed with Et_2O. Vacuum distillation of the combined residues gave **11** (1.07 g, 81%) as a colorless oil. B.p. 39°/32 Torr. IR (neat): 2980*vs*, 2865*vs*, 1670*w*. ^{1}H-NMR[10]): 5.72 (*m*, H–C(2), H–C(3)); 3.94 (*d*, J = 6.9, 2 H–C(1)); 2.03 (*qd*, J = 7.2, 0.9, 2 H–C(4)); 1.40 (*sext.*, J = 7.2, 2 H–C(5)); 0.89 (*t*, J = 7.2, 3 H–C(6)). ^{13}C-NMR[10]): 136.51 (*d*); 126.42 (*d*); 34.08 (*t*); 33.65 (*t*); 21.97 (*t*); 13.58 (*q*). MS: 164/162 (7,8, $M^{+\cdot}$), 149/147 (6, 6, $[M-CH_3]^+$), 135/133 (7, 6), 95/93 (4, 4), 83 (100, $[M-Br]^+$), 82/80 (15, 15), 81/79 (14, 12), 69 (6), 55 (48).

7. *[(*E*)-Hex-2-enyl]triphenylphosphonium Bromide* (**12**). A mixture of **11** (0.85 g, 5.2 mmol) and Ph_3P (1.42 g, 5.4 mmol) in dry benzene (10 ml) was heated at reflux with stirring for 5 h, then cooled, whereby a white precipitate was formed, filtered, dried *in vacuo* at 60°, and stored over P_4O_{10} (2.2 g, 100%).

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[11]) When not superimposed, resonances for the (6*Z*)-isomer are given within square brackets.

8. *(4E,6Z,8E)-1-[(3,4,5,6-Tetrahydro-2H-pyran-2-yl)oxy]dodeca-4,6,8-triene* (**13z**) *and Its (6E)-Isomer* **13e**. In a two necked flask, to a mixture of **12** (1.7 g, 4.0 mmol) in dry THF (30 ml), cooled to −5°, BuLi (1.6M, 2.5 ml) was added dropwise, whereby a deep red color immediately developed. This heterogeneous mixture was brought to 15° and stirred for 30 min whereby to give a homogeneous soln. which was then cooled to 0°, **9e** (0.4 g, 2.0 mmol, dissolved in THF, 5 ml) was added dropwise, and the mixture stirred for 1 h at r.t. and then for 1 h at reflux. The resulting mixture was added of H_2O (20 ml) and extracted with Et_2O (3 × 30 ml). The combined org. phase was washed with H_2O, dried (Na_2SO_4), and evaporated to give a residue which was subjected to FC (hexane/Et_2O 9:1) to give a 55:45 mixture **12z**/**13e** (0.43 g, 1.63 mmol, 81%) as a colorless oil. IR (neat): 3040*m*, 2975*vs*, 2840*s*, 1637*w* (C=C), 1136*m*, 1034*s*, 990*m*, 960*m*. ^{1}H-NMR[10])[12]): 6.51, 6.47 (*dd*, *J* = 15.0, 10.2, H–C(5), H–C(8)); 5.84 (*m*, H–C(6), H–C(7)) [6.10–5.95 *m*, H–C(5)–H–C((8)]; 5.74–5.58 (*m*, H–C(4), H–C(9)); 4.56 (*m*, H–C(2′)); 3.85–3.35 (series of *m*, 2 H–C(1), 2 H–C(6′)); 2.16 (*m*, 2 H–C(3)); 2.07 (*m*, 2 H–C(10)); 1.90–1.40 (series of *m*, 2 H–C(2), 2 H–C(11), 2 H–C(3′), 2 H–C(4′), 2 H–C(5′)); 0.90 [0.88] (*t*, *J* = 7.2, 3 H–C(12)). ^{13}C-NMR[10])[12]): 135.21, 134.36, 127.88, 127.49, 126.27, 125.98 [134.21, 133.35, 131.06, 130.91, 130.69, 130.62] (6*d*, C(4)–C(9)); 98.83 (*d*, C(2′)); 66.90 (*t*, C(1)); 62.20 (*t*, C(6′)); 34.97 [34.83] (*t*, C(10)); 30.77, 29.59, 29.44, 25.53, 22.49, 19.60 (6*t*, C(2), C(3), C(11), C(3′), C(4′), C(5′)); 13.61 (*q*, C(12)). MS: 264 (9, $M^{+\cdot}$), 181 (12), 180 (69), 164 (8), 162 (8), 133 (10), 121 (8), 119 (26), 105 (20), 91 (38), 85 (100), 79 (15), 67 (12), 55 (6).

9. *(4E,6Z,8E)-Dodeca-4,6,8-trien-1-ol* (**14z**) *and Its (6E)-Isomer* **14e**. To the mixture **13z**/**13e** (0.42 g, 1.6 mmol) in MeOH (3 ml), *Amberlyst-15* (0.050 g) was added and the mixture stirred at 40° for 2 h, until complete disappearance of both **13z** and **13e**. The resulting mixture was filtered on basic Al_2O_3 (70–230 mesh) and the filter washed with Et_2O. The filtrate and Et_2O washing were evaporated to give a 55:45 mixture **14z**/**14e** as a colorless oil (0.27 g, 94%). IR (neat): 3020*w*, 2922*s*, 2854*s*, 1638*w* (C=C), 995*m*, 963*m*. ^{1}H-NMR[10]): 6.51, 6.43 (br. *dd*, *J* = 14.7, 9.9, H–C(5), H–C(8)); 5.83 (*m*, H–C(6), H–C(7)); [6.11–5.95 (series of *m*, H–C(5)–H–C(8))]; 5.68 (*dt*, *J* = 14.7, 7.2) and 5.69 (*m*) (H–C(4), H–C(9)); 3.65 [3.63] (*t*, *J* = 6.6, H–C(1)); 2.21 or 2.17 [2.17 or 2.21] (*q*, *J* = 7.2, 2 H–C(3)); 2.09 or 2.05 [2.05 or 2.09] (*q*, *J* = 7.2, 2 H–C(10)); 1.68 [1.65] (*quint.*, *J* = 6.9, 2 H–C(2)); 1.41 (*sext.*, *J* = 7.2, 2 H–C(11)); 0.90 [0.88] (*t*, *J* = 7.2, 3 H–C(12)). ^{13}C-NMR[10]): 135.59, 134.61, 128.07, 127.22, 126.36, 125.78 [134.11, 133.08, 131.29, 131.04, 130.44, 130.43] (6*d*, C(4)–C(9)); 62.38 (*t*, C(1)); 34.99 [34.85] (*t*, C(10)); 32.20, 29.18, 22.46 [32.15, 29.05, 22.41] (3*t*, C(2), C(3), C(11)); 13.70 [13.65] (*q*, C(12)). MS: 180 (73, $M^{+\cdot}$), 133 (19), 119 (35), 105 (66), 81 (38), 79 (84), 67 (60), 55 (49).

10. *(S)-4-{[(4E,6Z,8E)-Dodeca-4,6,8-trienyl]oxy}-2,2-dimethyl-1,3-dioxolane* (**16z**) *and Its (6E)-Isomer* **16e**. To a mixture of NaH (0.02 g, 0.83 mmol) in dry THF (1 ml), at 0° under N_2 was added dropwise **14z**/**14e** (0.12 g, 0.67 mmol) in THF (1 ml). The resulting mixture was stirred at r.t. for 30 min and then at reflux for 1 h, then, in turn, cooled to 0°, (−)-**15** (0.286 g, 1.00 mmol) in THF (1 ml) was added dropwise, the mixture heated at reflux for 4 h, and stirred at r.t. overnight, H_2O (5 ml) was added, and the org. solvent was removed *in vacuo*. The residue was extracted with Et_2O (3 × 10 ml) and the org. extract was washed with H_2O, dried (Na_2SO_4), and evaporated. The residue was subjected to FC (hexane/Et_2O 4:1) to give a dextrorotatory 52:48 mixture **16z**/**16e** as a colorless oil (0.11 g, 56%). IR (neat): 3035*m*, 1638*w*, 1382*w*, 1371*w*, 1118*w*, 1056*w*. ^{1}H-NMR[10]): 6.56–6.40 (*m*, H–C(5), H–C(8)) [6.10–5.95 (series of *m*, H–C(5)–H–C(8))]; 5.83 (*m*, H–C(6), H–C(7)); 5.69, 5.68 (2*dt*, *J* = 14.7, 7.2, H–C(4), H–C(9)); 4.25 [4.26] (*X* of *ABX* and *A′B′X*, *pseudo-quint.*, *J* ≈ 6.3, H–C(2′)); 4.06, 3.71 [4.5, 3.72] (*A′B′* of *A′B′X*, *J*(*A′B′*) = 8.4, *J*(*A′X*) = *J*(*B′X*) = 6.3, 2 H–C(3′)); 3.48 (*m*, 2 H–C(1)); 3.49, 3.41 [3.50, 3.42] (*AB* of *ABX*, *J*(*AB*) = 11.1, *J*(*AX*) = 4.8, *J*(*BX*) = 5.7, 2 H–C(1′)); 2.18 or 2.14 [2.14 or 2.18] (*q*, *J* = 6.9, 2 H–C(3)); 2.08 or 2.05 [2.05 or 2.08] (*q*, *J* = 6.9, 2 H–C(10)); 1.68 (*quint.*, *J* = 6.9, 2 H–C(2)); 1.41, 1.35 (2*s*, Me_2C=); 1.41 (*sext.*, *J* = 7.2, 2 H–C(11)); 0.90 [0.88] (*t*, *J* = 7.2, 3 H–C(12)). ^{13}C-NMR[10]): 135.52, 134.53, 127.99, 127.37, 126.29, 125.86 [134.24, 133.21, 131.19, 130.99, 130.57, 130.52] (6*d*, C(4)–C(9)); 109.38 (*s*, Me_2C=); 74.74 (*d*, C(2′)); 71.87 or 71.02 [71.06] (*t*, C(1′)); 71.02 [71.06] or 71.87 (*t*, C(1)); 66.90 (*t*, C(3′)); 35.02 [34.87] (*t*, C(10)); 30.32 (*t*, C(2)); 29.18 (*t*, C(3)); 26.76, 25.42 (2*q*, Me_2C=); 22.50 (*t*, C(11)); 13.71 [13.68] (*q*, C(12)). MS: 265 (2), 221 (4), 207 (20), 115 (4), 85 (5), 73 (16).

11. *(R)-3-{[(4E,6Z,8E)-Dodeca-4,6,8-trienyl]oxy}propane-1,2-diol* (**17z**) *and Its (6E)-Isomer* **17e**. To a soln. of **16z**/**16e** (0.07 g, 0.24 mmol) in MeOH/H_2O 50:1 (2 ml) was added a *Dowex 50W-X8* resin in the H^+ form (0.1 g), and the resulting mixture was stirred for 1 h at 50°. The resin was then removed by filtration on basic Al_2O_3 and the filtrate was partly evaporated and then subjected to TLC with $CHCl_3$/i-PrOH 93:7 to give a levorotatory 52:48 mixture **17z**/**17e** as a colorless oil (0.053 g, 88%) at R_f 0.6. IR (neat): 3345*m*, 1638*w*, 1125*m*, 1060*m*. ^{1}H-NMR[10]): 6.51, 6.48 (2 br. *dd*, *J* = 14.7, 9.9, H–C(5), H–C(8)); 5.84 (*m*, H–C(6), H–C(7)) [6.10–5.95 (series of

[12]) When not superimposed, the resonances for the (6*E*)-isomer are given within square brackets. This holds also for **14z**/**14e**, **16z**/**16e**, **17z**/**17e**, **18**/**18e**, and **19z**/**19e**.

m, H–C(5)–H–C(8))]; 5.69, 5.66 (2*dt*, *J* = 15.0, 7.2, H–C(4), H–C(9)); 3.85 (*X* of *ABX* as a *m*, H–C(2′)); 3.70, 3.62 [3.71, 3.63] (*AB* of *ABX*, *J*(*AB*) = 11.4, *J*(*AX*) = 3.9, *J*(*BX*) = 5.1, 2 H–C(1′)); 3.50 (*m*, 2 H–C(3′), 2 H–C(1)); 2.16 (*m*, 2 H–C(3)); 2.06 (*m*, 2 H–C(10)); 1.67 [1.69] (*quint.*, *J* = 7.2, 2 H–C(2)); 1.39 (*sext.*, *J* = 7.2, 2 H–C(11)); 0.90 [0.88] (*t*, *J* = 7.2, 3 H–C(12)). ^{13}C-NMR[10]): 135.67, 134.69, 128.14, 127.22, 126.38, 125.78 [133.97, 132.92, 131.34, 131.09, 130.46, 130.45] (6*d*, C(4)–C(9)); 72.49 (*t*, C(1)); 70.99 [71.06] (*t*, C(1′)); 70.42 (*d*, C(2′)); 64.22 (*t*, C(3′)); 35.02 [34.88] (*t*, C(10)); 29.45 (*t*, C(2)); 29.16 [29.26] (*t*, C(3)); 22.50 (*t*, C(11)); 13.73 [13.69] (*q*, C(12)). MS: 254 (10, $M^{+\cdot}$), 180 (9), 163 (7), 162 (30), 133 (25), 121 (48), 119 (76), 105 (47), 95 (14), 91 (100), 82 (13), 75 (8).

12. p-*Acetoxybenzoylation of* **17z** *and* **17e**. To **17z**/**17e** (12.7 mg, 0.05 mmol) in pyridine (1 ml) were added 0.12 ml of a 0.46M soln. of 4-acetoxybenzoyl chloride (0.055 mmol) (obtained from 4-acetoxybenzoic acid, *Aldrich*, with excess $SOCl_2$ [26]) in CCl_4 under N_2, and the resulting mixture was stirred at r.t. overnight, then evaporated, H_2O was added and the mixture extracted with Et_2O (3 × 30 ml). The org. phase was washed first with aq. $CuSO_4$, then H_2O, dried (Na_2SO_4), and evaporated. The residue was subjected to FC with $CHCl_3$/i-PrOH 95:5 to give the **18z**/**18e** (10.4 mg) and the less polar **19z**/**19e** (6.4 mg) oily colorless mixtures, besides unreacted **17z**/**17e** (1.9 mg).

Data of the Dextrorotatory 52:48 Mixture **18z**/**18e**. IR (neat): 3400*w*, 3020*m*, 2930*s*, 2855*s*, 1745*m*, 1726*s*, 1638*w*, 1460*m*, 1374*m*, 1220*m*, 1118*m*. ^{1}H-NMR[10]): 8.07 (*d*, *J* = 8.7, H–C(2″), H–C(6″)); 7.16 (*d*, *J* = 8.7, H–C(3″), H–C(5″)); 6.56–6.40 (*m*, H–C(5), H–C(8)) [6.10–5.95 (series of *m*, H–C(5)–H–C(8))]; 5.83 (*m*, H–C(6), H–C(7)); 5.70–5.63 (*m*, H–C(4), H–C(9)); 4.41, 4.37 (*AB* of *ABX*, *J*(*AB*) = 11.4, *J*(*AX*) = 5.1, *J*(*BX*) = 5.7, 2 H–C(3′)); 4.13 (*X* of both *ABX* and *A′B′X* as a *m*, 2 H–C(2′)); 3.56, 3.50 (*A′B′* of *A′B′X*, *J*(*A′B′*) = 9.9, *J*(*A′X*) = 3.9, *J*(*B′X*) = 6.3, 2 H–C(1′)); 3.48 (*m*, 2 H–C(1)); 2.32 (*s*, CH_3CO); 2.19–2.06 (*m*, 2 H–C(3), 2 H–C(10)); 1.85–1.40 (*m*, 2 H–C(2), 2 H–C(11)); 0.90 [0.88] (*t*, *J* = 7.2, 3 H–C(12)).

Data of the Levorotatory 52:48 Mixture **19z**/**19e**. ^{1}H-NMR[10]): 8.08 (*d*, *J* = 9.0, H–C(2″), C(6″)); 7.17 (*d*, *J* = 9.0, H–C(3″), H–C(5″)); 6.56–6.40 (*m*, H–C(5), H–C(8)) [6.10–5.94 (series of *m*, H–C(5)–H–C(8))]; 5.83 (*m*, H–C(6), H–C(7)); 5.69–5.63 (*m*, H–C(4), H–C(9)); 5.22 [5.23] (*quint.*, *J* = 5.1, H–C(2′)); 3.93 (*d*, *J* = 4,2, 2 H–C(3′)); 3.76, 3.71 [3.77, 3.72] (*AB* of *ABX*, *J*(*AB*) = 10.5, *J*(*AX*) = 4.8, *J*(*BX*) = 5.1, 2 H–C(1′)); 3.49 (*m*, 2 H–C(1)); 2.32 (*s*, CH_3CO); 2.18–2.06 (*m*, 2 H–C(3), 2 H–C(10)); 1.80–1.40 (*m*, 2 H–C(2), 2 H–C(11)); 0.91 [0.88] (*t*, *J* = 7.2, 3 H–C(12)).

13. *Isobretonin A* (= *(+)-(S)-3-{[(4E,6E,8E)-Dodeca-4,6,8-trienyl]oxy}-2-hydroxypropyl 4-hydroxybenzoate;* (+)-**2**). The **18z**/**18e** mixture (8.8 mg, 0.021 mmol) was stirred overnight at r.t. in pyridine containing 4-(dimethylamino)pyridine (2.5 mg, 0.021 mmol). The resulting mixture was then shaken with an aq. $CuSO_4$ soln. to remove pyridine, then AcOEt was added, and finally the mixture was filtered on a *Whatman* phase-separation filter. The raw product was purified by reversed-phase HPLC with MeCN/H_2O 75:25 to give pure (+)-**2z** (t_R 8.4 min, 2.8 mg) and (+)-**2** (t_R 9.6 min, 2.7 mg) as colorless oils.

Data of (+)-(S)-3-{[(4E,6Z,8E)-Dodeca-4,6,8-trienyl]oxy}-2-hydroxypropyl 4-Hydroxybenzoate ((+)-**2z**). $[\alpha]^{25}(\lambda\,[\text{nm}])$ = +4.6 (589), +7.4 (546), +13.9 (435), +20.4 (365; *c* = 0.18, MeOH). IR (neat): 3350*m*, 3020*s*, 2940*s*, 2850*s*, 1710*s*, 1640*w*, 1500*m*, 1460*m*, 1223*s*, 1112*m*, 1095*m*. ^{1}H-NMR[10]): 7.94 (*d*, *J* = 8.7, H–C(2″), H–C(6″)); 6.84 (*d*, *J* = 8.7, H–C(3″), H–C(5″)); 6.56–6.40 (*m*, H–C(5), H–C(8)); 5.84 (*m*, H–C(6), H–C(7)); 5.69, 5.66 (2*dt*, *J* = 15.0, 7.2, H–C(4), H–C(9)); 4.39, 4.35 (*AB* of *ABX*, *J*(*AB*) = 11.4, *J*(*AX*) = 5.1, *J*(*BX*) = 5.4, 2 H–C(3′)); 4.10 (*X* of both *ABX* and *A′B′X* as a *m*, H–C(2′)); 3.56, 3.50 (*A′B′* of *A′B′X*, *J*(*A′B′*) = 9.9, *J*(*A′X* = 4.2, *J*(*B′X*) = 6.0, 2 H–C(1′)); 3.47 (*m*, 2 H–C(1)); 2.16–2.06 (*m*, 2 H–C(3), 2 H–C(10)); 1.80–1.35 (*m*, 2 H–C(2), 2 H–C(11)); 0.90 [0.88] (*t*, *J* = 7.2, 3 H–C(12)). MS: 281 (9), 236 (4), 195 (6), 163 (12), 138 (24), 137 (10), 121 (100), 95 (40), 93 (32), 82 (27), 69 (51).

*Data of (+)-***2**: $[\alpha]^{25}(\lambda\,[\text{nm}])$ = +5.4 (589), +8.6 (546), +15.2 (435), +22.6 (365; *c* = 0.16, MeOH). NMR and MS data superimposable to those for natural (+)-**2** [5].

14. *Acetylation Products (+)-(S)-1-[(Acetoxy)methyl]-2-{[(4E,6E,8E)-dodeca-4,6,8-trienyl]oxy}ethyl 4-Acetoxybenzoate* ((+)-**1b**) *and Its (6Z)-Isomer* ((+)-**20**). The **19z**/**19e** mixture (5.9 mg) was stirred overnight in excess Ac_2O/pyridine at r.t., then AcOEt was added and the mixture shaken with aq. $CuSO_4$ to remove pyridine, then filtered on a *Whatman* phase-separation filter, and finally evaporated to give a residue which was subjected to HPLC with hexane/AcOEt 3:1 to give (+)-**1b** (t_R 7.1 min) and (+)-**20** (t_R 7.8 min). These products were further purified by reversed-phase HPLC with MeCN/H_2O 4:1 to give pure (+)-**20** (t_R 12.0 min, 1.7 mg) and (+)-**1b** (t_R 13.3 min, 1.8 mg) as colorless oils.

*Data of (+)-***20**. ^{1}H-NMR[10]): 8.07 (*d*, *J* = 8.7, H–C(2″), H–C(6″)); 7.17 (*d*, *J* = 8.7, H–C(3″), H–C(5″)); 6.56–6.40 (*m*, H–C(5), H–C(8)); 5.84 (*m*, H–C(6), H–C(7)); 5.69, 5.66 (2*dt*, *J* = 14.8, 7.2, H–C(4), H–C(9)); 4.41, 4.33 (*AB* of *ABX*, *J*(*AB*) = 12.0, *J*(*AX*) = 3.9, *J*(*BX*) = 6.6, 2 H–C(3′)); 5.40 (*X* of both *ABX* and *A′B′X* as a *m*, H–C(2′)); 3.67, 3.64 (*A′B′X*, *J*(*A′B′*) = 10.2, *J*(*A′X*) ≈ *J*(*B′X*) = 5.1, 2 H–C(1′)); 3.48 (*m*, 2 H–C(1)); 2.32 (*s*,

CH_3COO–C(4″)); 2.12–2.05 (*m*, 2 H–C(3), 2 H–C(10)); 2.04 (*s*, CH_3COO–C(3′)); 1.63, 1.40 (*m*, 2 H–C(2), 2 H–C(11)); 0.90 (*t*, J = 7.2, 3 H–C(12)). MS: 279 (7), 237 (12), 179 (7), 163 (33), 135 (12), 121 (100), 116 (11), 95 (28), 82 (20), 69 (39).

*Data of (+)-***1b**. $[\alpha]^{25}(\lambda$ [nm]) = +5.6 (589), +7.4 (546), +13.9 (435), +20.6 (365; c = 0.14, MeOH). CD (MeOH): $\Delta\varepsilon$ (λ [nm]) = +0.016 (279), −0.060 (266), +0.125 (230). NMR and MS data superimposable to those for (−)-**1b** [5].

15. *Bretonin B* (= *(*S*)-2-{[(4*E*,6*Z*,8*E*)-Dodeca-4,6,8-trienyl]oxy}-1-(hydroxymethyl)ethyl 4-hydroxybenzoate;* **3**). Compound **3** was isolated from the sponge extract and was purified by reversed-phase HPLC (MeCN/H_2O 65:35, t_R 15 m) during the isolation of **1a** and (+)-**2** [5].

Data of **3**. ^{1}H-NMR[10]): 7.96 (*d*, J = 8.7, H–C(2″), H–C(6″)); 6.85 (*d*, J = 8.7, H–C(3″), H–C(5″)); 6.54–6.40 (*m*, H–C(5), H–C(8)); 5.83 (*m*, H–C(6), H–C(7)); 5.69, 5.65 (2*dt*, J = 14.7, 7.0, H–C(4), H–C(9)); 5.20 (*quint.*, J = 4.8, H–C(2′)); 3.92 (*d*, J = 4.8, 2 H–C(3′)); 3.77, 3.75 (*AB* of *ABX*, $J(AB)$ = 10.5, $J(AX)$ = 4.8, $J(BX)$ = 5.1, 2 H–C(1′)); 3.50 (*m*, 2 H–C(1)); 2.15, 2.08 (*q*, J = 7.2, 2 H–C(3), 2 H–C(10)); 1.68 (*quint.*, J = 7.2, 2 H–C(2)); 1.42 (*sext.*, J = 7.2, 2 H–C(11)); 0.90 (*t*, J = 7.2, 3 H–C(12)). MS: 357 (3, $[M - OH]^+$), 356 (4, $[M - H_2O]^{+\cdot}$), 281 (54), 253 (1), 236 (1), 195 (5), 163 (4), 149 (15), 138 (16), 121 (79), 95 (15), 93 (17), 82 (12), 69 (32), 56 (25).

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