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# Synthesis of Polyprenylated Benzoylphloroglucinols by Regioselective Prenylation of Phloroglucinol in an Aqueous Medium

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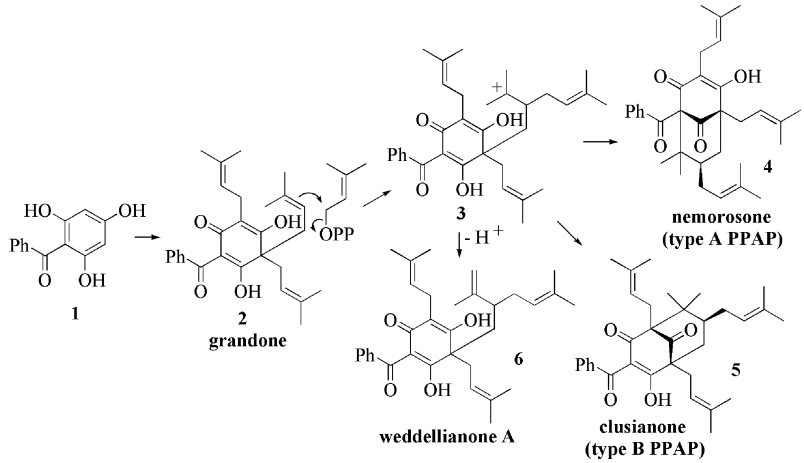
**Keywords:** Phloroglucinols / Prenylation / *C*-Benzoylation / Electrophilic cyclization / Natural products / Biomimetic synthesis

Regioselective tri-*C*-prenylation of phloroglucinol, leading to a compound with *gem*-disubstitution, has been achieved with prenyl bromide in the presence of potassium hydroxide in an aqueous medium. Geranyl- and isolavandulylphloroglucinol, obtained by *ortho*-lithiation, were diprenylated under the same conditions. *C*-Benzoylation of the trialkylated derivatives using benzoyl cyanide in the presence of triethylamine afforded two natural products, grandone and kolanone, and an isomer of weddellianone A. Attemped electrophilic cyclization reactions, aimed at a biomimetic synthesis of polycyclic polyprenylated acylphloroglucinols (PPAPs), are also reported.


## Introduction

A large number of phloroglucinol derivatives have a natural origin,[1] most of them possessing an acyl group and isoprenyl-type chains as substituents. In some cases, prenyl cyclization onto the nucleus leads to compounds with a bicyclo[3.3.1]nonane-2,4,9-trione core skeleton which are named polycyclic polyprenylated acylphloroglucinols (PPAPs).[2] The biosynthesis of PPAPs starting from benzoylphloroglucinol (**1**) as an example is illustrated in Scheme 1.[3] Formation of **1** followed by *C*-prenylations at the nucleus affords grandone (**2**) which, by further reaction with dimethylallyl pyrophosphate, could generate the cation **3** (or an equivalent). This is supposed to evolve, through cyclization or deprotonation, to the natural products nemorosone (**4**) (type A PPAP), clusianone (**5**) (type B PPAP) or weddellianone A (**6**). The type-A PPAP should result from electrophilic attack at the nucleus-C bearing the benzoyl




Scheme 1. Probable biosynthesis of PPAPs exemplified with benzoylphloroglucinol derivatives.

group, cyclization at the prenyl-substituted centre leading to the type-B compound.

Our interest in the field of PPAPs came from the observation[4] that xanthochymol was active in a tubulin disassembly inhibition test and from our recent results concerning the isolation of compounds belonging to this family,

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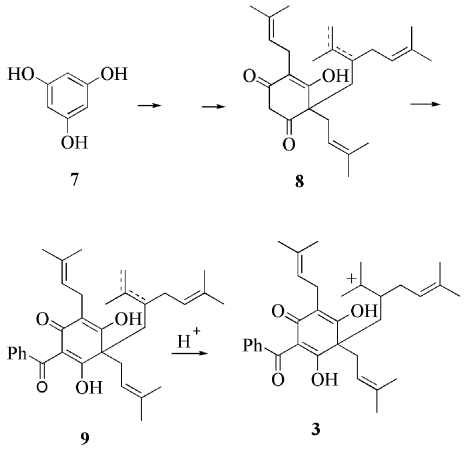
oblongifolins A–D.[5] We also undertook synthetic studies relating to type B PPAPs which led to a short synthesis of (±)-clusianone (**5**) based on a Lewis acid catalyzed α,α′-annulation of a suitably substituted cyclohexanone silyl enol ether using malonyl chloride.[6] Efforts were also devoted to the construction of bridgehead diprenyl-substituted bicyclo[3.3.1]nonane-2,9-diones as models for the further elaboration of PPAPs.[7]

As a part of a programme directed towards the biomimetic synthesis of PPAPs, we first investigated the transfer of isoprenyl chains to benzoylphloroglucinol (**1**) and its trimethyl ether by using sulfonium salts.[8] A slightly different strategy, shown in Scheme 2, involved tri-*C*-isoprenylation of phloroglucinol (**7**) which led to a compound such as **8** before *C*-acylation of the β-dicarbonyl moiety of **8** with benzoyl cyanide to give **9**.[9] This pathway should be of interest for the introduction of a group sensitive to alkylating reagents such as a 3,4-dihydroxybenzoyl which is present in several bioactive PPAPs.[2] Generation of cation **3** by protonation of the $C_{10}$ isoprenyl chain of **9** could then lead to type A and/or type B PPAPs, in accord with Scheme 1. We were encouraged to examine this possibility by the probable intervention of a species analogous to **3** in the formation of a bicyclo[3.3.1]nonane-2,4,9-trione derivative during our synthesis of (±)-clusianone (**5**).[6a]




Scheme 2. Synthetic approach to PPAPs by triisoprenylated benzoylphloroglucinols.

Although prenylation of acylphloroglucinols has been relatively well documented,[10] reports of prenyl transfer to phloroglucinol itself is more scarce. Thus, *C*-prenylation of phloroglucinol with 2-methyl-3-buten-2-ol in the presence of citric acid and in an aqueous medium led to chromanes through acid-catalyzed cyclization involving the trisubstituted olefin.[11] Changing the acid to $BF_3{\cdot}Et_2O$ and the solvent to dioxane gave mono-,[12] di- and even trialkylated[13] aromatic derivatives. It should be emphasized that the formation of *gem*-disubstituted compounds has not been reported under these conditions. To the best of our knowledge, and unlike the prenylation of acylphloroglucinols,[10] the *C*-alkylation of phloroglucinol itself with prenyl bromide in basic conditions has not been described.

On the other hand, Mioskowski and co-workers reported that the *C*-alkylation of phloroglucinol with allyl bromide in an aqueous medium provided different proportions of mono- and *meta*-dialkyl derivatives, depending on the conditions (without base, with sodium hydroxide or in a pH 7.8 buffer).[14]

The formation of *gem*-substituted products was described recently, but in this case the reaction involved the palladium-catalyzed hexa-*C*-allylation of phloroglucinol with allyl alcohol in the presence of triethylborane.[15]

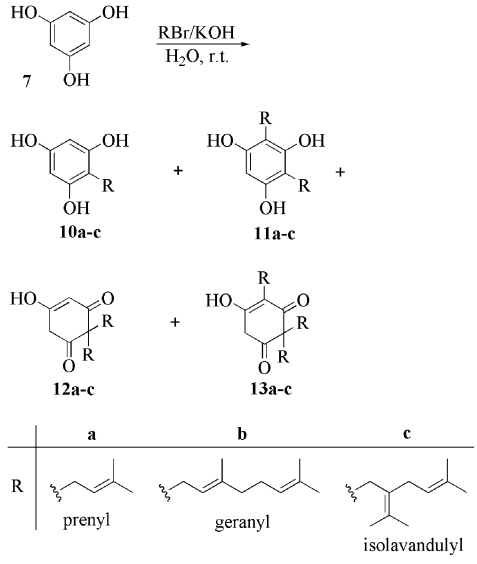
Very recently Qi and Porco reported a one-pot alkylative dearomatization followed by annulation by intramolecular Michael addition which led to the formation of bicyclo-[3.3.1]nonane-2,4,9-triones. This was achieved starting from *meta*-diprenylbenzoylphloroglucinol and allowed a new synthesis of (±)-clusianone (**5**).[6c]

In this paper we present new results concerning the introduction of isoprenyl chains into the phloroglucinol nucleus and the subsequent formation of trialkylated derivatives possessing *gem*-disubstitution. Subsequent *C*-benzoylation and tentative biomimetic-type electrophilic cyclizations are also reported.

## Results and Discussion

### *C*-Polyisoprenylation of Phloroglucinol in Water

Mioskowski and co-workers' procedure for the *C*-allylation of phloroglucinol (**7**) in water[14] was first chosen, using prenyl bromide as the alkylating reagent. We noted different behaviour and were pleased to observe the formation of *gem*-substituted derivatives **12a** and **13a** in a pH 7.9 phosphate buffer (with few or no *meta*-disubstituted compounds). The triprenylphloroglucinol **13a** could be obtained in better yield in the presence of KOH (Scheme 3 and Table 1) and 4 equivalents of prenyl bromide. As deduced from Table 1, the formation of the *gem*-disubstituted com-




Scheme 3. Isoprenylation of phloroglucinol in water.

pound **12a** preceded that of **13a** as the second alkylation took place at the carbon bearing the substituent. We also obtained *gem*-diallyl compounds (results not shown) by this procedure. This result is in sharp contrast to the formation of dialkylated compounds in which the aromaticity is retained, as is the case for the prenylation of acylphloroglucinols[10b,10c] and also for the aforementioned allylation.[14]

Table 1. *C*-Polyisoprenylation of phloroglucinol in water.

| R | RBr [equiv.] | KOH [equiv.] | Products (% yield) | | | |
|---|---|---|---|---|---|---|
| Prenyl | 0.5 | 1 | **10a** (55) | – | **12a** (20) | – |
| | 4 | 5 | – | – | **12a** (13) | **13a** (38) |
| Geranyl | 0.5 | 1 | **10b** (7) | – | – | – |
| | 4 | 5 | **10b** (7) | – | **12b** (16) | **13b** (7) |
| Isolavandulyl | 0.5 | 1 | **10c** (17) | **11c** (16) | – | – |

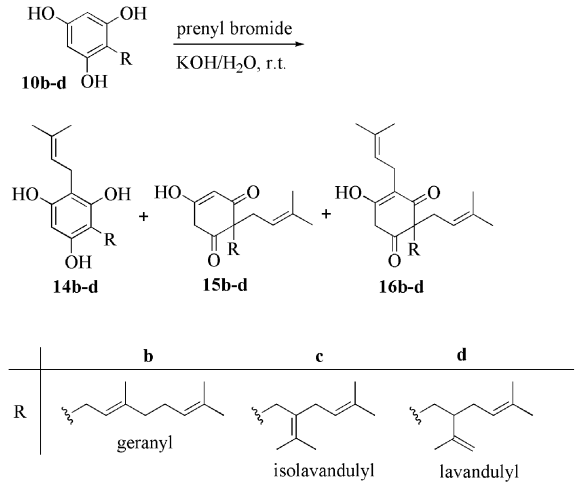
Thus, in only one step and under simple conditions, it is possible to obtain a phloroglucinol derivative with three prenyl groups that is also *gem*-disubstituted. This hitherto unknown procedure is interesting from the point of view of PPAP synthesis (see Scheme 2).

*gem*-Dialkylation was also observed with geranyl bromide (with less efficiency), but not with the more sterically demanding isolavandulyl bromide[8] which led, instead, to the *meta* derivative **11c**. Under these conditions, the monoalkylated product was more reactive than phloroglucinol itself and, even with a substoichiometric amount of the allylic bromide, it was not possible to obtain a satisfactory yield of geranyl- and isolavandulyl-phloroglucinol **10b** and **10c**.

### *C*-Prenylation of Monosubstituted Phloroglucinols

In order to obtain compounds with two prenyls and a $C_{10}$ unsaturated chain bound to a prenyl-bearing carbon (like product **8** in Scheme 2) by prenylation in water, we prepared phloroglucinols monosubstituted with a geranyl (**10b**), an isolavandulyl (**10c**) and a lavandulyl (**10d**) group. This was achieved through an indirect *ortho*-lithiation route (see below).

Diprenylation of **10b–d** in water was then investigated in the presence of prenyl bromide (2.5 equiv.) and KOH (4 equiv.) (see Scheme 4 and Table 2) and trialkylated derivatives **16b** and **16c** were obtained in moderate yields. Curiously, the lavandulyl compound **10d** did not lead to the expected *gem*-disubstituted product, but afforded instead the *meta*-dialkyltriphenol **14d** in 23% yield. This result can possibly be explained by differences in the conformational behaviour of the lavandulyl and isolavandulyl chains due to folding of the former in the aqueous medium which renders the carbon bearing this substituent sterically hindered with respect to further addition.



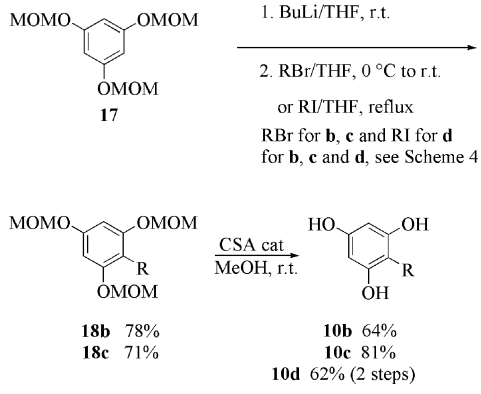

Scheme 4. Prenylation of monosubstituted phloroglucinols in water.

Table 2. Prenylation of monosubstituted phloroglucinols in water.

| Phloroglucinol | Prenyl bromide [equiv.] | KOH [equiv.] | Products (% yield) | | |
|---|---|---|---|---|---|
| **10b** | 2.5 | 4 | – | **15b** (18) | **16b** (37) |
| **10c** | 2.5 | 4 | – | **15c** (14) | **16c** (40) |
| **10d** | 2.5 | 4 | **14d** (23) | – | – |

It should be noted that the presence of phenolic and enolic products makes purification difficult and this is one of the reasons for the moderate yields. For the *gem*-disubstituted compounds, NMR analysis is often complicated by the presence of different proportions of dicarbonyl and enolic forms and so, in some cases, enol methylation was carried out to simplify the analysis.

For the preparation of **10b–d** we used a classic *ortho*-lithiation methodology starting from the tris-MOM ether **17**.[16] Following this route, we could prepare the geranyl and isolavandulyl derivatives **10b** and **10c** by alkylation with the corresponding allylic bromides (Scheme 5).




Scheme 5. Preparation of geranyl-, isolavandulyl- and lavandulyl-phloroglucinols.

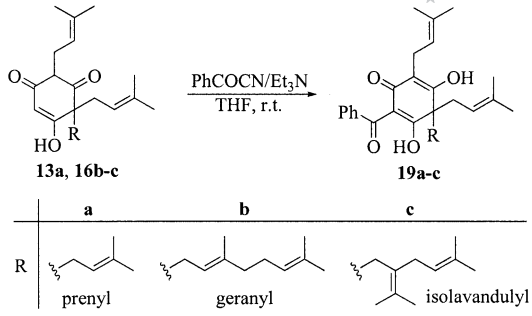
  

The lavandulyl group, although non-allylic, could be introduced by using lavandulyl iodide, but at a higher temperature. Interestingly, cleavage of the MOM ethers with CSA in methanol[16] was carried out without cyclization of the olefinic bonds, providing phenolic compounds **10b**–**10d** in satisfactory yields.

It is known, since the work of Kornblum and co-workers,[17] that *C*-alkylation of an ambident anion such as a phenoxide is favoured by reactive halides (allyl or benzyl bromide). Solvents with a powerful hydrogen-bonding capacity, and particularly water, also favour the regiochemistry observed here because of the selective solvation of the oxygen atom. Breslow and co-workers suggested that differences in the hydrophobic character of the transition states for the *O*- and *C*-alkylations could be significant for discriminating between the two pathways.[18] Generally, an aqueous solvent effect has been observed to accelerate heterogeneous organic reactions[19] and this could be the case here even though phloroglucinol is soluble in aqueous potassium hydroxide. Claisen rearrangement of α,α-dimethylallyl phenol ethers has recently been shown to be accelerated in water or in aqueous media.[20] However, Mioskowski and co-workers ruled out *O*-alkylation followed by such a rearrangement for the allylation of phloroglucinol in an aqueous medium.[14] On the other hand, phloroglucinol can be regarded as 1,3,5-cyclohexanetrione and, in some aspects, its behaviour is reminiscent of that of a cyclic β-diketone. Thus, the present prenylation could be related to the reported *C*-mono- and *gem*-dicrotylation of 1,3-cyclohexanedione in the presence of potassium hydroxide in water.[21] Schick and co-workers have shown that the *O*/*C* ratio for the alkylation of 2-methyl-1,3-cyclopentanedione was minimized when using a reactive halide, such as allyl bromide, and water as the solvent.[22] The results reported here are consistent with these different observations and proposals.

## *C*-Benzoylation of Polyprenylated Phloroglucinols

*C*-Benzoylation of 1,3-cyclohexanediones, without the formation of enol esters, can be achieved by using benzoyl cyanide in the presence of triethylamine in THF.[6a,9] Application of these conditions to triprenylated phloroglucinols **13a**, **16b** and **16c** provided benzoyl derivatives **19a**–**c** (Scheme 6 and Table 3). It is interesting to note that acylation took place at the unsubstituted position. Two of these compounds are natural products: grandone (**19a** ≡ **2**), isolated from the *Clusia grandiflora* floral resin,[23] and kolanone (**19b**), from *Garcinia kola*, the latter presenting antimicrobial properties.[24] Compound **19c** is an isomer of the natural weddellianone A, isolated from several *Clusia* floral resins,[25] in which the lavandulyl group has been replaced by an isolavandulyl. Owing to the presence of several tautomeric forms, **19a** and **19c** were, respectively, acetylated and methylated in order to simplify the NMR analysis.




Scheme 6. *C*-Benzoylation of triprenylated phloroglucinols **13a**, **16b** and **16c**.

Table 3. *C*-Benzoylation of triprenylated phloroglucinols **13a**, **16b** and **16c**.

| Triprenylphloroglucinol | Products (% yield) |
|---|---|
| **13a** | Grandone **19a** (51) |
| **16b** | Kolanone **19b** (63) |
| **16c** | Weddellianone A isomer **19c** (58) |

This two-step synthesis of grandone (**19a**) requires simpler experimental conditions than those used for the preparation of benzoylphloroglucinol[26] followed by triprenylation.[10c,10d] Compounds analogous to **19a** (with *i*Pr, *i*Bu or *s*Bu groups instead of phenyl), which are named β-acids and are found in hops (*Humulus lupulus*), present radical scavenging, lipid peroxidation and antimicrobial activities.[27] The procedure reported here could thus be useful for the synthesis of such derivatives.

## Electrophilic Cyclization Reactions

Cyclizations involving a prenyl group bonded to a β-dicarbonyl derivative have been reported as suitable methods for the construction of the bicyclo[3.3.1]nonane skeleton,[28] as well as being key steps in the synthesis of the PPAP core.[6d,29,30] In these cases, tin tetrachloride,[28] a selenium-containing reagent [*N*-(phenylseleno)phthalimide, *N*-PSP][29] or iodine[6d,30] has been used as promoters. More generally, electrophilic *C*-cyclizations of a prenyl onto β-dicarbonyl compounds, without introducing any heteroatoms, are best achieved by using stoichiometric amounts of $SnCl_4$ in dichloromethane[31] or catalytic palladium derivatives.[32]

Having compound **19c** in hand, biomimetic-like cyclizations were considered, as shown in Schemes 1 and 2. To test the feasibility of such a pathway, we first attempted the cyclizations with the triprenyl compounds **13a** and **19a** under classical tin tetrachloride conditions.[31] In fact the reactions were messy and only *O*-cyclized derivatives **20** (9%) and **21** (12%) from **13a** and **22** (14%) from **19a** were isolated as pure compounds (Figure 1). It should be noted that only the prenyl group bound to the $sp^2$ carbon was involved in the formation of **20**, **21** and **22**. The sole case of a *C*-cyclization was observed starting from the *gem*-disubsti-

tuted product **12a**; a bicyclo[3.3.1]nonane-2,4,9-trione was isolated as cyclic enol ether derivative **23**, but in a low yield (7%).

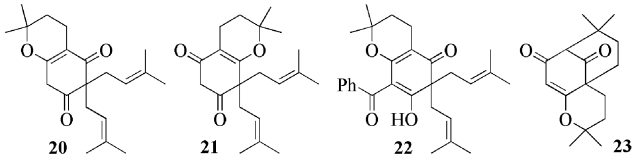
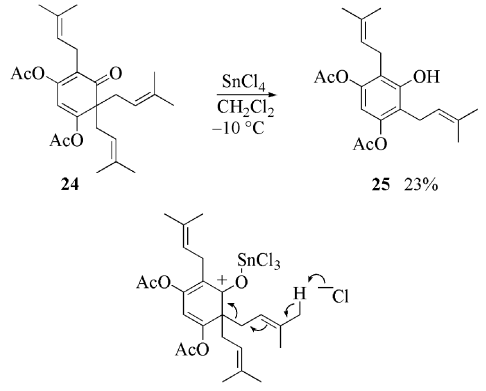



Figure 1. Products obtained by $SnCl_4$-induced cyclization of **13a**, **19a** and **12a**.

These conditions were also applied to the isolavandulyl derivative **19c**, the more nucleophilic tetrasubstituted olefin, in order to obtain type A or B PPAPs by an intermediate analogous to cation **3** (see Scheme 1 and Scheme 2), but we could not isolate any *C*-cyclized products.

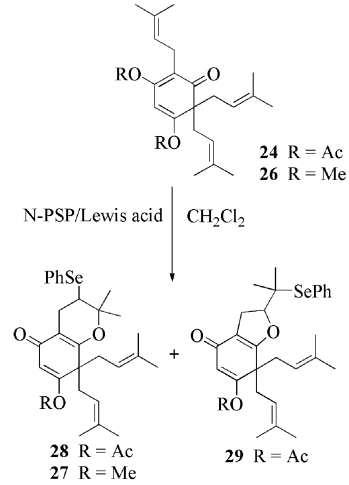
With the bis(enol acetate) **24**, obtained as a major product by acetylation of **13a** and chosen in order to minimize *O*-cyclization,[29b] a deprenylation reaction leading to **25** was observed (Scheme 7). This could be ascribed to a mechanism similar to that proposed by Nicolaou et al. for the acidic hydrolysis of a related vinylogous ester, the driving force being aromatization.[33]




Scheme 7. Deprenylation of **24** with $SnCl_4$.

Formation of the bicyclo[3.3.1]nonane-2,4,9-trione skeleton was also attempted starting from **24** and the corresponding bis(methyl enol ether) **26** using *N*-PSP.[29] Only *O*-cyclized products were obtained (also with the participation of the prenyl bound to the $sp^2$ carbon) and, depending on the conditions, six- or five-membered heterocycles were isolated (Scheme 8 and Table 4).

Thus, so far we have not been able to induce an electrophilic *C*-cyclization with polyprenylated benzoylphloroglucinols or their deacylated counterparts to construct the bicyclo[3.3.1]nonane-2,4,9-trione core of PPAPs (the sole exception is the low-yielding formation of the bridged compound **23** also involving *O*-cyclization).




Scheme 8. *N*-PSP-induced cyclizations with **24** and **26**.

Table 4.

| | Lewis acid | Temperature | Products (% yield) |
|---|---|---|---|
| **26** | $SnCl_4$ | –78 °C | **27** (41) |
| **24** | – | –78 °C → room temp. | **28** (43) **29** (20) |
| | $SnCl_4$ | –78 °C | **29** (69) |

## Conclusions

*C*-Alkylation of phloroglucinol with prenyl bromide in water and in the presence of potassium hydroxide provided, in one step, the triprenylated derivative with *gem*-disubstitution in 38% yield. Formation of geranyl-, isolavandulyl- and even lavandulylphloroglucinol was best achieved by *ortho*-lithiation of the tris-MOM ether. Their prenylation in water afforded, in the first two cases, compounds possessing a prenyl and a $C_{10}$ chain at the same position. *C*-Benzoylation of the triisoprenylated derivatives with benzoyl cyanide allowed the synthesis of two natural products, grandone and kolanone, and a double-bond isomer of weddellianone A. This two-step procedure is simpler and easier than those previously reported for the preparation of triprenyl acylphloroglucinols. Biomimetic-like electrophilic cyclizations using tin tetrachloride and/or *N*-(phenylseleno)-phthalimide were attempted with the aim of constructing polycyclic polyprenylated acylphloroglucinols (PPAPs). A bicyclo[3.3.1]nonane-2,4,9-trione was isolated only in one case (as a cyclic enol ether) and in low yield, but not by starting from a triisoprenylated phloroglucinol. To reach this goal studies are being continued using modified conditions and the results will be reported in due course.

## Experimental Section

**General Remarks:** NMR spectra were recorded with the following Bruker spectrometers: AC250 (250 MHz), AC300 (300 MHz), Avance 300 (300 MHz), DPX 400 (400 MHz) and Avance 500 (500 MHz). FTIR spectra were recorded as a film on NaCl or a diamond (SensIR Durasamp*IRII*) cell with a Perkin–Elmer Spectrum BX FT-IR spectrophotometer. Mass spectra were recorded

by electrospray ionization with a Micromass LCT (ESI-TOF) spectrometer.

**Prenylation of Phloroglucinol**

**Procedure A:** KOH (85%, 129 mg, 1.96 mmol) was added to a suspension of phloroglucinol (**7**) (250 mg, 1.96 mmol) in $H_2O$ (2 mL) at room temperature. The mixture was stirred for 5 min and prenyl bromide (90%, 128 μL, 0.98 mmol) was added dropwise. The resulting mixture was allowed to stir for an additional 8 h, quenched by the addition of 1 N HCl solution until becoming acidic and extracted with diethyl ether. The organic layer was washed with water and brine, dried with $Na_2SO_4$ and concentrated in vacuo. The crude product was purified by flash chromatography (heptane/EtOAc, 90:10) to obtain compounds **10a** (104 mg, 55%) and **12a** (51 mg, 20%) as viscous light-yellow oils.

**Procedure B:** KOH (85%, 3.9 g, 59.0 mmol) was added to a suspension of phloroglucinol (**7**) (1.5 g, 11.8 mmol) in $H_2O$ (118 mL) at room temperature. The mixture was stirred for 5 min and prenyl bromide (90%, 6.1 mL, 47.1 mmol) was added dropwise. The resulting mixture was allowed to stir for an additional 8 h, quenched by the addition of 1 N HCl solution until becoming acidic and extracted with diethyl ether. The organic layer was washed with water and brine, dried with $Na_2SO_4$ and concentrated in vacuo. The crude product was purified by flash chromatography (heptane/EtOAc, 95:5) to obtain compound **12a** (401 mg, 13%) and compound **13a** (1.5 g, 38%) as viscous light-yellow oils.

**2-(3-Methylbut-2-enyl)benzene-1,3,5-triol (10a):** FTIR: $\tilde{\nu}$ = 3362, 2974, 1614, 1612, 1463, 1144 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ = 1.73 (s, 3 H, 11-H), 1.79 (s, 3 H, 10-H), 3.30 (d, $J$ = 7.0 Hz, 2 H, 7-H), 5.22 (br. t, $J$ = 7.0 Hz, 1 H, 8-H), 5.94 (s, 2 H, 4-H, 6-H) ppm. $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ = 17.8 (C-10), 22.0 (C-7), 25.8 (C-11), 96.1 (C-4, C-6), 106.3 (C-2), 122.2 (C-8), 135.0 (C-9), 154.7 (C-5), 155.6 (C-1, C-3) ppm. HRMS (ESI): calcd. for $C_{11}H_{15}O_3$ $[M + H]^+$ 195.1021; found 195.1059.

**5-Hydroxy-2,2-bis(3-methybut-2-enyl)cyclohex-4-ene-1,3-dione (12a):** FTIR: $\tilde{\nu}$ = 3369, 2976, 1617, 1456, 1142 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ = 1.58 (s, 6 H, 10-H, 15-H), 1.62 (s, 6 H, 11-H, 16-H), 2.58 (m, 4 H, 7-H, 12-H), 3.21 (s, 2 H, 4-H), 4.89 (br. t, $J$ = 7.0 Hz, 2 H, 8-H, 13-H), 5.89 (s, 1 H, 6-H) ppm. $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ = 17.8 (C-10, C-15), 25.9 (C-11, C-16), 35.7 (C-7, C-12), 47.8 (C-4), 61.0 (C-2), 106.8 (C-6), 117.9 (C-8, C-13), 135.9 (C-9, C-14), 185.2 (C-5), 190.4 (C-1), 206.9 (C-3) ppm. HRMS (ESI): calcd. for $C_{16}H_{23}O_3$ $[M + H]^+$ 263.1647; found 263.1640.

**5-Hydroxy-2,2,4-tris(3-methylbut-2-enyl)cyclohex-4-ene-1,3-dione (13a):** FTIR: $\tilde{\nu}$ = 3332, 2973, 1656, 1632, 1445, 1376 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ = 1.54 (s, 6 H, 10-H, 15-H), 1.59 (s, 6 H, 11-H, 16-H), 1.72 (s, 3 H, 21-H), 1.74 (s, 3 H, 20-H), 2.45 (dd, $J$ = 14.0, 8.0 Hz, 2 H, 7-$H^B$, 12-$H^B$), 2.57 (dd, $J$ = 14.0, 8.0 Hz, 2 H, 7-$H^A$, 12-$H^A$), 3.14 (d, $J$ = 7.0 Hz, 2 H, 17-H), 3.24 (s, 2 H, 4-H), 4.82 (br. t, $J$ = 8.0 Hz, 2 H, 8-H, 13-H), 5.11 (br. t, $J$ = 7.0 Hz, 1 H, 18-H) ppm. $^{13}C$ NMR (125 MHz, $CDCl_3$): $\delta$ = 17.7 (C-10, C-15), 17.8 (C-20), 21.9 (C-17), 25.7 (C-21), 25.8 (C-11, C-16), 35.7 (C-7, C-12), 47.8 (C-4)*, 61.3 (C-2)*, 116.6 (C-6), 118.2 (C-8, C-13), 121.2 (C-18), 134.4 (C-19), 135.5 (C-9, C-14), 170.5 (C-1)*, 188.9 (C-5)*, 206.7 (C-3) ppm; * deduced from HMQC/HMBC experiments. HRMS (ESI): (–): calcd. for $C_{21}H_{29}O_3$ $[M - H]^-$ 329.2117; found 329.2093.

**Geranylation of Phloroglucinol:** This experiment was performed using procedure B described for the preparation of **12a** and **13a**, but with geranyl bromide, to obtain **10b** (7%), **12b** (16%) and **13b** (7%) as viscous light-yellow oils.

**(*E*)-2-(3,7-Dimethylocta-2,6-dienyl)benzene-1,3,5-triol (10b):** See below.

**2,2-Bis[(*E*)-3,7-dimethylocta-2,6-dienyl]-5-hydroxycyclohex-4-ene-1,3-dione (12b):** FTIR: $\tilde{\nu}$ = 3413, 2922, 1719, 1629, 1453, 1376, 1159, 1079 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ = 1.56 (s, 6 H, 14-H, 24-H), 1.58 (s, 6 H, 16-H, 26-H), 1.64 (s, 6 H, 15-H, 25-H), 1.94 (t, $J$ = 6.0 Hz, 4 H, 10-H, 20-H), 1.98 (t, $J$ = 6.0 Hz, 4 H, 11-H, 21-H), 2.53 (dd, $J$ = 13.7, 7.2 Hz, 2 H, 7-$H^B$, 17-$H^B$), 2.63 (dd, $J$ = 14.0, 8.1 Hz, 2 H, 7-$H^A$, 17-$H^A$), 3.21 (s, 2 H, 4-H), 4.93 (t, $J$ = 7.6 Hz, 2 H, 8-H, 18-H), 4.99 (t, $J$ = 7.1 Hz, 2 H, 12-H, 22-H), 5.87 (s, 1 H, 6-H) ppm. $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ = 16.1 (C-16, C-26), 17.7 (C-14, C-24), 25.7 (C-15, C-25), 26.5 (C-11, C-21), 35.6 (C-7, C-17), 39.8 (C-10, C-20), 48.0 (C-4), 60.9 (C-2), 107.0 (C-6), 118.0 (C-8, C-18), 123.9 (C-12, C-22), 131.7 (C-13, C-23), 139.4 (C-9, C-19), 184.1 (C-1), 206.9 (C-3) ppm. HRMS (ESI): calcd. for $C_{26}H_{38}NaO_3$ $[M + Na]^+$ 421.2719; found 421.2758.

**2,2,4-Tris[(*E*)-3,7-dimethylocta-2,6-dienyl]-5-hydroxycyclohex-4-ene-1,3-dione (13b):** FTIR: $\tilde{\nu}$ = 3363, 2925, 1607, 1578, 1435, 1153, 1153, 1049, 927, 830 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ = 1.55 (s, 3 H, 34-H), 1.56 (s, 6 H, 14-H, 24-H), 1.59 (s, 3 H, 35-H), 1.64 (s, 6 H, 16-H, 26-H), 1.67 (s, 6 H, 15-H, 25-H), 1.76 (s, 3 H, 36-H), 1.87–1.94 (m, 4 H), 1.94–2.05 (m, 4 H), 2.05–2.15 (m, 4 H, 10-H, 11-H, 20-H, 21-H, 30-H, 31-H), 2.51 (dd, $J$ = 13.1, 7.5 Hz, 2 H, 7-$H^B$, 17-$H^B$), 2.56–2.66 (m, 2 H, 7-$H^A$, 17-$H^A$), 3.20 (d, $J$ = 7.5 Hz, 2 H, 27-H), 3.22 (s, 2 H, 4-H), 4.88 (t, $J$ = 7.5 Hz, 1 H, 32-H), 4.99 (t, $J$ = 7.5 Hz, 2 H, 12-H, 22-H), 5.01–5.12 (m, 2 H, 8-H, 18-H), 5.19 (t, $J$ = 7.5 Hz, 1 H, 28-H) ppm.

**Isolavandulylation of Phloroglucinol:** KOH (85%, 259 mg, 3.92 mmol) was added to a suspension of phloroglucinol (**7**) (500 mg, 3.92 mmol) in $H_2O$ (4 mL) at room temperature. The mixture was stirred for 5 min and isolavandulyl bromide[8] (71%, 600 mg, 1.96 mmol) was added dropwise. The resulting mixture was allowed to stir for an additional 3 h, quenched by the addition of 1 N HCl solution until becoming acidic and extracted with diethyl ether. The organic layer was washed with water and brine, dried with $Na_2SO_4$ and concentrated in vacuo. The crude product was purified by flash chromatography (heptane/EtOAc, 80:20) to obtain compounds **10c** (85 mg, 17%) and **11c** (127 mg, 16%) as viscous light-yellow oils.

**2-[5-Methyl-2-(propan-2-ylidene)hex-4-enyl]benzene-1,3,5-triol (10c):** See below.

**2,4-Bis[5-methyl-2-(propan-2-ylidene)hex-4-enyl]benzene-1,3,5-triol (11c):** FTIR: $\tilde{\nu}$ = 3411, 2912, 1625, 1449, 1084, 1039 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ = 1.50 (s, 6 H, 12-H, 22-H), 1.65 (s, 6 H, 13-H, 23-H), 1.77 (s, 6 H, 16-H, 26-H or 15-H, 25-H), 1.91 (s, 6 H, 15-H, 25-H or 16-H, 26-H), 2.66 (d, $J$ = 7.0 Hz, 4 H, 9-H, 19-H), 3.43 (s, 4 H, 7-H, 17-H), 4.98 (br. t, $J$ = 7.0 Hz, 2 H, 10-H, 20-H), 5.57 (br. s, 1 H, OH), 5.85 (br. s, 1 H, OH), 5.93 (s, 1 H, 4-H) ppm. $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ = 17.6 (C-12, C-22), 20.6 (C-15, C-25 or C-16, C-26), 20.8 (C-25, C-15 or C-26, C-16), 25.7 (C-13, C-23), 26.1 (C-7, C-17), 29.9 (C-9, C-19), 96.0 (C-4), 104.5 (C-2, C-6), 122.3 (C-10, C-20), 128.6 (C-8, C-18), 131.0 (C-14, C-24), 132.2 (C-11, C-21), 154.3 (C-3, C-5), 155.0 (C-1) ppm. HRMS (ESI): calcd. for $C_{26}H_{39}O_3$ $[M + H]^+$ 399.2899; found 399.2919.

**Prenylation of Geranylphloroglucinol:** Compound **10b** (100 mg, 0.38 mmol) was added to a solution of KOH (85%, 100 mg, 1.52 mmol) in water (2 mL) and the mixture was stirred for 5 min at room temp. Then prenyl bromide (90%, 110 μL, 0.85 mmol) was added dropwise. The resulting mixture was allowed to stir for an additional 8 h, quenched by the addition of 1 N HCl solution (2 mL) and extracted with diethyl ether. The organic layer was

washed with water and brine, dried with $Na_2SO_4$ and the solvents evaporated in vacuo. The crude product was purified by flash chromatography (heptane/EtOAc, 50:50) to give compounds **15b** (23 mg, 18%) and **16b** (56 mg, 37%) as viscous light-yellow oils.

**(*E*)-2-(3,7-Dimethylocta-2,6-dienyl)-5-hydroxy-2-(3-methylbut-2-enyl)cyclohex-4-ene-1,3-dione (15b):** FTIR: $\tilde{\nu}$ = 3465, 2915, 1719, 1647, 1565, 1444, 1375, 1327, 1214, 1180, 1061, 851 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ = 1.55 (s, 3 H, 14-H), 1.57 (s, 6 H, 20-H, 15-H), 1.60 (s, 3 H, 21-H), 1.63 (s, 3 H, 16-H), 1.95 (t, $J$ = 6.4 Hz, 2 H, 10-H), 1.99 (q, $J$ = 6.3 Hz, 2 H, 11-H), 2.44–2.77 (m, 4 H, 7-H, 17-H), 3.21 (s, 2 H, 4-H), 4.83–5.11 (m, 3 H, 8-H, 12-H, 18-H), 5.93 (s, 1 H, 6-H), 6.50–7.22 (br. s, 1 H, OH) ppm. $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ = 16.1 (C-16), 17.6 (C-20), 17.8 (C-14), 25.6 (C-21), 25.9 (C-15), 26.5 (C-11), 35.4 (C-7), 35.8 (C-17), 39.8 (C-10), 47.8 (C-4), 60.9 (C-2), 106.8 (C-6), 117.8 (C-18), 118.0 (C-8), 123.9 (C-12), 131.6 (C-13), 135.7 (C-19), 139.5 (C-9), 184.7 (C-5), 190.1 (C-1), 206.8 (C-3) ppm. HRMS (ESI): calcd. for $C_{21}H_{31}O_3$ $[M + H]^+$ 331.2273; found 331.2282.

**(*E*)-2-(3,7-Dimethylocta-2,6-dienyl)-5-hydroxy-2,4-bis(3-methylbut-2-enyl)cyclohex-4-ene-1,3-dione (16b):** FTIR: $\tilde{\nu}$ = 3450, 2920, 1716, 1652, 1591, 1447, 1375, 1225, 1176, 1046, 845 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ = 1.56 (s, 9 H, 14-H, 20-H, 25-H), 1.61 (s, 3 H, 15-H), 1.64 (s, 3 H, 21-H), 1.78 (s, 6 H, 16-H, 26-H), 1.92 (t, $J$ = 7.2 Hz, 2 H, 10-H), 1.97 (q, $J$ = 7.2 Hz, 2 H, 11-H), 2.43–2.78 (m, 4 H, 7-H, 17-H), 3.18 (d, $J$ = 7.6 Hz, 2 H, 22-H), 3.23 (s, 2 H, 4-H), 4.79–4.95 (m, 2 H, 8-H, 18-H), 4.95–5.08 (m, 1 H, 12-H) 5.16 (t, $J$ = 7.9 Hz, 1 H, 23-H) ppm. $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ = 16.1 (C-16), 17.6 (C-25), 17.8 (C-20), 17.9 (C-14), 22.0 (C-22), 25.6 (C-26), 25.8 (C-21), 25.9 (C-15), 26.5 (C-11), 31.2 (C-4)*, 35.7 (C-7), 35.9 (C-17), 39.8 (C-10), 60.3 (C-2)*, 116.2 (C-6), 118.0 (C-18), 118.2 (C-8), 121.1 (C-23), 123.9 (C-12), 131.7 (C-13), 135.5 (C-19), 137.2 (C-24), 139.3 (C-9), 170.5 (C-5)*, 189.9 (C-1)*, 206.5 (C-3) ppm; * deduced from HMQC/HMBC experiments. HRMS (ESI): calcd. for $C_{26}H_{39}O_3$ $[M + H]^+$ 399.2899; found 399.2914.

**Prenylation of Isolavandulylphloroglucinol:** The experiment was performed using the same procedure as that described for the prenylation of geranylphloroglucinol to obtain compounds **15c** (14%) and **16c** (40%) as viscous light-yellow oils.

**5-Hydroxy-2-[5-methyl-2-(propan-2-ylidene)hex-4-enyl]-2-(3-methylbut-2-enyl)cyclohex-4-ene-1,3-dione (15c):** FTIR: $\tilde{\nu}$ = 3387, 2916, 1721, 1643, 1557, 1437, 1372, 1210, 1097, 838 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ = 1.58 (s, 6 H, 12-H, 20-H), 1.60 (s, 3 H, 15-H or 16-H), 1.61 (s, 6 H, 13-H, 21-H), 1.63 (s, 3 H, 16-H or 15-H), 2.47–2.64 (m, 3 H, 9-H, 17-H), 2.67 (s, 2 H, 7-H), 2.71–2.80 (m, 1 H, 9-H or 17-H), 3.16 (d, $J$ = 20.7 Hz, 1 H, 4-$H^B$), 3.26 (d, $J$ = 20.7 Hz, 1 H, 4-$H^A$), 4.76 (t, $J$ = 7.0 Hz, 1 H, 18-H), 4.84 (t, $J$ = 5.6 Hz, 1 H, 10-H), 5.86 (s, 1 H, 6-H) ppm. $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ = 17.8 (C-12, C-20), 20.6 (C-15 or C-16), 21.2 (C-16 or C-15), 25.6 (C-13 or C-21), 25.8 (C-21 or C-13), 31.7 (C-9), 35.2 (C-17), 41.3 (C-7), 48.3 (C-4), 60.6 (C-2), 106.9 (C-6), 118.3 (C-18), 122.5 (C-10), 127.4 (C-8), 130.7 (C-14), 131.9 (C-11), 135.2 (C-19), 185.7 (C-5), 190.2 (C-1), 207.0 (C-3) ppm. HRMS (ESI): calcd. for $C_{21}H_{30}NaO_3$ $[M + Na]^+$ 353.2093; found 353.2102.

**5-Hydroxy-2-[5-methyl-2-(propan-2-ylidene)hex-4-enyl]-2,4-bis(3-methylbut-2-enyl)cyclohex-4-ene-1,3-dione (16c):** FTIR: $\tilde{\nu}$ = 3450, 2914, 2361, 1700, 1632, 1437, 1374, 1215, 1096 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ = 1.58 (s, 9 H, 12-H, 20-H, 25-H), 1.60 (s, 3 H, 15-H or 16-H), 1.64 (s, 6 H, 13-H, 21-H), 1.76 (s, 3 H, 26-H), 1.77 (s, 3 H, 16-H or 15-H), 2.45–2.59 (m, 3 H, 9-H, 17-H), 2.62 (d, $J$ = 5.9 Hz, 2 H, 7-H), 2.66–2.80 (m, 1 H, 17-H or 9-H), 3.15 (d, $J$ = 7.1 Hz, 1 H, 22-H), 3.18 (d, $J$ = 7.1 Hz, 1 H, 22-H), 3.20 (d, $J$ = 20.0 Hz, 1 H, 4-$H^B$), 3.28 (d, $J$ = 20.0 Hz, 1 H, 4-$H^A$), 4.74 (t, $J$ = 7.2 Hz, 1 H, 18-H), 4.84 (t, $J$ = 6.6 Hz, 1 H, 10-H), 5.14 (t, $J$ = 7.5 Hz, 1 H, 23-H) ppm. $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ = 17.8 (C-12, C-20, C-25), 20.6 (C-15 or C-16), 21.1 (C-16 or C-15), 22.1 (C-22), 25.7 (C-13 or C-21 or C-26), 25.8 (C-21 or C-26 or C-13), 25.9 (C-26 or C-13 or C-21), 29.7 (C-9), 31.7 (C-7, C-17), 35.4 (C-4)*, 58.7 (C-2)*, 116.2 (C-6), 118.4 (C-23), 121.1 (C-18), 122.6 (C-10), 127.6 (C-8), 130.9 (C-14), 131.9 (C-11), 135.1 (C-19), 137.3 (C-24), 188.6 (C-5)*, 201.5 (C-1)*, 206.4 (C-3) ppm; * deduced from HMQC/HMBC experiments. HRMS (ESI): calcd. for $C_{26}H_{39}O_3$ $[M + H]^+$ 399.2899; found 399.2880.

**Prenylation of Lavandulylphloroglucinol:** The experiment was performed using the same procedure as that described for the prenylation of geranylphloroglucinol to obtain compound **14d** (23%) as a viscous light-yellow oil.

**2-[5-Methyl-2-(prop-1-en-2-yl)hex-4-enyl]-4-(3-methyl-2-but-2-enyl)-benzene-1,3,5-triol (14d):** FTIR: $\tilde{\nu}$ = 3331, 2921, 1620, 1445, 1376, 1125, 1001, 898 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ = 1.57 (s, 3 H, 15-H), 1.67 (s, 6 H, 12-H, 20-H), 1.74 (s, 3 H, 13-H or 21-H), 1.80 (s, 3 H, 21-H or 13-H), 2.08 (t, $J$ = 7.0 Hz, 2 H, 9-H), 2.16–2.28 (m, 1 H, 8-H), 2.54 (dd, $J$ = 13.0, 9.5 Hz, 1 H, 7-$H^B$), 2.67 (dd, $J$ = 13.0, 5.1 Hz, 1 H, 7-$H^A$), 3.35 (d, $J$ = 7.0 Hz, 2 H, 17-H), 4.86 (s, 1 H, 16-H), 4.93–5.02 (m, 2 H, 10-H, 16-H), 5.25 (tq, $J$ = 7.0, 1.5 Hz, 1 H, 18-H), 5.49–5.76 (br. s, 1 H, OH), 6.10 (s, 1 H, 4-H), 6.35 (s, 1 H, OH), 6.65 (s, 1 H, OH) ppm. $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ = 17.8 (C-12 or C-20), 17.9 (C-20 or C-12), 18.9 (C-15), 22.8 (C-17), 25.7 (C-13 or C-21), 25.8 (C-21 or C-13), 31.6 (C-9), 39.4 (C-7), 47.1 (C-8), 94.6 (C-4), 96.8 (C-2), 105.4 (C-6), 113.7 (C-16), 121.4 (C-10), 122.3 (C-18), 133.2 (C-19), 133.9 (C-11), 145.5 (C-14), 155.7 (C-3), 156.3 (C-5), 158.0 (C-1) ppm.

**1,3,5-Tris(methoxymethoxy)benzene (17):** NaH (60% dispersion in mineral oil, 0.53 g, 13.3 mmol) was added to a mixture of dry DMF (5 mL) and ether (10 mL). The mixture was cooled to 0 °C and phloroglucinol (**7**) (0.5 g, 3.96 mmol) was added portionwise over a period of 10 min. The mixture was warmed to room temp. and stirred for an additional 1 h. Methoxymethyl chloride (990 μL, 13.0 mmol) was added and the mixture was stirred for 10 h at room temp. Excess NaH was destroyed by the addition of water (15 mL). The mixture was diluted with diethyl ether, washed with water and brine, dried with $Na_2SO_4$, filtered and concentrated in vacuo. The crude product was purified by flash chromatography (heptane/EtOAc, 90:10) to give **17** (680 mg, 66%) as viscous colourless oil. FTIR: $\tilde{\nu}$ = 2906, 1595, 1470, 1398, 1137, 1079, 1026, 920, 832 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ = 3.47 (s, 9 H, $CH_3$), 5.13 (s, 6 H, $CH_2$), 6.41 (s, 3 H, Ar-H) ppm. $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ = 56.1 ($CH_3$), 94.5 ($CH_2$), 98.4 (*C*-H), 158.9 (*C*-O) ppm.

**(*E*)-2-(3,7-Dimethylocta-2,6-dienyl)-1,3,5-tris(methoxymethoxy)benzene (18b):** *n*-BuLi (1.4 M solution in hexane, 3.65 mL, 5.11 mmol) was added dropwise over a period of 10 min to a solution of **17** (1.10 g, 4.26 mmol) in THF (12 mL) at room temp. After 2 h, the solution was cooled to 0 °C and geranyl bromide (97%, 840 μL, 4.1 mmol) was added dropwise. The reaction mixture was stirred for 1 h at 0 °C, warmed to room temperature over 30 min and stirred for 4 h. The resulting solution was quenched by the addition of water, stirred for 1 h and extracted with EtOAc. The organic layer was washed with water and brine, dried with $Na_2SO_4$ and concentrated in vacuo. The resulting residue was purified by flash chromatography (heptane/EtOAc, 80:20) to afford **18b** (1.26 g, 78%) as a viscous colourless oil. FTIR: $\tilde{\nu}$ = 2924, 1595, 1467, 1397, 1215, 1136, 1021, 920, 831 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ = 1.57 (s, 3 H, 14-H), 1.65 (s, 3 H, 15-H), 1.77 (s, 3 H, 16-H), 1.90–2.11 (m, 4 H, 10-H, 11-H), 3.33 (d, $J$ = 7.9 Hz, 2 H, 7-H), 3.47 (s, 9 H, O-$CH_3$), 5.02–5.26 (m, overlapping s at 5.12 and 5.16, 8 H, 8-

H, 12-H and O-$CH_2$-O), 6.50 (s, 2 H, 4-H, 6-H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 16.0 (C-16), 17.6 (C-14), 22.2 (C-7), 25.6 (C-15), 26.7 (C-11), 39.8 (C-10), 56.0 (3 × O-$CH_3$), 94.6 (2 × O-$CH_2$-O), 94.8 (O-$CH_2$-O), 97.1 (C-4, C-6), 114.0 (C-2), 123.1 (C-8), 124.4 (C-12), 131.2 (C-13), 134.2 (C-9) 156.1 (C-1, C-3), 156.5 (C-5) ppm. HRMS (ESI): calcd. for $C_{22}H_{34}NaO_6$ $[M + Na]^+$ 417.2253; found 417.2239.

**(*E*)-2-(3,7-Dimethylocta-2,6-dienyl)benzene-1,3,5-triol (10b):** CSA (148 mg, 0.64 mmol) was added to a solution of compound **18b** (1.26 g, 3.19 mmol) in MeOH (10 mL). The resulting solution was stirred for 15 h at room temp., quenched by the addition of saturated $NaHCO_3$ and extracted with EtOAc. The organic phase was washed with water and brine and dried with $Na_2SO_4$. Concentration in vacuo followed by purification by flash chromatography (heptane/EtOAc, 80:20) afforded **10b** (540 mg, 64%) as a viscous colourless oil. FTIR: $\tilde{\nu}$ = 3355, 2914, 1613, 1514, 1462, 1376, 1157, 1039, 818 $cm^{-1}$. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 1.57 (s, 3 H, 14-H), 1.66 (s, 3 H, 15-H), 1.77 (s, 3 H, 16-H), 1.94–2.15 (m, 4 H, 10-H, 11-H), 3.31 (d, $J$ = 7.6 Hz, 2 H, 7-H), 5.04 (t, $J$ = 5.9 Hz, 1 H, 12-H), 5.23 (t, $J$ = 5.9 Hz, 1 H, 8-H), 5.69–5.90 (br. s, 2 H, OH), 5.93 (s, 2 H, 4-H, 6-H), 5.99–6.18 (br. s, 1 H, OH) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 16.1 (C-16), 17.6 (C-14), 21.9 (C-7), 25.6 (C-15), 26.4 (C-11), 39.6 (C-10), 96.3 (C-4, C-6), 106.9 (C-2), 121.8 (C-8), 123.7 (C-12), 132.1 (C-13), 139.2 (C-9), 154.4 (C-5), 155.6 (C-1, C-3) ppm. HRMS (ESI): calcd. for $C_{16}H_{23}O_3$ $[M + H]^+$ 263.1647; found 263.1640.

**1,3,5-Tris(methoxymethoxy)-2-[5-methyl-2-(propan-2-ylidene)hex-4-enyl]benzene (18c):** The experiment was performed using the same procedure as that described for the preparation of **18b**, except that the reaction mixture was stirred for 20 h at room temp. after the addition of isolavandulyl bromide[8] to obtain, after purification, compound **18c** in 71% yield as a viscous colourless oil. FTIR: $\tilde{\nu}$ = 2908, 1593, 1490, 1434, 1394, 1214, 1151, 1137, 1041, 1023, 920, 826 $cm^{-1}$. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 1.52 (s, 3 H, 12-H), 1.61 (s, 3 H, 13-H), 1.64 (s, 3 H, 15-H or 16-H), 1.84 (s, 3 H, 16-H or 15-H), 2.59 (d, $J$ = 6.8 Hz, 2 H, 9-H), 3.44 (s, 9 H, O-$CH_3$), 3.47 (s, 2 H, 7-H), 4.95 (t, $J$ = 7.1 Hz, 1 H, 10-H), 5.12 (s, 6 H, O-$CH_2$-O), 6.49 (s, 2 H, 4-H, 6-H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 17.6 (C-12), 20.6 (C-15 or C-16), 20.7 (C-16 or C-15), 25.6 (C-13), 25.9 (C-7), 30.0 (C-9), 55.8 (2 × O-$CH_3$), 56.0 (O-$CH_3$), 94.4 (2 × O-$CH_2$-O), 94.7 (O-$CH_2$-O), 96.6 (C-4, C-6), 112.9 (C-2), 124.0 (C-10), 124.6 (C-8), 129.4 (C-14), 130.4 (C-11), 156.6 (C-5), 156.8 (C-1, C-3) ppm. HRMS (ESI): calcd. for $C_{22}H_{34}NaO_6$ $[M + Na]^+$ 417.2253; found 417.2245.

**2-[5-Methyl-2-(propan-2-ylidene)hex-4-enyl]benzene-1,3,5-triol (10c):** The experiment was performed using the same procedure as that described for the preparation of **10b**, affording **10c** in 81% yield. FTIR: $\tilde{\nu}$ = 3357, 2914, 1608, 1514, 1466, 1374, 1268, 1205, 1138, 1094, 1035, 1003, 819 $cm^{-1}$. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 1.50 (s, 3 H, 12-H), 1.65 (s, 3 H, 13-H), 1.77 (s, 3 H, 15-H or 16-H), 1.90 (s, 3 H, 16-H or 15-H), 2.68 (d, $J$ = 7.3 Hz, 2 H, 9-H), 3.42 (s, 2 H, 7-H), 4.99 (t, $J$ = 7.0 Hz, 1 H, 10-H), 5.12–5.26 (br. s, 1 H, OH), 5.51–5.68 (br. s, 2 H, OH), 5.94 (s, 2 H, 6-H, 4-H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 17.6 (C-12), 20.6 (C-16 or C-15), 20.8 (C-15 or C-16), 25.7 (C-13), 25.8 (C-7), 29.9 (C-9), 96.1 (C-4, C-6), 104.5 (C-2), 122.1 (C-10), 129.2 (C-8), 130.5 (C-14), 132.8 (C-11), 155.0 (C-5), 156.4 (C-1, C-3) ppm. HRMS (ESI): calcd. for $C_{16}H_{23}O_3$ $[M + H]^+$ 263.1647; found 263.1680.

**2-[5-Methyl-2-(prop-1-en-2yl)hex-4-enyl]benzene-1,3,5-triol (10d):** *n*-BuLi (1.4 M solution in hexane, 1.25 mL, 1.74 mmol) was added dropwise over a period of 10 min to a solution of **17** (0.15 g, 0.58 mmol) in THF (2 mL) at room temp. After 2 h, lavandulyl iodide (prepared from commercially available lavandulol by reaction with iodine, triphenylphosphane and imidazole in dichloromethane) (0.384 g, 1.45 mmol) was added dropwise. The reaction mixture was heated at 70 °C for 8 h. The resulting solution was quenched by the addition of water, stirred for 1 h and extracted with EtOAc. The organic layer was washed with water and brine, dried with $Na_2SO_4$ and concentrated in vacuo. The resulting residue was subjected to CSA hydrolysis, as described for the preparation of **10b**, to yield, after purification by flash chromatography (heptane/EtOAc, 80:20), compound **10d** (94 mg, 62%) as a viscous colourless oil. FTIR: $\tilde{\nu}$ = 3394, 2920, 1620, 1587, 1454, 1337, 1130, 1039, 1001, 838 $cm^{-1}$. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 1.57 (s, 3 H, 12-H), 1.67 (s, 6 H, 13-H, 15-H), 2.08 (t, $J$ = 7.0 Hz, 2 H, 9-H), 2.16–2.28 (m, 1 H, 8-H), 2.54 (dd, $J$ = 13.0, 9.7 Hz, 1 H, 7-H), 2.67 (dd, $J$ = 13.0, 5.0 Hz, 1 H, 7-H), 4.87 (s, 1 H, 16-H), 4.94–5.02 (m, 2 H, 10-H, 16-H), 5.30–5.44 (br. s, 1 H, OH), 6.09 (s, 2 H, 4-H, 6-H), 6.49–6.61 (br. s, 2 H, OH) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 17.9 (C-12), 18.9 (C-15), 25.7 (C-13), 31.7 (C-9), 39.5 (C-7), 47.1 (C-8), 94.6 (C-4, C-6), 97.4 (C-2), 113.8 (C-16), 121.3 (C-10), 133.4 (C-11), 145.6 (C-14), 158.5 (C-1, C-3), 159.0 (C-5) ppm.

**3,5-Dihydroxy-2,4,4-tris(3-methylbut-2-enyl)-6-(phenylcarbonyl)-cyclohexa-2,5-dienone (Grandone, 19a):** Freshly distilled $Et_3N$ (127 μL, 0.91 mmol) and, dropwise, benzoyl cyanide (55 μL, 0.45 mmol) were successively added to a solution of **13a** (150 mg, 0.45 mmol) in THF (760 μL). The mixture was stirred overnight at room temperature, diluted with EtOAc and quenched with a small amount of saturated aqueous $NH_4Cl$. The organic phase was separated and washed with water and brine, dried with $Na_2SO_4$ and concentrated to give a yellow oil. Purification by flash chromatography (heptane/EtOAc, 95:5) gave grandone **19a** (101 mg, 51%) as a white powder. HRMS (ESI): calcd. for $C_{28}H_{34}NaO_4$ $[M + Na]^+$ 457.2355; found 457.2373.

Owing to the presence of a certain number of tautomeric forms, grandone (**19a**) was acetylated with acetic anhydride under classical conditions in order to determine the major form.

**2,2,4-Tris(3-methylbut-2-enyl)-5-oxo-6-(phenylcarbonyl)cyclohexa-3,6-diene-1,3-diyl Diethanoate (Acetylated Grandone):** FTIR: $\tilde{\nu}$ = 2988, 2869, 1786, 1768, 1681, 1661, 1626, 1141 $cm^{-1}$. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 1.60 (s, 3 H, 20-H), 1.61 (s, 6 H, 10-H, 15-H), 1.66 (s, 3 H, 21-H), 1.70 (s, 6 H, 11-H, 16-H), 2.00 (s, 3 H, 30-H or 32-H), 2.26 (s, 3 H, 32-H or 30-H), 2.53 (m, 4 H, 7-H, 12-H), 2.95 (d, $J$ = 7.0 Hz, 2 H, 17-H), 4.88 (br. t, $J$ = 7.0 Hz, 1 H, 18-H), 5.09 (br. t, $J$ = 7.0 Hz, 2 H, 8-H, 13-H), 7.39 (t, $J$ = 7.0 Hz, 2 H, 25-H, 27-H), 7.51 (tt, $J$ = 7.0, 2.0 Hz, 1 H, 26-H), 7.78 (dd, $J$ = 7.0, 2.0 Hz, 2 H, 24-H, 28-H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 17.7 (C-20), 18.0 (C-10, C-15), 20.7 (C-30, C-32), 23.5 (C-17), 25.7 (C-21), 25.9 (C-11, C-16), 34.9 (C-7, C-12), 52.1 (C-2), 117.5 (C-8, C-13), 120.4 (C-18), 128.2 (C-25, C-27), 128.9 (C-4), 129.0 (C-24, C-28), 130.5 (C-6), 132.6 (C-19), 133.0 (C-26), 135.5 (C-9, C-14), 136.8 (C-23), 160.0 (C-1), 163.2 (C-3), 165.6 (C-29, C-31), 184.6 (C-5), 192.3 (C-22) ppm. HRMS (ESI): calcd. for $C_{32}H_{38}NaO_6$ $[M + Na]^+$ 541.2566; found 541.2564.

**(*E*)-4-(3,7-Dimethylocta-2,6-dienyl)-3,5-dihydroxy-2,4-bis(3-methylbut-2-enyl)-6-(phenylcarbonyl)cyclohexa-2,5-dienone (Kolanone) (19b):** TEA (50 μL, 0.36 mmol) followed by benzoyl cyanide (30 μL, 0.25 mmol) were added to a solution of **16b** (73 mg, 0.18 mmol) in dry THF (2 mL). The reaction mixture was stirred for 12 h at room temp., by which time the starting material had been completely consumed. $Et_2O$ was added and the organic layer was washed with saturated aqueous $NH_4Cl$, dried with $Na_2SO_4$ and concentrated in vacuo. The crude residue was purified by flash chromatography (heptane/EtOAc, 90:10) to give **19b** (58 mg, 63%)

as a viscous light-yellow oil which solidified upon standing. An analytical sample was obtained by recrystallization from heptane/EtOAc (80:20); m.p. 104–106 °C (ref.[24] 107–109 °C, recrystallized from ethanol/water). FTIR: $\tilde{\nu}$ = 3300, 2920, 1644, 1587, 1556, 1510, 1493, 1446, 1374, 1217, 1185, 1152, 1099, 796, 694 $cm^{-1}$. $^1H$ NMR (300 MHz, $C_6D_6$): $\delta$ = 1.51 (s, 3 H, 14-H), 1.54 (s, 9 H, 15-H, 20-H, 25-H), 1.57 (s, 3 H, 21-H), 1.61 (s, 3 H, 26-H), 1.63 (s, 3 H, 16-H), 1.91–2.02 (m, 2 H, 10-H), 2.02–2.15 (m, 2 H, 11-H), 2.51–2.67 (m, 1 H, 7-H), 2.72–3.03 (m, 3 H, 7-H, 17-H), 3.23 (d, $J$ = 7.6 Hz, 2 H, 22-H), 5.11 (t, $J$ = 7.6 Hz, 1 H, 12-H), 5.19 (t, $J$ = 7.0 Hz, 2 H, 8-H, 18-H), 5.26 (t, $J$ = 7.1 Hz, 1 H, 23-H), 7.05–7.23 (m, 3 H, 30-H, 31-H 32-H), 7.61–7.76 (m, 2 H, 29-H, 33-H) ppm. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ = 1.51–1.85 (m, 21 H, 14-H, 15-H, 16-H, 20-H, 21-H, 25-H, 26-H), 1.87–2.07 (m, 4 H, 10-H, 11-H), 2.43–2.82 (m, 4 H, 7-H, 17-H), 3.14 (minor tautomer) and 3.23 (major tautomer) (d, $J$ = 6.8 Hz, 2 H, 22-H), 4.81–5.24 (m, 4 H, 8-H, 12-H, 18-H, 23-H), 7.30–7.56 (m, 5 H, Ar-H) ppm. $^{13}C$ NMR (75 MHz, $C_6D_6$): $\delta$ = 17.3 (C-16), 18.4 (C-20, C-25), 18.8 (C-14), 22.1 (C-22), 26.4 (C-21, C-26), 26.6 (C-15), 27.6 (C-11), 38.1 (C-7), 38.4 (C-17), 40.8 (C-10), 58.2 (C-2), 109.1 (C-4), 111.6 (C-6), 119.5 (C-8), 119.8 (C-18), 122.4 (C-23), 125.1 (C-12), 128.3 (C-29, C-33), 129.0 (C-30, C-32), 129.4 (C-31), 131.6 (C-28), 132.2 (C-13), 135.7 (C-19), 139.6 (C-24), 140.1 (C-9), 173.7 (C-1), 190.2 (C-5), 195.0 (C-3), 197.1 (C-27) ppm. $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ = 16.4 (C-16), 17.6 (C-20), 17.9 (C-25), 18.0 (C-14), 21.1 (C-22), 25.6 (C-21), 25.8 (C-26), 25.9 (C-15), 26.6 (C-11), 37.1 (C-7), 37.3 (C-17), 39.8 (C-10), 57.2 (C-2), 107.8 (C-4), 109.7 (C-6), 118.1 (C-8), 118.4 (C-18), 120.9 (C-23), 123.9 (C-12), 127.5 (C-29, C-33), 127.7 (C-30, C-32), 128.4 (C-31), 130.1 (C-28), 130.8 (C-13), 134.9 (C-19), 136.7 (C-24), 138.8 (C-9), 173.4 (C-1), 188.6 (C-5), 194.5 (C-3), 196.0 (C-27) ppm. HRMS (ESI): calcd. for $C_{33}H_{42}NaO_4$ $[M + Na]^+$ 525.2981; found 525.2987.

**3,5-Dihydroxy-4-[5-methyl-2-(propan-2-ylidene)hex-4-enyl]-2,4-bis(3-methylbut-2-enyl)-6-(phenylcarbonyl)cyclohexa-2,5-dienone (19c):** The experiment was performed, starting from **16c**, using the same procedure as that described for the preparation of **19b** to afford **19c** (58%) as a viscous light-yellow oil. Compound **19c** was found to be composed of an inseparable mixture of tautomeric forms. The major tautomer was characterized as described below. FTIR: $\tilde{\nu}$ = 3421, 2921, 1691, 1601, 1584, 1449, 1374, 1242, 1092, 1067, 709 $cm^{-1}$. $^1H$ NMR (300 MHz, $C_6D_6$): $\delta$ = 1.46–1.74 (m, 24 H, 12-H, 13-H, 15-H, 16-H, 20-H, 21-H, 25-H, 26-H), 2.57–3.06 (m, 6 H, 7-H, 9-H, 17-H), 3.27 (d, $J$ = 6.6 Hz, 1 H, 22-H), 3.39–3.48 (m, 1 H, 22-H), 4.99–5.39 (m, 3 H, 10-H, 18-H, 23-H), 7.01–7.26 (m, 3 H, 30-H, 31-H, 32-H), 7.61–7.72 (m, 2 H, 29-H, 33-H) ppm. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ = 1.51–1.70 (m, 18 H, 12-H, 13-H, 15-H or 16-H, 20-H, 21-H, 25-H), 1.74–1.86 (m, 6 H, 16-H or 15-H, 26-H), 2.46–2.91 (m, 6 H, 7-H, 9-H, 17-H), 3.08–3.35 (m, 2 H, 22-H), 4.80–4.97 (m, 2 H, 10-H, 18-H), 5.11–5.23 (m, 1 H, 23-H), 7.31–7.66 (m, 5 H, Ar-H) ppm. $^{13}C$ NMR (75 MHz, $C_6D_6$): $\delta$ = 17.6, 17.9, 18.1 (C-12, C-20, C-25), 20.4 (C-15 or C-16), 20.9 (C-16 or C-15), 21.5 (C-22), 25.7, 25.9 (C-13, C-21, C-26), 28.1 (C-9), 30.2 (C-7 or C-17), 37.9 (C-17 or C-7), 57.3 (C-2), 108.6 (C-4), 110.8 (C-6), 118.5 (C-23), 119.3 (C-18), 121.6 (C-10), 123.9 (C-8), 128.5 (C-31), 128.6 (C-29, C-33), 130.4 (C-30, C-32), 131.9 (C-14), 133.4 (C-28), 134.6 (C-11), 136.0 (C-19), 139.1 (C-24), 173.2 (C-1), 189.6 (C-5), 193.5 (C-3), 196.1 (C-27) ppm. $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ = 17.8, 18.0 (C-12, C-20, C-25), 20.8 (C-15 or C-16), 21.2 (C-16 or C-15), 21.3 (C-22), 25.6, 25.8, 25.9 (C-13, C-21, C-26), 31.3 (C-9), 38.2 (C-7 or C-17), 41.6 (C-17 or C-7), 57.0 (C-2), 107.5 (C-4), 109.5 (C-6), 118.4 (C-23), 120.8 (C-18), 123.1 (C-10), 127.4 (C-8), 127.7 (C-31), 128.4 (C-29, C-33), 130.6 (C-30, C-32), 131.4 (C-14), 133.6 (C-28), 134.9 (C-11), 136.8 (C-19), 139.0 (C-24), 173.9 (C-1), 188.7 (C-5), 194.0 (C-3), 196.0 (C-27) ppm. HRMS (ESI): calcd. for $C_{33}H_{42}NaO_4$ $[M + Na]^+$ 525.2981; found 525.2956.

**3,5-Dimethoxy-4-[5-methyl-2-(propan-2-ylidene)hex-4-enyl]-2,4-bis(3-methylbut-2-enyl)-6-(phenylcarbonyl)cyclohexa-2,5-dienone:** $K_2CO_3$ (48 mg, 348 μmol) followed by $Me_2SO_4$ (22 μL, 231 μmol) were added to a solution of **19c** (27 mg, 54 μmol) in acetone (1 mL). The mixture was stirred for 18 h at room temp., diluted with EtOAc, washed with water and brine, dried with $Na_2SO_4$ and concentrated in vacuo. The residue was purified by flash chromatography (heptane/EtOAc, 90:10) to yield the bis(methyl enol ether) (17 mg, 60%) as a viscous light-yellow oil which was also found to be composed of an inseparable mixture of regioisomers, the major form being characterized as follows. FTIR: $\tilde{\nu}$ = 2921, 1744, 1673, 1647, 1598, 1449, 1259, 1222, 1090, 1023, 708 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ = 1.46–1.97 (m, 24 H, 12-H, 13-H, 15-H, 16-H, 20-H, 21-H, 25-H, 26-H), 2.47–2.48 (m, 6 H, 7-H, 9-H, 17-H), 2.99–3.33 (m, 2 H, 22-H), 3.55 (s, 3 H, 34-H), 3.95 (s, 3 H, 35-H), 4.80–5.17 (m, 3 H, 10-H, 18-H, 23-H), 7.31–7.61 (m, 3 H, 30-H, 31-H, 32-H), 7.75–8.00 (m, 2 H, 29-H, 33-H) ppm. $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ = 17.8, 18.0, 18.1 (C-12, C-20, C-25), 20.8 (C-15 or C-16), 21.0 (C16 or C-15), 22.9 (C-22), 25.7, 25.9, 26.0 (C-13, C-21, C-26), 31.3 (C-9), 35.9 (C-7 or C-17), 40.1 (C-17 or C-7), 53.9 (C-34), 59.1 (C-2), 61.4 (C-35), 89.0 (C-4)*, 104.9 (C-6)*, 118.8 (C-23), 122.7 (C-18), 123.6 (C-10), 128.1 (C-8), 128.4 (C-29, C-33), 129.1 (C-30, C-32), 129.3 (C-31), 130.1 (C-14), 131.3 (C-11), 132.9 (C-28), 134.5 (C-19), 138.6 (C-24), 169.5 (C-1), 170.7 (C-3), 187.9 (C-5), 196.3 (C-27) ppm; * deduced from HMQC/HMBC experiments. HRMS (ESI): calcd. for $C_{35}H_{46}NaO_4$ $[M + Na]^+$ 553.3294; found 553.3314.

**Electrophilic Cyclization Reactions:** $SnCl_4$ (53 μL, 0.44 mmol) was slowly added to a solution of **13a** (98 mg, 0.30 mmol) in $CH_2Cl_2$ (4 mL) at –10 °C. The mixture was stirred for 3 h at –10 °C, diluted with $CH_2Cl_2$ (10 mL) and quenched with water. The aqueous phase was extracted with $CH_2Cl_2$ and the organic layers were washed with brine, dried with $Na_2SO_4$ and concentrated to give a yellow oil. Purification by flash chromatography (heptane/EtOAc, 70:30) gave **20** (9 mg, 9%) and **21** (12 mg, 12%) as yellow oils.

**2,2-Dimethyl-6,6-bis(3-methylbut-2-enyl)-3,4-dihydro-2*H*-chromen-5,7(6*H*,8*H*)-dione (20):** FTIR: $\tilde{\nu}$ = 3021, 2915, 1718, 1651, 1624, 1386, 1114 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ = 1.31 (s, 6 H, 20-H, 21-H), 1.57 (s, 6 H, 10-H, 15-H), 1.60 (s, 6 H, 11-H, 16-H), 1.73 (t, $J$ = 6.5 Hz, 2 H, 18-H), 2.34 (tt, $J$ = 6.5, 2.0 Hz, 2 H, 17-H), 2.51 (d, $J$ = 7.5 Hz, 4 H, 7-H, 12-H), 3.10 (t, $J$ = 2.0 Hz, 2 H, 4-H), 4.83 (br. t, $J$ = 7.5 Hz, 2 H, 8-H, 13-H) ppm. $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ = 16.3 (C-17), 17.8 (C-10, C-15), 25.9 (C-11, C-16), 26.4 (C-20, C-21), 32.1 (C-18), 35.9 (C-7, C-12), 43.3 (C-4), 64.6 (C-2), 78.3 (C-19), 111.5 (C-6), 118.7 (C-8, C-13), 134.9 (C-9, C-14), 164.1 (C-5), 197.6 (C-1), 207.3 (C-3) ppm. HRMS (ESI): calcd. for $C_{21}H_{30}NaO_3$ $[M + Na]^+$ 353.2093; found 353.2140.

**2,2-Dimethyl-8,8-bis(3-methylbut-2-enyl)-3,4-dihydro-2*H*-chromen-5,7(6*H*,8*H*)-dione (21):** FTIR: $\tilde{\nu}$ = 2972, 2916, 1654, 1590, 1155, 1115 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ = 1.32 (s, 6 H, 20-H, 21-H), 1.57 (s, 6 H, 10-H, 15-H), 1.60 (s, 6 H, 11-H, 16-H), 1.67 (t, $J$ = 6.5 Hz, 2 H, 18-H), 2.40 (t, $J$ = 6.5 Hz, 2 H, 17-H), 2.43 (dd, $J$ = 14.0, 7.0 Hz, 2 H, 7-$H^B$, 12-$H^B$), 2.62 (dd, $J$ = 14.0, 7.0 Hz, 2 H, 7-$H^A$, 12-$H^A$), 3.24 (s, 2 H, 4-H), 4.82 (br. t, $J$ = 7.0 Hz, 2 H, 8-H, 13-H) ppm. $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ = 16.3 (C-17), 17.9 (C-10, C-15), 25.9 (C-11, C-16), 26.5 (C-20, C-21), 31.7 (C-18), 35.7 (C-7, C-12), 52.5 (C-4), 58.2 (C-2), 78.3 (C-19), 112.6 (C-6), 118.3 (C-8, C-13), 135.2 (C-9, C-14), 170.4 (C-1), 191.4 (C-5),

206.7 (C-3) ppm. HRMS (ESI): calcd. for $C_{21}H_{30}NaO_3$ $[M + Na]^+$ 353.2093; found 353.2135.

**7-Hydroxy-2,2-dimethyl-6,6-bis(3-methylbut-2-enyl)-8-(phenylcarbonyl)-3,4-dihydro-2*H*-chromen-5(6*H*)-one (22):** $SnCl_4$ (15 μL, 0.13 mmol) was slowly added to a solution of **19a** (56 mg, 0.13 mmol) in $CH_2Cl_2$ (1.6 mL) at 0 °C. The mixture was stirred for 3 h at 0 °C, diluted with $CH_2Cl_2$ (10 mL) and quenched with a solution of 1 N HCl (10 mL). The aqueous phase was extracted with $CH_2Cl_2$ and the organic layers were washed with brine, dried with $Na_2SO_4$ and concentrated to give a yellow oil. Purification by flash chromatography (heptane/EtOAc, 80:20) gave **22** (8 mg, 14%) as a yellow oil. $^1H$ NMR (500 MHz, $C_6D_6$): $\delta$ = 0.59 (s, 6 H, 20-H, 21-H), 1.10 (t, $J$ = 7 Hz, 2 H, 18-H), 1.51 (s, 6 H, 11-H, 16-H), 1.62 (s, 6 H, 10-H, 15-H), 2.46 (t, $J$ = 7 Hz, 2 H, 17-H), 2.89 (dd, $J$ = 13.0, 7.0 Hz, 2 H, 7-$H^B$, 12-$H^B$), 3.06 (dd, $J$ = 13.0, 7.0 Hz, 2 H, 7-$H^A$, 12-$H^A$), 5.22 (br. t, $J$ = 7.0 Hz, 2 H, 8-H, 13-H), 6.99 (dd, $J$ = 7.5, 7.0 Hz, 2 H, 25-H, 27-H), 7.05 (br. t, $J$ = 7.5 Hz, 1 H, 26-H), 7.35 (br. d, $J$ = 7.0 Hz, 2 H, 24-H, 28-H) ppm. $^{13}C$ NMR (125 MHz, $C_6D_6$): $\delta$ = 16.8 (C-17), 18.0 (C-10, C-15), 25.5 (C-20, C-21), 26.0 (C-11, C-16), 31.9 (C-18), 38.9 (C-7, C-12), 60.6 (C-2), 77.1 (C-19), 106.4 (C-6), 107.9 (C-4), 119.3 (C-8, C-13), 127.4 (C-25, C-27), 128.3 (C-24, C-28), 130.3 (C-26), 134.9 (C-9, C-14), 139.5 (C-23), 161.9 (C-5), 188.4 (C-22), 195.1 (C-1), 200.0 (C-3) ppm. HRMS (ESI): calcd. for $C_{28}H_{34}NaO_4$ $[M + Na]^+$ 457.2355; found 457.2378.

**6,6,12,12-Tetramethyl-5-oxatricyclo[7.3.1.0$^{4,9}$]tridec-3-ene-2,13-dione (23):** $SnCl_4$ (98 μL, 0.83 mmol) was slowly added to a solution of **12a** (198 mg, 0.75 mmol) in $CH_2Cl_2$ (9 mL) at –10 °C. The mixture was stirred for 3 h at –10 °C, diluted with $CH_2Cl_2$ (10 mL) and quenched with a solution of 1 N HCl (10 mL). The aqueous phase was extracted with $CH_2Cl_2$ and the organic layers were washed with brine, dried with $Na_2SO_4$ and concentrated to give a yellow oil. Purification by flash chromatography (heptane/EtOAc, 50:50) gave **23** (14 mg, 7%) as a yellow oil. FTIR: $\tilde{\nu}$ = 2972, 2933, 1728, 1646, 1595, 1120 $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ = 0.95 (s, 3 H, 15-H), 1.04 (s, 3 H, 16-H), 1.20 (s, 3 H, 10-H), 1.40 (m, 1 H, 13-$H^B$), 1.43 (s, 3 H, 11-H), 1.60 (m, 2 H, 7-$H^B$, 12-$H^B$), 1.71 (dt, $J$ = 14.0, 4.0 Hz, 1 H, 8-$H^B$), 1.80 (dt, $J$ = 14.0, 7.0 Hz, 1 H, 13-$H^A$), 1.92 (td, $J$ = 14.0, 5.0 Hz, 1 H, 8-$H^A$), 2.20 (ddd, $J$ = 14.0, 5.0, 2.0 Hz, 1 H, 12-$H^A$), 2.37 (td, $J$ = 14.0, 5.0 Hz, 1 H, 7-$H^A$), 2.86 (s, 1 H, 6-H), 5.83 (s, 1 H, 4-H) ppm. $^{13}C$ NMR (125 MHz, $CDCl_3$): $\delta$ = 22.6 (C-7), 25.5 (C-10, C-15), 28.5 (C-16), 29.9 (C-11), 30.6 (C-8), 32.1 (C-13), 32.3 (C-12), 39.4 (C-14), 48.3 (C-2), 73.1 (C-6), 80.6 (C-9), 113.8 (C-4), 173.7 (C-3), 194.3 (C-5), 207.4 (C-1) ppm. HRMS (ESI): calcd. for $C_{16}H_{22}NaO_3$ $[M + Na]^+$ 285.1467; found 285.1446.

**4,6,6-Tris(3-methylbut-2-enyl)-5-oxocyclohexa-1,3-diene-1,3-diyl Diethanoate (24):** $Ac_2O$ (316 μL, 3.28 mmol) was added to a solution of **13a** (361 mg, 1.09 mmol) in pyridine (1.0 mL). The mixture was stirred for 3 h at room temperature, diluted with $Et_2O$ and quenched with water. The aqueous phase was extracted with $Et_2O$ and the organic layers were washed with brine, dried with $Na_2SO_4$ and concentrated to give a yellow oil. Purification by flash chromatography (heptane/EtOAc, 80:20) gave **24** (407 mg, 90%) as a yellow oil. FTIR: $\tilde{\nu}$ = 2967, 2913, 1773, 1661, 1595, 1171 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ = 1.54 (s, 6 H, 10-H, 15-H), 1.59 (s, 6 H, 11-H, 16-H), 1.65 (s, 3 H, 21-H), 1.68 (s, 3 H, 20-H), 2.22 (s, 3 H, 23-H or 25-H), 2.24 (s, 3 H, 25-H or 23-H), 2.38 (dd, $J$ = 14.0, 7.0 Hz, 2 H, 7-$H^B$, 12-$H^B$), 2.65 (dd, $J$ = 14.0, 7.0 Hz, 2 H, 7-$H^A$, 12-$H^A$), 2.92 (d, $J$ = 7.0 Hz, 2 H, 17-H), 4.79–4.89 (m, 3 H, 8-H, 13-H, 18-H), 6.36 (s, 1 H, 4-H) ppm. $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ = 17.7 (C-20), 17.8 (C-10, C-15), 20.8 (C-23 or C-25), 21.5 (C-25 or C-23), 21.9 (C-17), 25.6 (C-11, C-16, C-21), 37.7 (C-7, C-12), 57.6 (C-2), 111.1 (C-4), 117.7 (C-8, C-13), 120.7 (C-18), 123.6 (C-6),132.0 (C-19), 134.6 (C-9, C-14), 156.6 (C-3), 158.8 (C-5), 167.2 (C-22, C-24), 200.8 (C-1) ppm. HRMS (ESI): calcd. for $C_{25}H_{34}NaO_5$ $[M + Na]^+$ 437.2304; found 437.2299.

**5-Hydroxy-4,6-bis(3-methylbut-2-enyl)-1,3-phenylene Diethanoate (25):** $SnCl_4$ (20 μL, 0.17 mmol) was slowly added to a solution of **24** (63 mg, 0.15 mmol) in $CH_2Cl_2$ (2 mL) at –10 °C. The mixture was stirred for 3 h at –10 °C, diluted with $CH_2Cl_2$ (10 mL) and quenched with water. The aqueous phase was extracted with $CH_2Cl_2$ and the organic layers were washed with brine, dried with $Na_2SO_4$ and concentrated to give a yellow oil. Purification by flash chromatography (heptane/EtOAc, 80:20) gave **25** (12 mg, 23%) as a yellow oil. FTIR: $\tilde{\nu}$ = 3443, 2921, 1768, 1198 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ = 1.72 (s, 6 H, 11-H, 16-H), 1.77 (s, 6 H, 10-H, 15-H), 2.27 (s, 6 H, 18-H, 20-H), 3.22 (d, $J$ = 7.0 Hz, 4 H, 7-H, 12-H), 5.16 (br. t, $J$ = 7.0 Hz, 2 H, 8-H, 13-H), 5.73 (s, 1 H, OH), 6.44 (s, 1 H, 4-H) ppm. $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ = 17.8 (C-10, C-15), 20.8 (C-18, C-20), 23.5 (C-7, C-12), 25.7 (C-11, C-16), 108.6 (C-4), 117.9 (C-2, C-6), 121.0 (C-8, C-13), 134.5 (C-9, C-14), 147.1 (C-3, C-5), 154.5 (C-1), 169.2 (C-17, C-19) ppm. HRMS (ESI): calcd. for $C_{20}H_{26}NaO_5$ $[M + Na]^+$ 369.1678; found 369.1671.

**3,5-Dimethoxy-2,6,6-tris(3-methylbut-2-enyl)cyclohexa-2,4-dienone (26):** $K_2CO_3$ (26 mg, 187 μmol) followed by $Me_2SO_4$ (13 μL, 137 μmol) were added to a solution of **13a** (15 mg, 45.4 μmol) in acetone (1 mL). The mixture was stirred for 18 h at room temp., diluted with EtOAc, washed with water and brine, dried with $Na_2SO_4$ and concentrated in vacuo. The residue was purified by flash chromatography (heptane/EtOAc, 90:10) to yield the bis(methyl enol ether) **26** (11 mg, 69%) as a viscous light-yellow oil. FTIR: $\tilde{\nu}$ = 2912, 1643, 1609, 1535, 1445, 1403, 1375, 1328, 1215, 1068, 978, 814 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ = 1.52 (s, 6 H, 10-H, 15-H), 1.54 (s, 6 H, 11-H, 16-H), 1.63 (s, 3 H, 20-H), 1.69 (s, 3 H, 21-H), 2.43 (dd, $J$ = 13.5, 7.9 Hz, 2 H, 7-$H^B$, 12-$H^B$), 2.58 (dd, $J$ = 13.5, 7.1 Hz, 2 H, 7-$H^A$, 12-$H^A$), 2.96 (d, $J$ = 7.1 Hz, 2 H, 17-H), 3.68 (s, 3 H, 22-H), 3.85 (s, 3 H, 23-H), 4.73 (tq, $J$ = 7.6, 1.3 Hz, 2 H, 8-H, 13-H), 4.99 (tq, $J$ = 7.0, 1.3 Hz, 1 H, 18-H), 5.46 (s, 1 H, 4-H) ppm. $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ = 17.7 (C-10, C-15, C-20), 21.0 (C-17), 25.7, 25.8 (C-11, C-16, C-21), 38.5 (C-7, C-12), 55.1 (C-22), 55.6 (C-23), 56.8 (C-2), 88.2 (C-4), 113.1 (C-6), 118.8 (C-8, C-13), 123.3 (C-18), 130.3 (C-19), 133.4 (C-9, C-14), 168.7 (C-5), 172.1 (C-3), 198.7 (C-1) ppm. HRMS (ESI): calcd. for $C_{23}H_{35}O_3$ $[M + H]^+$ 359.2586; found 359.2560.

**7-Methoxy-2,2-dimethyl-8,8-bis(3-methylbut-2-enyl)-3-(phenylselanyl)-3,4-dihydro-2*H*-chromen-5(8*H*)-one (27):** *N*-PSP (46.4 mg, 0.15 mmol) and 1 M $SnCl_4$ in dichloromethane (0.14 mL, 0.14 mmol) were added to a solution of **26** (50 mg, 0.14 mmol) in dichloromethane (5 mL) at –78 °C. The mixture was stirred at –78 °C for 2 h, quenched with saturated aqueous $NaHCO_3$ and warmed to room temperature. The mixture was extracted with diethyl ether, the organic layer was washed with water and brine and dried with $Na_2SO_4$. Concentration in vacuo followed by purification by flash chromatography (heptane/EtOAc, 80:20) afforded **27** (29 mg, 41%) as a viscous colourless oil. FTIR: $\tilde{\nu}$ = 2917, 1655, 1621, 1601, 1436, 1396, 1222, 1155, 1112, 1078, 835, 738, 690 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ = 1.32 (s, 3 H, 20-H or 21-H), 1.44 (s, 3 H, 21-H or 20-H), 1.53 (s, 3 H, 10-H or 15-H), 1.55 (s, 3 H, 15-H or 10-H), 1.57 (s, 3 H, 11-H or 16-H), 1.58 (s, 3 H, 16-H or 11-H), 2.42–2.61 (m, 5 H, 7-H, 12-H, 17-H), 2.90 (dd, $J$ = 17.4, 5.6 Hz, 1 H, 17-H), 3.18 (dd, $J$ = 9.4, 5.6 Hz, 1 H, 18-H), 3.62 (s, 3 H, 28-H), 4.70 (t, $J$ = 7.3 Hz, 1 H, 8-H or 13-H), 4.79 (t, $J$ = 7.2 Hz, 1 H, 13-H or 8-H), 5.51 (s, 1 H, 4-H), 7.23–7.32 (m, 3 H, 24-H, 25-H,

26-H), 7.53–7.62 (m, 2 H, 23-H, 27-H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 18.0 (C-10, C-15), 22.9 (C-20 or C-21), 25.3 (C-17), 25.8 (C-11, C-16), 27.6 (C-21 or C-20), 35.6, 35.8 (C-7, C-12), 47.2 (C-18), 50.3 (C-2), 55.4 (C-28), 80.1 (C-19), 102.7 (C-4), 110.1 (C-6), 118.2, 118.5 (C-8, C-13), 127.8 (C-25), 129.2 (C-24, C-26), 130.6 (C-22), 133.7, 133.8 (C-9, C-14)), 134.7 (C-23, C-27), 165.5 (C-1), 173.4 (C-3), 187.4 (C-5) ppm. HRMS (ESI): calcd. for $C_{28}H_{37}O_3Se$ $[M + H]^+$ 501.1908; found 501.1931.

**2,2-Dimethyl-8,8-bis(3-methylbut-2-enyl)-5-oxo-3-(phenylselanyl)-3,4,5,8-tetrahydro-2*H*-chromen-7-yl Ethanoate (28):** The experiment was performed starting from **24** using the same procedure as that described for the preparation of **27**, except that it was carried out in the absence of $SnCl_4$ and the mixture was stirred for 10 h after the addition of *N*-PSP to obtain, after purification, **28** (43%) and **29** (20%) as viscous colourless oils. FTIR: $\tilde{\nu}$ = 2923, 1773, 1731, 1658, 1605, 1366, 1181, 1135, 1110, 1062, 738, 690 cm$^{-1}$. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 1.32 (s, 3 H, 20-H or 21-H), 1.45 (s, 3 H, 21-H or 20-H), 1.55 (s, 3 H, 10-H or 15-H), 1.56 (s, 3 H, 15-H or 10-H), 1.60 (s, 6 H, 11-H, 16-H), 2.21 (s, 3 H, 29-H), 2.32–2.43 (m, 1 H), 2.43–2.56 (m, 1 H), 2.50–2.62 (m, 3 H, 7-H, 12-H, 17-H$^B$), 2.90 (dd, $J$ = 17.2, 5.7 Hz, 1 H, 17-H$^A$), 3.16 (dd, $J$ = 9.4, 5.7 Hz, 1 H, 18-H), 4.78 (tq, $J$ = 9.5, 1.5 Hz, 1 H, 8-H or 13-H), 4.84 (tq, $J$ = 9.2, 1.3 Hz, 1 H, 13-H or 8-H), 7.24–7.31 (m, 3 H, 24-H, 25-H, 26-H), 7.52–7.60 (m, 2 H, 23-H, 27-H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 18.1, 18.2 (C-10, C-15), 21.4 (C-29), 22.7 (C-20 or C-21), 25.2 (C-17), 25.8 (C-11, C-16), 27.6 (C-21 or C-20), 34.9, 35.1 (C-7, C-12), 46.9 (C-18), 50.0 (C-2), 80.7 (C-19), 111.1 (C-6), 117.8 (C-4), 118.0, 118.1 (C-8, C-13), 127.9 (C-25), 129.2 (C-24, C-26), 129.3 (C-22), 134.1, 134.3 (C-9, C-14), 134.7 (C-23, C-27), 162.5 (C-1), 166.5 (C-3), 167.9 (C-28), 186.6 (C-5) ppm. HRMS (ESI): calcd. for $C_{29}H_{36}NaO_4Se$ $[M + Na]^+$ 551.1677; found 551.1636.

**7,7-Bis(3-methylbut-2-enyl)-4-oxo-2-(2-phenylselanyl)propan-2-yl)-2,3,4,7-tetrahydrobenzofuran-6-yl Ethanoate (29):** The experiment was performed using the same procedure as that described for the preparation of **27** to yield **29** (69%) as a viscous colourless oil. FTIR: $\tilde{\nu}$ = 2924, 1764, 1605, 1421, 1366, 1192, 1055, 903 cm$^{-1}$. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 1.32 (s, 3 H), 1.35 (s, 3 H, 20-H, 21-H), 1.52 (s, 3 H), 1.56 (s, 3 H, 10-H, 15-H), 1.65 (s, 3 H), 1.72 (s, 3 H, 11-H, 16-H), 2.20 (s, 3 H, 29-H), 2.69 (dd, $J$ = 17.0, 11.1 Hz, 1 H, 17-H$^B$), 2.93 (dd, $J$ = 17.1, 5.9 Hz, 1 H, 17-H$^A$), 3.07 (t, $J$ = 6.6 Hz, 1 H, 7-H or 12-H), 3.13–3.21 (m, 3 H, 7-H, 12-H), 4.72 (t, $J$ = 9.1 Hz, 1 H, 18-H), 5.06 (tq, $J$ = 7.3, 1.3 Hz, 1 H), 5.09 (tq, $J$ = 7.5, 1.3 Hz, 1 H, 8-H, 13-H), 6.41 (s, 1 H, 4-H), 7.27–7.39 (m, 3 H, 24-H, 25-H, 26-H), 7.55–7.68 (m, 2 H, 23-H, 27-H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 17.8, 19.9 (C-10, C-15), 20.7 (C-29), 20.8 (C-20 or C-21), 23.0 (C-17), 25.7 (C-11, C-16), 27.6 (C-21 or C-20), 29.7 (C-7, C-12), 46.3 (C-19), 48.9 (C-2)*, 78.6 (C-18), 107.7 (C-6), 118.8 (C-4), 119.8, 121.7 (C-8, C-13), 127.8 (C-25), 128.7 (C-22), 129.1 (C-24, C-26), 134.7 (C-9, C-14), 138.3 (C-23, C-27), 168.6 (C-1), 169.1 (C-3), 169.2 (C-28), 185.2 (C-5) ppm; * deduced from HMQC/HMBC experiments. MS (ESI): $m/z$ = 525.1.

**Supporting Information** (see also the footnote on the first page of this article): Structures of the described compounds drawn with the numbering scheme used for the NMR analysis.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