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Illustrating the Power of Singlet Oxygen Chemistry in a Synthetic Context: Biomimetic Syntheses of Litseaverticillols A–G, I and J and the Structural Reassignment of Litseaverticillol E

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Abstract: Biomimetic syntheses of the litseaverticillols A–G, I and J are reported herein. The syntheses rely heavily on the application of two different modes of reaction for photochemically generated singlet oxygen, namely, the [4+2] cycloaddition of singlet oxygen ($^1O_2$) with furans and the ene reaction of $^1O_2$ with double bonds. The highlight of these syntheses is a one-pot cascade sequence, involving five synthetic operations initiated by a [4+2] reaction, to form the fully functionalised litseaverticillol core. A series of regioselective ene reactions are then used to appositely functionalise the side chains. The synthesis of litseaverticillol E (both its originally proposed and its actual structures) allows a structural reassignment of this natural product.

Keywords: biomimetic synthesis · cascade reactions · litseaverticillol · natural products · singlet oxygen

Introduction

A recently isolated family of potent anti-HIV natural products, the litseaverticillols, presented us with a unique opportunity to blend the aims of developing both environmentally friendly chemistry and atom-efficient synthetic methods, by allowing us to devise and realise a highly efficient biomimetic strategy for their synthesis. The plan, which made use of a sophisticated cascade sequence[1] and the immense versatility of singlet oxygen ($^1O_2$) chemistry, was completely devoid of wasteful hindrances, such as protecting groups. The full evolution of this design from inception to execution is described herein.[2,3]

The litseaverticillols as a family all possess a 4-hydroxycyclopentenone core substituted at the 5-position with a variable, but always unsaturated, side chain (Scheme 1). The isolation and structure elucidation of this novel class of naturally occurring sesquiterpenes, alongside initial biological activity data, were reported in a series of papers,[4] with the full details for all family members appearing in print in 2003.[4c] The litseaverticillols originated in the leaves and twigs of a perennial shrub or arbor, named *Litsea verticillata* Hance, which was found growing in the Cuc Phuong National Park, Vietnam. Following bioassay-guided fractionation of the chloroform extract taken from the biomass, eight members of this new litseane skeletal class were identified, litseaverticillols A–H (**1**–**8**, Scheme 1), all of which exhibited inhibitory activity against HIV-1 replication in HOG.R5 cells with IC_{50} values ranging from 2–15 $\mu g\,mL^{-1}$.[4c] Crucially, their potent antiviral activity did not affect the growth of the host cell, so the compounds were considered to have low in vitro toxicity and were deemed to be important targets for further biological investigation. Due to the short supply of several members of this class and the desire for access to selected analogues, synthetic studies were seen as imperative.

Development of a proposal for the biogenesis of the litseaverticillols: Close inspection of the litseaverticillols' structures revealed to us several important features which were to inform our subsequent hypothesis relating to their biogenetic origins (Scheme 2). Firstly, the group could be de-

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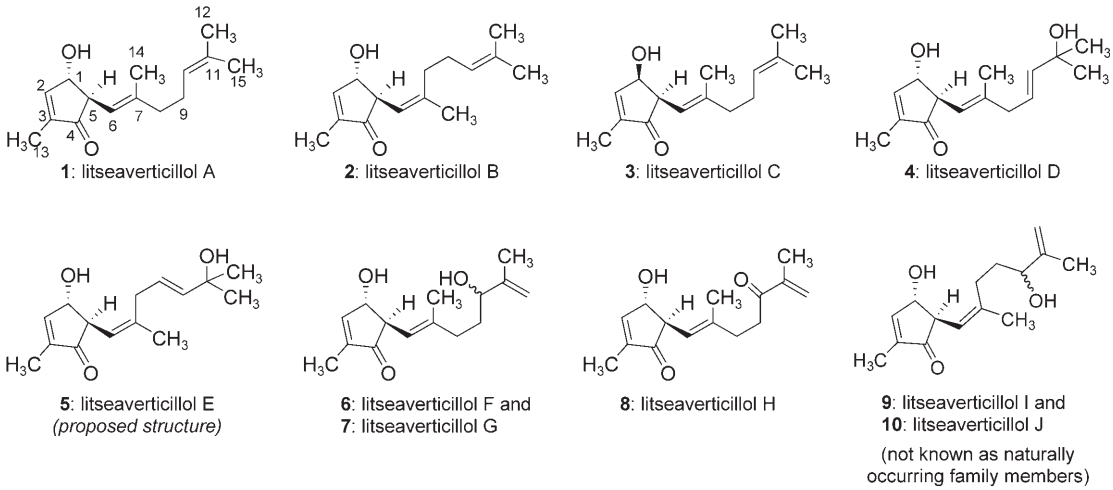
Supporting Information for this article (comprising copies of ^1H and ^{13}C NMR spectra for compounds **1**, **2**, **4**–**7**, **9**, **10**, **11a**, **11b**, **13a**, **13b**, **18a**, **18b**, and **25** and HRMS data for **25**) is available on the WWW under http://www.chemeurj.org/ or from the authors.



Scheme 1. Structures of litseaverticillols A–J.

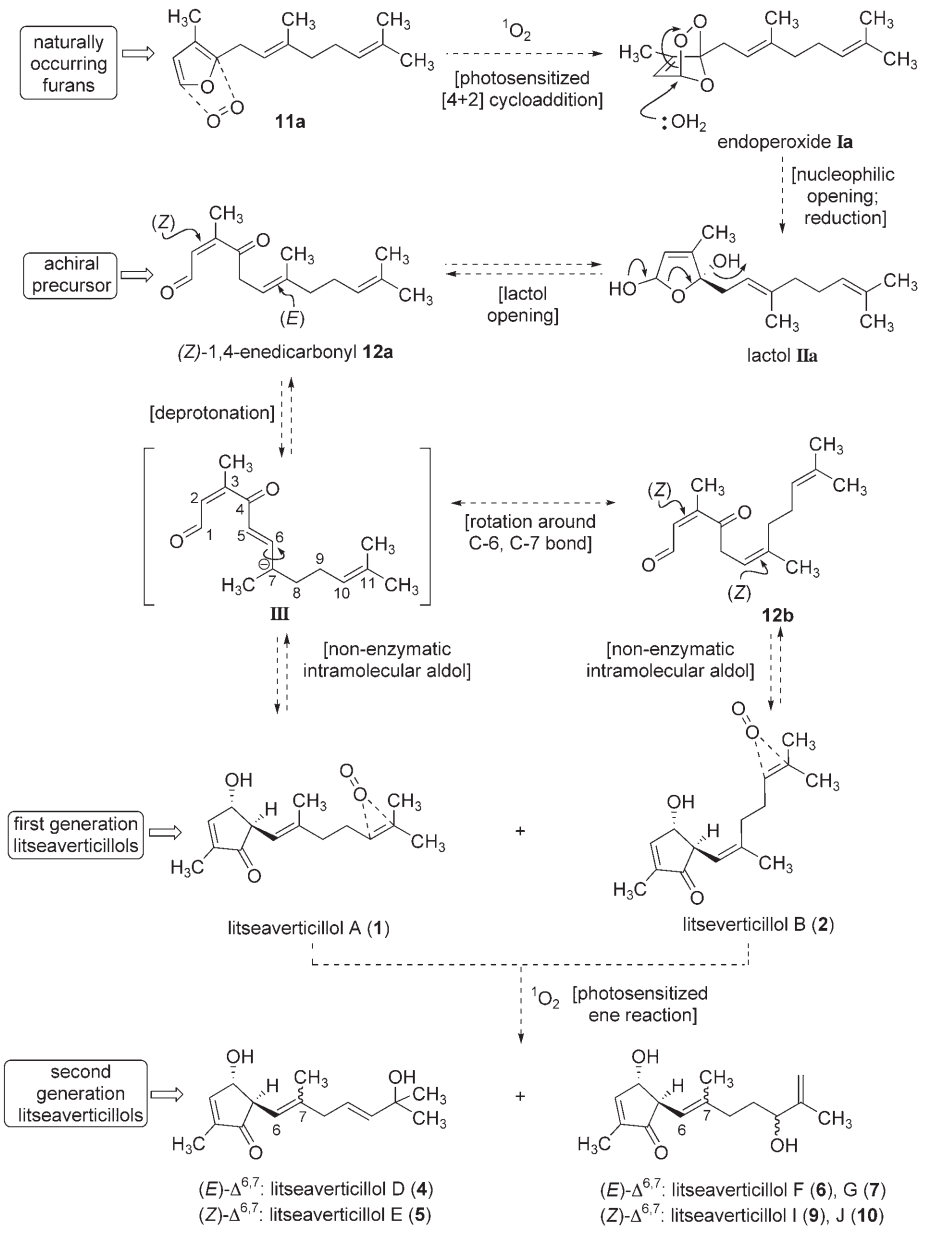
lineated into first (litseaverticillols A–C (**1**–**3**)) and second (litseaverticillols D–H (**4**–**8**)) generations, with the latter arising directly from oxidation of the unsaturated side chain present in the former. The classical modes by which singlet oxygen ($^1O_2$) is known to react with trisubstituted double bonds[5] support the idea that $^1O_2$ could be responsible for this conversion of the first-generation compounds into the second. For example, litseaverticillols D (**4**), F (**6**) and G (**7**) together represent the three possible products that could be derived from a chemoselective ene reaction between $^1O_2$ and the $\Delta^{10,11}$ double bond of the side chain of litseaverticillol A (**1**), that is, the double bond most distal from the 4-hydroxycyclopentenone core. Litseaverticillol A (**1**) could also be responsible for fathering litseaverticillol H (**8**) through two consecutive oxidations. Likewise, litseaverticillol B (**2**) could furnish the compound with the proposed structure for litseaverticillol E (**5**). Furthermore, the litseaverticillol core could conceivably arise from a cascade initiated by another common reaction of $^1O_2$, a [4+2] cycloaddition occurring with the electron-rich diene moiety of a naturally occurring furan,[6] such as sesquirosefuran (**11a**).[7] The endoperoxide **IIa** resulting from this transformation might reasonably be expected to be susceptible to nucleophilic opening; this followed by base-mediated collapse of the lactol intermediate **IIa** would give the acyclic (*Z*)-1,4-enedicarbonyl **12a**. A nonenzymatic intramolecular aldol reaction of this achiral precursor **12a** would then complete the assembly of the litseaverticillol core. At this stage we also entertained the possibility that the deviation in geometry at the $\Delta^{6,7}$ double bond exhibited amongst the various litseaverticillols could arise by isomerisation of **12a**, under mildly basic conditions, to afford a mixture of **12a** and **12b**; thus, just one naturally occurring furan might be the biogenetic precursor to the entire litseaverticillol family. This proposed derivation of the litseverticillols A–H (**1**–**8**) is in full accord with the high natural abundance in plants of the three components necessary for photochemically generating the reactive $^1O_2$ species; these components are a) molecular dioxygen (approximately 20% in atmospheric air), b) photosensitisers, such as, tannins, chlorophylls and porphyrins, and c) visible light.

Finally, our newly developed hypothesis that the achiral 1,4-enedicarbonyls **12a** and **12b** might be key intermediates in the biogenesis of all the litseaverticillols could be further justified by the observation that all the litseaverticillols exist as racemic mixtures. Racemates are found relatively rarely in nature because of the heavy reliance on homochiral enzyme-templated reactions. However, the concept of nonenzymatic biological assembly[1] of whole classes of natural products is not without precedent. Most notably, Black and co-workers proposed such a biosynthesis for the endiandric acids,[8] a hypothesis later supported by a total synthesis of these racemates accomplished by Nicolaou and co-workers.[9]

Retrosynthetic analysis and strategy: With our proposed biogenetic blueprint in hand, we now turned our attention to how its directives might be implemented in a laboratory setting and to how our hypothesis might be supported by empirical results. It was envisioned that the furans **11a** and **11b**, required as substrates for our investigation into the pivotal $^1O_2$-initiated cascade sequence, could be accessed by alkylation of the known furan **14** with either neryl or geranyl bromide (**15** and **16**, respectively), as detailed in the retrosynthetic scheme (Scheme 3).

Results and Discussion

Synthesis of the first-generation litseaverticillols A–C: Now that our full strategy for accomplishing a biomimetic synthesis of the litseverticillol family (A–J, **1**–**10**) had been clearly delineated, we were ready to embark on the synthetic phase of the project. Thus, 2-triisopropylsilyloxyfuran **14** was prepared according to a two-step literature precedent[10,11] from the cheap and readily available citraconic anhydride (**17**, Scheme 4). *Ortho*-metallation at the 5-position of **14** by

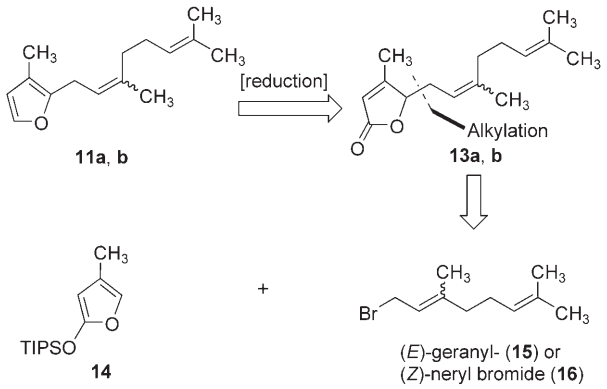


Scheme 2. Our proposal for the biogenesis of the litseaverticillol family.

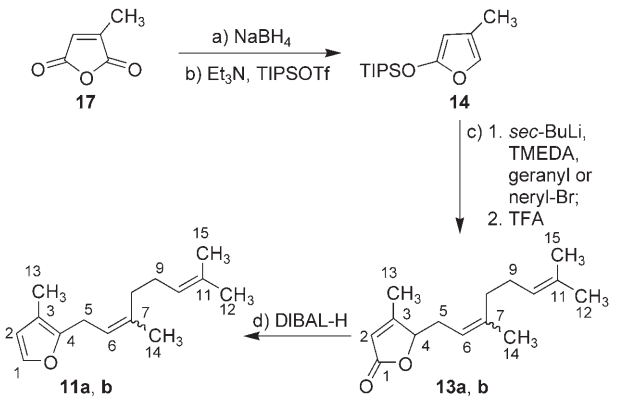
using *sec*-butyllithium, followed by a quench of the resultant anion with either neryl or geranyl bromide (**15** and **16**, respectively) and subsequent in situ acidic hydrolysis of the triisopropylsilyloxy moiety, furnished the lactones **13a** and **13b** in moderate yields. DIBAL-H was eventually found to be the reducing agent of choice[12] for effecting the transformation of the lactones **13a** and **13b** into sesquirosefuran (**11a**) and furan **11b**, respectively, under carefully controlled reaction conditions.

With the synthesis of the sesquirosefuran (**11a**) and furan **11b** substrates efficiently concluded, the time had come to test the key singlet oxygen ($^1O_2$) cascade sequence from which we hoped to derive the complete litseaverticillol core.

A significant hurdle that execution of this ambitious one-pot, five-synthetic-operations cascade faced was the problem of chemoselectivity. The sequence was required to initiate at the site of the furan core without concomitant reaction at either of the two susceptible double bonds present in the appended side chain. Indeed, applications of several literature protocols known as methods for the direct oxidation of furans to the corresponding (*Z*)-1,4-enediones, including treatment with either Br_2/MeOH/dilute H_2SO_4[13] or magnesium monoperoxyphthalate,[14] were unsuccessful as they led primarily to extensive unwanted bromination or epoxidation of the side-chain double bonds. This apparent lack of chemoselectivity prompted us to examine more closely the pioneering work of Foote, Schenck and co-workers[15] relating to the photosensitised oxidation of alkyl-substituted furans. In this case, the conditions used would closely mimic our biogenetic scenario for the oxidation of naturally occurring furans into the litseaverticillols. Gratifyingly, it was found that upon subjecting sesquirosefuran (**11a**), in a methanolic solution containing 10^{-4} M methylene blue (as a photosensitiser) and having O_2 gently bubbled through it, to irradia-

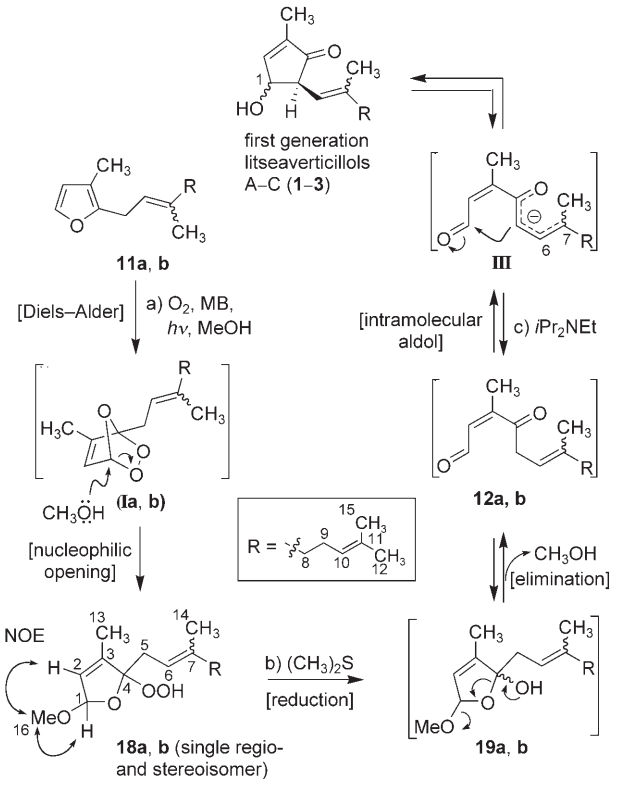


Scheme 3. Retrosynthetic analysis of furans **11a** and **11b**, precursors for the proposed biomimetic cascade sequence. TIPS = triisopropylsilyl.



Scheme 4. Preparation of sesquirosefuran **11a** and its *Z* analogue **11b**. Reagents and conditions: a) see ref. [10,11]; b) Et_3N (1.4 equiv), TIPSOTf (1.2 equiv), CH_2Cl_2, 0→25 °C, 6 h, 81 %; c) TMEDA (1.8 equiv), *sec*-BuLi (1.8 equiv), THF, 0 °C, 2 h, geranyl-Br (**15**) or neryl-Br (**16**, 2.0 equiv), 0 °C, 3 h; then TFA (3.0 equiv), 25 °C, 1 h, 63–65 %; d) DIBAL-H (1.7 equiv), THF, −78→−5 °C, 3 h, 80–85 %. TIPSOTf = triisopropylsilyltrifluoromethanesulfonate, TMEDA = *N*,*N*,*N*′,*N*′-tetramethylethylenediamine, TFA = trifluoroacetic acid, DIBAL-H = diisobutylaluminium hydride.

tion with visible light for 1 min, hydroperoxide **18a** was exclusively formed as the adduct in a quantitative yield (Scheme 5). It was possible to isolate and fully characterise hydroperoxide **18a**; in addition, it was the subject of NOE studies, as indicated in Scheme 5, which confirmed that it was the opposite regioisomer to that previously proposed for the analogous photooxidation of 2-methylfuran and menthofuran.[15] These studies of the structure of hydroperoxide **18a** also proved that the nucleophilic addition of MeOH to the endoperoxide (**Ia**, Scheme 5) was not only regioselective but also diastereoselective. The hydroperoxide moiety of **18a** was reduced by treatment with 5.0 equivalents of $(CH_3)_2S$ in CH_2Cl_2 with progress monitored by use of ^{1}H NMR spectroscopy. After 2 h, the intermediate anomeric hemiketals (**19a**, Scheme 5) could be observed in the ^{1}H NMR spectra along with small amounts of keto aldehyde **12a**, however, the reaction was left for a further 6 h until complete conversion into the keto aldehyde **12a** had occurred. The labile keto aldehyde **12a** could be isolated in high yield (90 %); alternatively, once it was formed, in situ treatment with 1 equivalent of Hünig's base furnished, after 6 h stirring, a 19:1 mixture of litseaverticillols A (**1**) and C (**3**). Triethylamine was initially employed as the base in an attempt to promote this reaction, which mimics the nonenzymatic intramolecular aldol reaction proposed in our biogenetic hypothesis; however, this choice of base led to a major degradation of the fragile substrate.



Scheme 5. Biomimetic total synthesis of the first-generation litseaverticillols A–C from furans **11a** and **11b**, including the mechanistic rationale. Reagents and conditions: a) 10^{-4} M MB, O_2 (bubbling), MeOH, *hν*, 0 °C, 1 min, 97 %; b) $(CH_3)_2S$ (5.0 equiv), CH_2Cl_2, 25 °C, 8 h; c) *i*Pr_2NEt (1.0 equiv), 25 °C, 6 h, 51–55 % over two steps. MB = methylene blue.

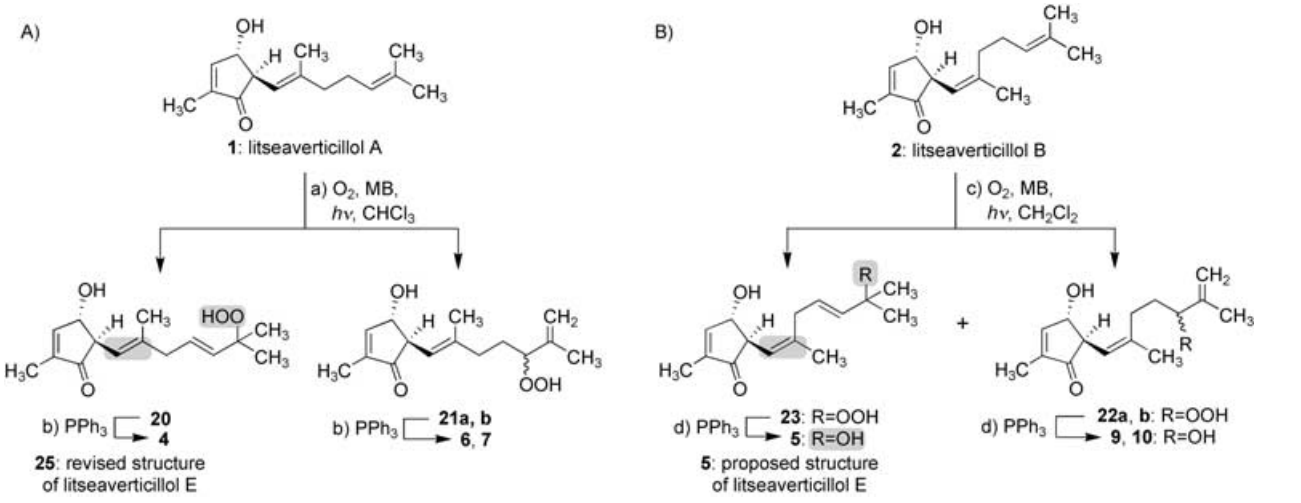
Optimisation of this reaction sequence enabled us to achieve the desired goal of undertaking the whole series of transformations (**11a**→**1**, **3**) in a single pot, with just one exchange of solvent from methanol to CH_2Cl_2 (or $CHCl_3$) at the appropriate stage (prior to the addition of $(CH_3)_2S$), in 55 % overall yield. It was also found that premature addition of the Hünig's base halted the cascade; apparently, anomeric hemiketals **19a** are stable under basic conditions. If Hünig's base was added to a solution containing the mixture of hemiketals and keto aldehyde (**19a**:**12a**, 7:3), the elimination of MeOH was suppressed, thereby leading to a 7:3 mixture of hemiketals and litseaverticillol A (**19a**:**1**), even after three days of stirring at room temperature. This observation had to be balanced, when seeking optimal timings with the observed lability of keto aldehyde **12a**, which was shown to decompose completely on standing in solution for two days.

Exactly the same protocol as had been developed for the one-pot cascade to furnish litseaverticillol A (**1**) from sesquirosefuran (**11a**) was repeated with furan **11b** to access litseaverticillol B (**2**) in 51 % overall yield. The formation of litseaverticillol B (**2**) was accompanied, in accordance with our previous experience regarding the formation of both litseaverticillols A (**1**) and C (**3**) from the same achiral precursor (**12a**), by production of trace amounts of its C-1 diastereoisomer (20:1). It should be noted at this stage that the spectra (^{1}H NMR, ^{13}C NMR, HRMS, see the Supporting Information) of the synthetic litseaverticillols A–C (**1**–**3**) were identical in every way to those of the naturally derived compounds. Perhaps the most intriguing and exciting observation of this phase of our investigations was that, if the reaction of **11b** was left for prolonged periods (12 h) subsequently to the addition of Hünig's base, then substantial amounts of litseaverticillol A (**1**, 15 %) were isolated in addition to the expected products, litseaverticillol B (**2**) and its

C-1 diastereoisomer. The furan **11b** employed in the reaction cascade is geometrically pure; therefore, this geometrical deviation must be a feature of the cascade itself. Since no formation of litseaverticillol A (**1**) was observed with shorter reaction times, we rationalised that litseaverticillol B (**2**) must be undergoing a retroaldol reaction to regenerate the stabilised anion **III** (Scheme 2 and Scheme 5). This anion, exhibiting extended conjugation, may allow stereochemical scrambling of the $\Delta^{6,7}$ double bond by permitting rotation around the C-6/C-7 bond. Thus, under these equilibration conditions, anion **III** can suffer one of two fates, either reformation of litseaverticillol B (**2**) or rotation around the C-6/C-7 bond followed by an intramolecular aldol reaction to afford the thermodynamically more stable litseaverticillol A (**1**). These results provide a stark indication that our biogenetic proposal, including the proposal that the whole litseaverticillol family might arise from a single naturally occurring furan, is a valid and substantiated hypothesis. Further to our proposals presented thus far, we now suggest that the distribution of isolated natural products may be correlated to their thermodynamic stability, as it represents an equilibrium mixture.

Synthesis of the second-generation litseaverticillols D–G, I and J: Not content to rest upon our laurels with the synthesis of the first-generation litseaverticillols A–C (**1**–**3**) secured, we continued to probe the scope of the $^1O_2$ paradigm by attempting to synthesise the second-generation litseaverticillols by using $^1O_2$-mediated oxidation of the distal double bond ($\Delta^{10,11}$) in the side chains appended to the litseaverticillol core. We rationalised that this regioselective reaction, targeting just one out of the three double bonds present in the first-generation litseaverticillols, was possible for both steric and electronic reasons. The $\Delta^{2,3}$ double bond present within the molecule's core is too electron deficient to readily participate in an ene reaction with $^1O_2$ and the $\Delta^{6,7}$ double bond suffers from greater steric encumberance than its $\Delta^{10,11}$ neighbour; therefore, reaction at the latter should be fastest. The first-generation parent litseaverticillol A (**1**), dissolved in $CDCl_3$ together with 10^{-4} M methylene blue as a photosenzitiser, was subjected to visible light irradiation for 3 min at 0 °C whilst O_2 was gently bubbled through the solution (Scheme 6). ^1H NMR analysis of the mixture that was produced identified the presence of tertiary hydroperoxide **20** and diastereomeric secondary hydroperoxides **21a** and **21b** (**20**:**21**, 1:1). In situ reduction of this mixture with PPh_3 instantaneously afforded the corresponding naturally occurring diols, litseaverticillols D (**4**), F (**6**) and G (**7**) in good overall yield (70%). Litseaverticillol D (**4**, 35%) could be separated by careful column chromatography from an inseparable equimolar mixture (35%) of litseaverticillols F (**6**) and G (**7**). Only trace amounts of the more polar triols arising from the indiscriminate oxidation of both side chain double bonds were observed. The favoured published mechanism[16,17] for describing the ene reaction of a trisubstituted double bond with $^1O_2$ accounts for the product distribution seen upon oxidation of litseaverticillol A (**1**, Scheme 6). Thus, the result is consistent with the formation of an intermediate perepoxide,[16] in which the negatively charged oxygen atom is orientated towards the more substituted side of the preceding double bond, in accordance with the so-called *cis* effect.[16] The subsequent abstraction of the allylic hydrogen atom, possible from either C-9 or C-15, furnishes a balanced 1:1 mixture of C-11 (tertiary) and C-10 (secondary) hydroperoxides (**20** and **21a**,**b**, respectively).

Gratified by the success of this oxidative strategy for the derivation of the second-generation litseaverticillols, we were anxious to proceed with the synthesis of the remaining congeners from the litseaverticillol family, a task which included the synthesis of litseaverticillols I and J (**9** and **10**),



Scheme 6. Transformation of litseaverticillols A and B (**1** and **2**) into the second-generation litseaverticillols D (**4**), F (**6**), G (**7**), E (**5**), I (**9**) and J (**10**) through a regioselelective singlet-oxygen ene reaction and the structural reassignment of litseaverticillol E. Reagents and conditions: a) 10^{-4} M MB, O_2 (bubbling), $CHCl_3$, *hν*, 0 °C, 3 min; b) PPh_3 (2.0 equiv), $CHCl_3$, 25 °C, 5 min, 35% of **4** plus 35% of **6** and **7** over two steps; c) 10^{-4} M MB, O_2 (bubbling), CH_2Cl_2, *hν*, 0 °C, 4 min, 90%; d) PPh_3 (2.0 equiv), CH_2Cl_2, 25 °C, 10 min, 35% of **5** plus 22% of **9** and 18% of **10**.

the, as yet, not isolated offspring of litseaverticillol B (**2**), and the natural isolate litseaverticillol E (**5**). We believed that litseaverticillols I (**9**) and J (**10**) had not yet been isolated precisely because they were the offspring of the minor $\Delta^{6,7}$-isomer first-generation compound litseaverticillol B (**2**) and these compounds, as previously discussed, possessed the less thermodynamically stable *Z* arrangement at the $\Delta^{6,7}$ double bond. Our interest in litseaverticillols I and J (**9** and **10**), which crucially bear both the $\Delta^{6,7}$ *Z* arrangement and side-chain oxidation, had been piqued by the initial structure–activity relationship data, which suggested that each of these two structural attributes was responsible for rises in the anti-HIV activity when like-with-like comparisons were made of the biological data for the known naturally occurring litseaverticillols A–H (**1**–**8**).[4c] To enable us to examine further the biological activity of litseaverticillols I and J (**9** and **10**) it was necessary to synthesise them; to this end, litseaverticillol B (**2**) was subjected to the optimal oxidation conditions as described above. After 4 min irradiation and subsequent PPh_3-mediated reduction, litseaverticillols I and J (**9** and **10**, 40%, 1.2:1) and compound **5** (35%) were isolated in 75% combined yield (Scheme 6). In contrast to litseaverticillols F (**6**) and G (**7**), litseaverticillols I (**9**) and J (**10**) were separable by column chromatography with pure samples of each being attained and subsequently submitted for biological investigations, the results of which will be reported at a later date.

Structural reassignment of litseaverticillol E: The completion of one synthesis of the so-called second-generation litseaverticillols did not provide the expected end to the tale. Whilst the spectra of synthetic litseaverticillols D, F and G (**4**, **6**, and **7**) matched exactly with those of the naturally occurring samples, the spectral data taken for the synthetically obtained compound **5** showed significant discrepancies with those of the natural sample of litseaverticillol E. Since, there could be no doubt that we had synthesised the compound with the proposed structure for litseaverticillol E (that is, compound **5**), we began to search for an alternative explanation for this apparent mismatch. Close inspection of the papers[4] reporting the isolation of the litseaverticillols revealed that the structure of litseaverticillol E (proposed structure **5**) had caused some concern to the group responsible.[4c] Fong and co-workers discuss the incongruous nature of some of the ^{13}C NMR peaks of the compound they supposed had the structure **5** in comparison to its closest litseaverticillol relatives. Specifically, they noted that the C-8 and C-14 signals in ^{13}C NMR spectrum were closer to those in the $\Delta^{6,7}$ *E* isomers than the $\Delta^{6,7}$ *Z* isomers; furthermore, the C-11 peak was shifted downfield from the comparable peak in litseaverticillol D (**4**). Our biogenetic proposal for the litseaverticillol family led us to consider that the spectral and physical properties of litseaverticillol E might be more in accordance with one of the hydroperoxide intermediates. However, the ^1H NMR spectrum of natural litseaverticillol E was distinctly different from each of the components of the mixture of hydroperoxides (**22a**, **22b**, and **23**) obtained upon oxidation of litseaverticillol B (**2**, Scheme 6). This prompted us to scrutinise the hydroperoxide intermediates obtained from the analogous oxidation of litseaverticillol A (**1**). Careful inspection of the ^1H NMR spectrum of the initially inseparable hydroperoxide intermediate mixture (**20**, **21a**, and **21b**, Scheme 6) convinced us that the true structure for litseaverticillol E was that of tertiary hydroperoxide **20**. In order to obtain full characterisation of hydroperoxide **20** to support this assertion, we needed to deconvolute the inseparable mixture obtained from the $^1O_2$-mediated oxidation of litseaverticillol A (**1**). We accomplished this task by selectively reducing the secondary hydroperoxides (**21a** and **21b**) with $(CH_3)_2S$ (5.0 equivalents, 25 °C, 12 h) to afford the more polar litseaverticillols F and G (**6** and **7**) accompanied by unreacted tertiary hydroperoxide **20**. The tertiary hydroperoxide **20**, which could now be isolated and purified with ease, had spectral data that matched those of naturally occurring litseaverticillol E in every respect (including a signal at 7.51 ppm in the ^1H NMR spectrum that was assignable to the hydroperoxide proton and HRMS data confirming that an error in the molecular formula was made upon isolation by the omission of one oxygen atom). The structure of naturally occurring litseaverticillol E was therefore reassigned as hydroperoxide **20**.

In conclusion, we have achieved the first syntheses of litseaverticillols A–G, I and J by using the biomimetic strategy which we had developed earlier. The syntheses include an elegant and highly efficient one-pot cascade, involving five synthetic operations and initiated by the [4+2] cycloaddition of a furan to $^1O_2$, to assemble the fully functionalised litseaverticillol core. The powerful chemistry of $^1O_2$ was then further commandeered to serve our purposes when the requisite regioselective side-chain oxidation was also accomplished by using ene reactions of $^1O_2$. The syntheses of compounds **20** and **5** allowed us to reassign the structure of naturally occurring litseaverticillol E as being the former rather than the latter, as was originally reported. Furthermore, the reassignment of litseaverticillol E to hydroperoxide structure **20** lent considerable credence to our proposal that $^1O_2$-mediated oxidation of the first-generation litseaverticillols is how nature constructs the second-generation litseaverticillols. Overall, these syntheses provide ample evidence that nature uses many of the modes of reaction known for $^1O_2$ and that this $^1O_2$ chemistry is easily adapted to the laboratory environment where it can provide a set of very valuable tools to the synthetic chemist.

Experimental Section

General techniques: Diethyl ether and THF were distilled from Na/benzophenone. TMEDA was refluxed for 24 h with $LiAlH_4$ and kept over 3 Å molecular sieves. Reagents were purchased at the highest available commercial quality and used without further purification. Irradiation experiments (photooxygenations) were performed with a xenon Variac Eimac Cermax 300 W lamp. Reactions were monitored by thin-layer chromatography (TLC) carried out on silica gel plates (60F-254) with UV light as the visualising method and an acidic mixture of phosphomo-

lybdic acid/cerium(IV) sulfate accompanied by heating of the plate as a developing system. The development agent contains H_2O (94 mL), concentrated H_2SO_4 (6 mL), $Ce(SO_4)_2{\cdot}(H_2O)_n$ (1.0 g) and phosphomolybdic acid (1.5 g). Column chromatography refers to flash column chromatography carried out on SiO_2 (silica gel 60, particle size 0.040–0.063 mm) with the specified eluent.

NMR spectra were recorded on a Bruker AMX-500 instrument and calibrated by using residual undeuterated solvent as an internal reference. The following abbreviations are used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. Electrospray ionisation mass spectrometry (ESIMS) experiments were performed on an API 100 Perkin–Elmer SCIEX single-quadrupole mass spectrometer at 4000 V emitter voltage. High-resolution mass spectra (HRMS) were recorded on a VG ZAB-ZSE mass spectrometer under matrix-assisted laser desorption/ionisation (MALDI) conditions with 2,5-dihydroxybenzoic acid (DHB) as the matrix.

Lactones 13a,b: *sec*-BuLi (2.0 mL of a 1.4 M solution in cyclohexane, 2.8 mmol) was added dropwise to a solution of furan **14** (400 mg, 1.56 mmol) and TMEDA (417 μL, 2.8 mmol) in anhydrous THF (8 mL) at 0 °C. After 2 h, geranyl bromide (**15**) or neryl bromide (**16**; 677 mg, 3.12 mmol) was added and the reaction was stirred for a further 3 h at the same temperature. A solution of H_2O and saturated aqueous $NaHCO_3$ (1:1, 10 mL) was added and the resulting mixture was extracted with Et_2O (15 mL). The organic phase was treated for 1 h with excess TFA (358 μL, 4.68 mmol) at ambient temperature. Saturated aqueous $NaHCO_3$ (10 mL) was added and the resulting mixture was extracted with Et_2O (2×10 mL). The organic phase was dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by flash column chromatography (silica gel, EtOAc/hexane (1:4)) to afford **13a** or **13b** (230–237 mg, 63–65 % over two steps) as colourless oils.

13a: R_f = 0.30 (silica gel, EtOAc/hexane (1:2)); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.79 (brs, 1H; H-2), 5.03 (brt, J = 6.7 Hz, 2H; H-4 and H-10), 4.87 (brt, J = 5.2 Hz, 1H; H-6), 2.64 (ddd, J_1 = 15.3, J_2 = 6.3, J_3 = 5.6 Hz, 1H; H-5a), 2.35 (ddd, J_1 = 15.3, J_2 = 7.3, J_3 = 6.4 Hz, 1H; H-5b), 2.03 (brs, 3H; H-13), 2.01 (m, 4H; H-8 and H-9), 1.67 (brs, 3H; CH_3), 1.63 (brs, 3H; CH_3), 1.58 ppm (brs, 3H; CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 173.1 (C-1), 168.2 (C-3), 139.8 (C-7), 131.6 (C-11), 123.9 (C-10), 117.3 (C-6 or C-2), 116.0 (C-2 or C-6), 84.3 (C-4), 39.7 (C-8), 30.2 (C-5), 26.4 (C-9), 25.7 (CH_3), 17.7 (CH_3), 16.3 (CH_3), 13.9 ppm (CH_3); HRMS (MALDI): calcd for $C_{15}H_{22}O_2Na$: 257.1512 $[M+Na]^+$; found: 257.1514.

13b: R_f = 0.31 (silica gel, EtOAc/hexane (1:2)); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.73 (brs, 1H; H-2), 5.03 (brt, J = 5.6 Hz, 1H; H-10), 4.99 (brt, J = 6.9 Hz, 1H; H-4), 4.78 (brt, J = 5.2 Hz, 1H; H-6), 2.58 (m, 1H; H-5a), 2.25 (ddd, J_1 = 15.3, J_2 = 7.4, J_3 = 6.5 Hz, 1H; H-5b), 1.98 (brs, 3H; H-13), 1.98 (brm, 4H; H-8 and H-9), 1.63 (brs, 3H; CH_3), 1.61 (brs, 3H; CH_3), 1.54 ppm (brs, 3H; CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 173.0 (C-1), 168.3 (C-3), 139.6 (C-7), 131.8 (C-11), 123.8 (C-10), 117.2 (C-2 or C-6), 116.8 (C-6 or C-2), 84.3 (C-4), 32.0 (C-8), 30.1 (C-5), 26.2 (C-9), 25.6 (CH_3), 23.3 (CH_3), 17.6 (CH_3), 13.9 ppm (CH_3); HRMS (MALDI): calcd for $C_{15}H_{22}O_2Na$: 257.1512 $[M+Na]^+$; found: 257.1514.

Sesquirosefuran 11a and its $\Delta^{6,7}$-*cis* analogue 11b: DIBAL-H (1.6 mL of a 1.0 M solution in THF, 1.6 mmol) was added dropwise to a solution of lactone **13a** or **13b** (220 mg, 0.94 mmol) in dry THF (9 mL) at −78 °C. The reaction solution was warmed slowly (3 h) to −5 °C and subsequently treated with 10 % HCl (2 mL). The mixture was extracted with Et_2O (10 mL), then the organic phase was dried with Na_2SO_4 and concentrated in vacuo. The residue was purified by flash column chromatography (silica gel, EtOAc/hexane (1:20→1:1)) to afford the unpolar sesquirosefuran **11a** or its $\Delta^{6,7}$-*cis* analogue **11b** (163–174 mg, 80–85 %) as colourless liquids, accompanied by the polar diol or its $\Delta^{6,7}$-*cis* analogue (18 mg, 8 %) as colourless syrups.

11a: R_f = 0.74 (silica gel, EtOAc/hexane (1:2)); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.21 (d, J = 1.4 Hz, 1H; H-1), 6.15 (d, J = 1.4 Hz, 1H; H-2), 5.26 (td, J_1 = 6.9, J_2 = 0.8 Hz, 1H; H-6), 5.08 (brt, J = 6.9 Hz, 1H; H-10), 3.29 (d, J = 7.0 Hz, 2H; H-5), 2.08 (m, 2H; H-9), 2.01 (t, J = 7.5 Hz, 2H; H-8), 1.97 (s, 3H; H-13), 1.71 (brs, 3H; CH_3), 1.67 (brs, 3H; CH_3), 1.59 ppm (brs, 3H; CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 150.1 (C-4), 139.8 (C-1), 136.5 (C-7), 131.5 (C-11), 124.2 (C-10), 119.9 (C-6), 113.4 (C-3), 112.8 (C-2), 39.6 (C-8), 26.6 (C-9), 25.7 (C-5 or CH_3), 25.2 (C-5 or CH_3), 17.6 (CH_3), 16.1 (CH_3), 9.8 ppm (CH_3); HRMS (MALDI): calcd for $C_{15}H_{23}O$: 219.1743 $[M+H]^+$; found: 219.1752.

11b: R_f = 0.75 (silica gel, EtOAc/hexane (1:2)); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.21 (d, J = 1.4 Hz, 1H; H-1), 6.16 (d, J = 1.4 Hz, 1H; H-2), 5.28 (brt, J = 7.0 Hz, H-6), 5.16 (brt, J = 6.3 Hz, 1H; H-10), 3.29 (d, J = 7.1 Hz, 2H; H-5), 2.14 (m, 4H; H-8 and H-9), 1.97 (s, 3H; H-13), 1.73 (brs, 3H; CH_3), 1.70 (brs, 3H; CH_3), 1.63 ppm (brs, 3H; CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 150.0 (C-4), 139.8 (C-1), 136.7 (C-7), 131.7 (C-11), 124.2 (C-10), 120.7 (C-6), 113.4 (C-3), 112.8 (C-2), 32.0 (C-8), 26.5 (C-9), 25.7 (C-5 or CH_3), 24.9 (C-5 or CH_3), 23.3 (CH_3), 17.6 (CH_3), 9.8 ppm (CH_3); HRMS (MALDI): calcd for $C_{15}H_{23}O$: 219.1743 $[M+H]^+$; found: 219.1752.

Tandem transformation of furans 11a,b into first-generation litseaverticillols A–C (1–3): A solution of **11a** or **11b** (150 mg, 0.69 mmol) in MeOH (20 mL) and containing 10^{-4} M methylene blue was placed in a test tube with O_2 gently bubbling through it. Irradiation with a xenon Variac Eimac Cermax 300 W lamp for 1 min at 0 °C led to complete tranformation of the starting material (based on TLC). The solvent was thoroughly removed in vacuo to yield the hydroperoxide **18a** or **18b** (188 mg, 97 % crude) as a gum.

18a: R_f = 0.40 (silica gel, EtOAc/hexane (1:2)); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.87 (brs, 1H; H-1), 5.59 (brs, 1H; H-2), 5.03 (brt, J = 6.4 Hz, 1H; H-10), 4.91 (brt, J = 6.7 Hz, 1H; H-6), 3.19 (s, 3H; H-16), 2.59 (dd, J_1 = 14.9, J_2 = 6.6 Hz, 1H; H-5a), 2.44 (dd, J_1 = 14.9, J_2 = 7.5 Hz, 1H; H-5b), 2.01 (m, 4H; H-8 and H-9), 1.70 (brs, 3H; CH_3), 1.67 (brs, 3H; CH_3), 1.62 (brs, 3H; CH_3) 1.59 ppm (brs, 3H; CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 144.7 (C-3), 138.4 (C-7), 131.4 (C-11), 124.1 (C-10), 121.5 (C-4), 117.0 (C-6), 115.2 (C-1), 108.4 (C-2), 50.1 (C-16), 39.7 (C-8), 35.5 (C-5), 26.4 (C-9), 25.7 (CH_3), 17.6 (CH_3), 16.3 (CH_3), 11.7 ppm (CH_3).

18b: R_f = 0.41 (silica gel, EtOAc/hexane (1:2)); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.90 (brs, 1H; H-1), 5.60 (brs, 1H; H-2), 5.09 (brs, 1H; H-10), 4.93 (brt, J = 6.7 Hz, 1H; H-6), 3.17 (s, 3H; H-16), 2.58 (dd, J_1 = 15.1, J_2 = 6.5 Hz, 1H; H-5a), 2.42 (dd, J_1 = 15.1, J_2 = 7.3 Hz, 1H; H-5b), 2.04 (brm, 4H; H-8 and H-9), 1.70 (brs, 3H; CH_3), 1.68 (brs, 3H; CH_3), 1.67 (brs, 3H; CH_3), 1.59 ppm (brs, 3H; CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 144.7 (C-3), 138.6 (C-7), 131.7 (C-11), 124.1 (C-10), 121.6 (C-4), 117.5 (C-6), 114.9 (C-1), 108.4 (C-2), 50.1 (C-16), 35.4 (C-5), 32.2 (C-8), 26.4 (C-9), 25.7 (CH_3), 23.6 (CH_3), 17.6 (CH_3), 11.7 ppm (CH_3).

The hydroperoxide **18a** or **18b** (188 mg, 0.67) was dissolved in CH_2Cl_2 (15 mL) at ambient temperature and $(CH_3)_2S$ (244 μL, 3.35 mmol) was added. After the mixture had been stirred for 8 h, iPr$_2$NEt (114 μL, 0.67 mmol) was added and the resultant solution was stirred for a further 6 h at the same temperature. Removal of the solvent in vacuo and purification of the residue by flash column chromatography (silica gel, EtOAc/hexane (1:5→1:4)) afforded an inseparable mixture of **1** and **3** (19:1, 86 mg, 55 %) or an inseparable mixture of **2** and its C-1 diastereoisomer (19:1, 80 mg, 51 %) as colourless gums.

Litseaverticillol A (**1**): R_f = 0.24 (silica gel, EtOAc/hexane (1:2)); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.11 (d, J = 1.7 Hz, 1H), 5.07 (brt, J = 6.1 Hz, 1H), 4.99 (brd, J = 9.0 Hz, 1H), 4.55 (brs, 1H), 3.13 (dd, J_1 = 9.0, J_2 = 2.3 Hz, 1H), 2.67 (brs, OH), 2.05 (m, 4H), 1.77 (t, J = 1.5 Hz, 3H), 1.72 (brs, 3H), 1.65 (brs, 3H) 1.57 ppm (brs, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 206.5, 155.0, 142.7, 141.8, 131.6, 123.9, 118.8, 76.4, 56.2, 39.6, 26.5, 25.6, 17.7, 17.1, 10.2 ppm; HRMS (MALDI): calcd for $C_{15}H_{22}O_2Na$: 257.1512 $[M+Na]^+$; found: 257.1523.

Litseaverticillol B (**2**): R_f = 0.29 (silica gel, EtOAc/hexane (1:2)); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.12 (brs, 1H), 5.16 (brs, 1H), 5.02 (brd, J = 9.5 Hz, 1H), 4.54 (brs, 1H), 3.15 (dd, J_1 = 9.5, J_2 = 2.4 Hz, 1H), 2.22 (brd, J = 4.9 Hz, OH), 2.15 (m, 4H), 1.80 (brs, 3H), 1.79 (brs, 3H), 1.69 (brs, 3H) 1.62 ppm (brs, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 206.2, 154.7, 142.8, 141.8, 132.4, 123.9, 119.7, 76.1, 56.3, 32.5, 26.6, 25.7, 23.3, 17.7, 10.2 ppm; HRMS (MALDI): calcd for $C_{15}H_{22}O_2Na$: 257.1512 $[M+Na]^+$; found: 257.1523.

Photooxygenation of litseaverticillols A (1) and B (2) to furnish the second-generation litseaverticillols D (4), E (5), F (6), G (7), I (9) and J (10): A solution of litseaverticillols A (**1**) or B (**2**) (80 mg, 0.34 mmol) in CH_2Cl_2 (15 mL) containing 10^{-4} M methylene blue was placed in a test tube with O_2 gently bubbling through it. The solutions were irradiated with a xenon Variac Eimac Cermax 300 W lamp for 3 and 4 min, respectively, at 0 °C to afford a mixture of tertiary and diastereomeric secondary hydroperoxides (83 mg, 91 % from **1**; 82 mg, 90 % from **2**) after evaporation of the solvent.

^{1}H NMR absorptions of the tertiary hydroperoxide **20** in the crude mixture arising from photooxygenation of litseaverticillol A (**1**) are identical to those reported[4c] for litseaverticillol E. Treatment of this chromatographically inseparable mixture of hydroperoxides (83 mg, 0.31 mmol) with $(CH_3)_2S$ (114 μL, 1.55 mmol) for 12 h at 25 °C leads to the selective reduction of the diastereomeric secondary hydroperoxides **21a,b** into the more polar (relative to the hydroperoxides), naturally occurring secondary alcohols litseaverticillols F (**6**) and G (**7**). The resulting mixture was separated by flash column chromatography (silica gel, EtOAc/hexane (1:2→2:1)) to allow purification and full characterisation of **20**.

Revised structure of litseaverticillol E (**20**): Colourless gum; R_f=0.22 (silica gel, EtOAc/hexane (1:1)); ^{1}H NMR (500 MHz, $CDCl_3$): δ=7.51 (brs, OOH), 7.14 (d, J=1.1 Hz, 1H; H-2), 5.70 (dt, J_1=15.8, J_2=6.6 Hz, 1H; H-9), 5.61 (brd, J=15.8 Hz, 1H; H-10), 5.05 (brd, J=9.1 Hz, 1H; H-6), 4.61 (brs, 1H; H-1), 3.17 (dd, J_1=9.1, J_2=2.3 Hz, 1H; H-5), 2.81 (brd, J=6.6 Hz, 2H; H-8), 2.12 (brs, OH), 1.81 (brs, 3H; CH_3), 1.74 (brs, 3H; CH_3) 1.34 ppm (s, 6H; 2×CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ=206.1 (C-4), 155.0 (C-2), 142.8 (C-3), 140.4 (C-7), 135.4 (C-10), 129.1 (C-9), 120.0 (C-6), 82.2 (C-11), 76.3 (C-1), 56.3 (C-5), 42.4 (C-8), 24.3 (CH_3), 24.2 (CH_3), 17.2 (CH_3), 10.2 ppm (CH_3); HRMS (MALDI): calcd for $C_{15}H_{22}O_4Na$: 289.1410 $[M+Na]^+$; found: 289.1416.

Prolonged treatment (72 h) of the crude mixture of the hydroperoxides **20** and **21a,b** (83 mg, 0.31 mmol) with $(CH_3)_2S$ under the previously described conditions resulted in complete reduction to the corresponding naturally occurring alcohols, litseaverticillols D (**4**), F (**6**) and G (**7**). Removal of the solvent in vacuo and purification by flash column chromatography (silica gel, EtOAc/hexane (1:1→2:1)) afforded **4** (26 mg, 35 %) and an inseparable mixture of **6** and **7** (25 mg, 35 %). Similar yields could be obtained when the mixture of hydroperoxides (**20**, **21a**, and **21b**) was treated for 5 min with PPh_3 (163 mg, 0.62 mmol) in CH_2Cl_2. The only disadvantage of this second protocol is the almost identical R_f value of diol **4** and the byproduct of the reduction (O=PPh_3), which makes separation difficult.

Litseaverticillols F and G (**6** and **7**): Colourless gum; R_f=0.14 (silica gel, EtOAc/hexane (1:1)); ^{1}H NMR (500 MHz, $CDCl_3$): δ=7.11 (brs, 2H), 5.04 (brd, J=9.0 Hz, 2H), 4.91 (s, 2H), 4.81 (t, J=1.3 Hz, 2H), 4.57 (brs, 2H), 4.04 (m, 2H), 3.14 (dd, J_1=9.0, J_2=2.1 Hz, 2H), 2.34 (brd, J=5.6 Hz, OH), 2.32 (brd, J=5.6 Hz, OH), 2.11 (m, 4H), 1.83 (brs, OH), 1.78 (t, J=1.5 Hz, 6H), 1.75 (brd, J=0.7 Hz, 3H), 1.74 (brs, 3H), 1.70 (brs, 6H), 1.65 ppm (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$): δ=206.2 (2× C), 155.1, 155.0, 147.4, 147.3, 142.7 (2×C), 141.7, 141.5, 119.4, 119.2, 111.0, 110.9, 76.3 (2×C), 75.6, 75.4, 56.3 (2×C), 35.9, 35.7, 33.0, 32.8, 17.7, 17.6, 17.0, 16.9, 10.2 ppm (2×C); HRMS (MALDI): calcd for $C_{15}H_{22}O_3Na$: 273.1461 $[M+Na]^+$; found: 273.1460.

Litseaverticillol D (**4**): Colourless gum; R_f=0.11 (silica gel, EtOAc/hexane (1:1)); ^{1}H NMR (500 MHz, $CDCl_3$): δ=7.12 (brs, 1H), 5.64 (d, J=15.6 Hz, 1H), 5.58 (dt, J_1=15.6, J_2=6.3 Hz, 1H), 5.02 (brd, J=9.0 Hz, 1H), 4.58 (brs, 1H), 3.14 (dd, J_1=9.0, J_2=2.3 Hz, 1H), 2.75 (brd, J=5.8 Hz, 2H), 2.26 (brd, J=6.2 Hz, OH), 1.79 (t, J=1.3 Hz, 3H), 1.71 (d, J=0.8 Hz, 3H), 1.51 (brs, OH), 1.29 ppm (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ=206.2, 155.0, 142.7, 140.6, 139.9, 124.4, 119.8, 76.3, 70.7, 56.3, 42.2, 29.8, 29.8, 17.1, 10.2 ppm; HRMS (MALDI): calcd for $C_{15}H_{22}O_3Na$: 273.1461 $[M+Na]^+$; found: 273.1464.

Complete reduction of the crude mixture of hydroperoxides **22a,b** and **23** to the corresponding secondary (**9**, **10**) and tertiary alcohols (**5**, Scheme 6) was achieved under the previously described conditions. In this particular case, not only could the separation of the tertiary alcohol **5** from the mixture of the secondary alcohols **9** and **10** be readily achieved but the separation of **9** from its diastereomer **10** was also accomplished. Full characterisation of **5** unambiguously confirmed our suspicions that the initially proposed structure for litseaverticillol E is incorrect.

Proposed structure of litseaverticillol E (**5**): Colourless gum; R_f=0.09 (silica gel, EtOAc/hexane (1:1)); ^{1}H NMR (500 MHz, $CDCl_3$): δ=7.13 (brs, 1H; H-2), 5.69 (m, 2H; H-9 and H-10), 5.10 (brd, J=9.6 Hz, 1H; H-6), 4.57 (brs, 1H; H-1), 3.14 (dd, J_1=9.6, J_2=2.3 Hz, 1H; H-5), 2.94 (dd, J_1=15.0, J_2=3.6 Hz, 1H; H-8a), 2.77 (dd, J_1=15.0, J_2=2.7 Hz, 1H; H-8b), 2.52 (brd, J=4.3 Hz, OH), 1.80 (t, J=1.3 Hz, 3H; CH_3), 1.79 (brs, 3H; CH_3), 1.67 (brs, OH), 1.33 (s, 3H; CH_3), 1.32 ppm (s, 3H; CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ=206.3 (C-4), 155.2 (C-2), 142.7 (C-3), 139.7 (C-7), 138.6 (C-10), 124.9 (C-9), 121.0 (C-6), 75.8 (C-1), 70.7 (C-11), 56.3 (C-5), 35.2 (C-8), 29.7 (CH_3), 29.5 (CH_3), 14.0 (CH_3), 10.2 ppm (CH_3); HRMS (MALDI): calcd for $C_{15}H_{22}O_3Na$: 273.1461 $[M+Na]^+$; found: 273.1464.

9 (less polar diastereoisomer): Colourless gum; R_f=0.24 (silica gel, EtOAc/hexane (1:1)); ^{1}H NMR (500 MHz, $CDCl_3$): δ=7.14 (brs, 1H; H-2), 5.15 (brd, J=9.3 Hz, 1H; H-6), 4.96 (brs, 1H; H-12a), 4.85 (brs, 1H; H-12b), 4.53 (q, J=1.7 Hz, 1H; H-1), 4.30 (brs, OH), 3.99 (brd, J=8.2 Hz, 1H; H-10), 3.26 (dd, J_1=9.3, J_2=1.9 Hz, 1H; H-5), 2.58 (ddd, J_1=14.0, J_2=10.3, J_3=6.4 Hz, 1H; H-8a), 2.36 (brs, OH), 2.06 (dt, J_1=14.0, J_2=5.4 Hz, 1H; H-8b), 1.81 (m, 1H; H-9a), 1.81 (brs, 3H; CH_3), 1.77 (brs, 3H; CH_3), 1.75 (brs, 3H; CH_3), 1.67 ppm (m, 1H; H-9b); ^{13}C NMR (125 MHz, $CDCl_3$): δ=207.4 (C-4), 155.7 (C-2), 147.6 (C-11), 142.8 (C-3), 140.0 (C-7), 121.9 (C-6), 110.5 (C-12), 76.1 (C-1), 73.7 (C-10), 56.2 (C-5), 32.4 (C-8), 27.8 (C-9), 22.8 (CH_3), 18.8 (CH_3), 10.4 ppm (CH_3); HRMS (MALDI): calcd for $C_{15}H_{22}O_3Na$: 273.1461 $[M+Na]^+$; found: 273.1462.

10 (more polar diastereoisomer): Colourless gum; R_f=0.20 (silica gel, EtOAc/hexane (1:1)); ^{1}H NMR (500 MHz, $CDCl_3$): δ=7.16 (brs, 1H; H-2), 5.06 (brd, J=8.8 Hz, 1H; H-6), 4.97 (brs, 1H; H-12a), 4.82 (brs, 1H; H-12b), 4.56 (brs, 1H; H-1), 4.07 (brd, J=8.7 Hz, 1H; H-10), 3.50 (brs, OH), 3.24 (brd, J=8.7 Hz, 1H; H-5), 2.89 (brs, OH), 2.29 (m, 2H; H-8), 1.86 (m, 1H; H-9a), 1.80 (d, J=1.1 Hz, 3H; CH_3), 1.77 (brs, 3H; CH_3), 1.74 (brs, 3H; CH_3), 1.51 ppm (m, 1H; H-9b); ^{13}C NMR (125 MHz, $CDCl_3$): δ=208.0 (C-4), 156.2 (C-2), 148.0 (C-11), 142.7 (C-3), 141.3 (C-7), 120.9 (C-6), 110.5 (C-12), 76.4 (C-1), 74.8 (C-10), 56.1 (C-5), 33.7 (C-8), 29.0 (C-9), 23.2 (CH_3), 18.2 (CH_3), 10.3 ppm (CH_3); HRMS (MALDI): calcd for $C_{15}H_{22}O_3Na$: 273.1461 $[M+Na]^+$; found: 273.1462.

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