DOI: 10.1002/ejoc.200600389

Transition-Metal-Catalyzed Allylic Substitution and Titanocene-Catalyzed Epoxypolyene Cyclization as a Powerful Tool for the Preparation of Terpenoids

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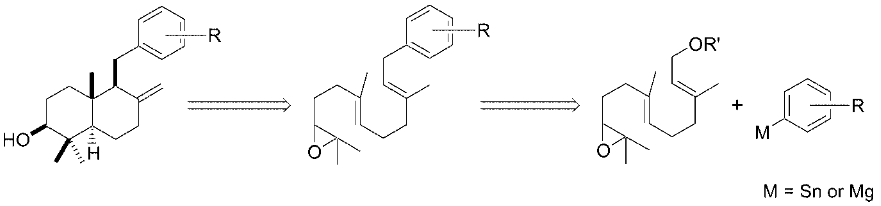
Keywords: Copper / Cyclization / Epoxides / Radicals / Titanium

Many biologically active substances are composed of sesquiterpene units linked to aromatic structures, especially substituted phenols. Here, we describe an efficient synthetic approach to this class of natural product from commercially available substances in a short sequence. The key transformations involve allylic substitution reactions using a palladium or copper catalyst and titanocene-catalyzed epoxypolyene cyclization reactions via radicals. The polycyclic core structures are accessed with high chemo- and stereocontrol.

Introduction

In contemporary natural product synthesis, the use of reactions that generate structurally complex molecules from simple starting materials catalytically and with atom economy in a tandem sequence is rightfully regarded as a most powerful strategy.[1] In this context the radical chemistry originating from titanocene-mediated or -catalyzed epoxide-opening has attracted considerable attention in recent years.[2] Nugent and RajanBabu introduced "Cp_2TiCl" as a mild and highly chemoselective reagent for the reductive opening of epoxides by electron transfer.[3] The first catalytic reaction conditions for mediating the reaction were developed by Gansäuer and co-workers using collidine hydrochloride.[4] This method has been used for enantioselective radical generation and a number of unusual radical reactions, such as a tandem sequence for the preparation of substituted tetrahydrofurans and the efficient synthesis of cyclopropanes.

The chlorotrimethylsilane/2,4,6-collidine-mediated catalytic conditions introduced by Cuerva and Oltra and their co-workers have been used in efficient transannular and epoxypolyene cyclization reactions.[5] In this manner a number of natural products have been efficiently synthesized in very few steps and with high stereoselectivity. This radical reaction has advantages over classical cationic polycyclization reactions[6] because radicals are generated under much milder conditions than cations. Most importantly, the tandem cyclization reaction is terminated by a highly regioselective β-hydride elimination process to yield exocyclic olefins, normally the side-products of biosynthesis. Thus, the incorporation of functional groups to terminate the cyclization reaction is rendered unnecessary.[7] Moreover, numerous functional groups are tolerated in titanocene catalysis.



Scheme 1. Retrosynthetic strategy for the preparation of meroterpenoids.

In this publication we describe a short and highly stereoselective approach to a class of biologically active compounds containing a sesquiterpene unit linked to substituted phenols. Our strategy features the pivotal atom-economical and highly stereoselective titanocene-catalyzed epoxypolyene cyclization reaction.[5b] The necessary starting

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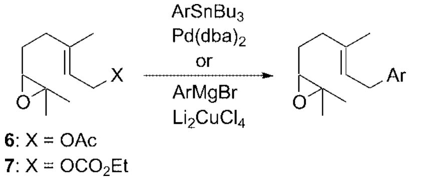
materials can be readily prepared by catalytic allylic substitution reactions.[8,9] The total syntheses of zonarol (**1**) and zonarone (**2**)[10] and the formal total syntheses of umbrosone (**3**),[11] puupehedione (**4**), and 8-*epi*-puupehedione (**5**) [12] were completed. These compounds are important because of their antifungal, antitumor, antiviral, and antibiotic properties. The general strategy is outlined in Scheme 1.

Results and Discussion

Synthesis of the Starting Materials by Allylic Substitution Reactions

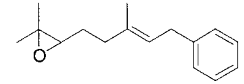
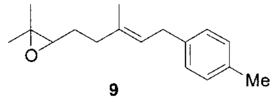
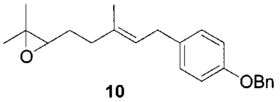
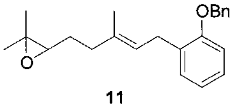
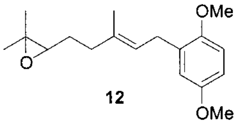
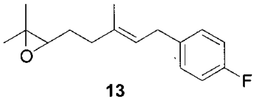
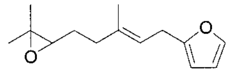
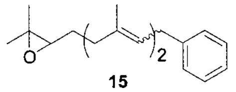
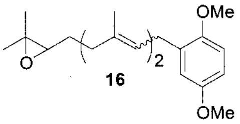
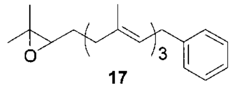
In order to develop an efficient overall synthetic strategy it is mandatory to elaborate simple starting materials into the desired products in a short sequence. Thus, we decided to synthesize arylepoxypolyenes as substrates for the epoxypolyene cyclization reaction from epoxygeranyl and epoxyfarnesyl acetates and carbonates through catalytic allylic substitution reactions with aromatic nucleophiles. For this purpose, palladium-catalyzed reactions, for example, the Stille coupling reaction,[8] and reactions with cuprates[9] seemed especially attractive as both are known to proceed with a high degree of retention of olefin geometry, as shown in Scheme 2.[13]



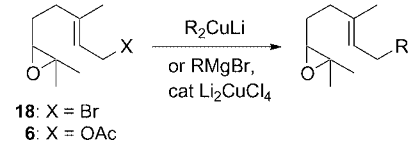
Scheme 2. Allylic substitution reactions for the preparation of epoxypolyenes.

One serious point of concern is immediately apparent, however. It is well documented that epoxides can react with nucleophiles in the presence of Lewis acids to give ring-opened products through nucleophilic substitution reactions. This is especially so for cuprate reagents derived from organolithium compounds or Grignard reagents.[14] Therefore, the essentially neutral conditions of the Stille-type coupling of allylic carbonates and trialkyl(aryl)stannanes developed by Echavarren and co-workers were investigated first.[15] The results are summarized in Table 1.[5c] The Stille coupling yielded the corresponding products with satisfactory yields (62–92%, Table 1). The procedure has two drawbacks, however. Extended reaction times are required and the coupling is limited to aryl- and alkenylstannanes, thereby excluding the preparation of other interesting epoxypolyenes with saturated groups.

Table 1. Products, yields, and reaction times in the palladium-catalyzed synthesis of compounds **8**–**17** from **7**.

Coupling product	Yield	Time
 **8**	92 %	48 h
 **9**	66 %	48 h
 **10**	68 %	48 h
 **11**	70 %	48 h
 **12**	67 %	72 h
 **13**	66 %	72 h
 **14**	62 %	48 h
 **15**	77 %	51 h
 **16**	68 %	120 h
 **17**	66 %	50 h

Encouraged by the stability of the epoxides formed under the Stille coupling conditions, and trying to overcome the drawbacks, we turned our attention to the use of cuprates and the copper-catalyzed coupling reactions of Grignard reagents, as exemplified in Scheme 3.[16]



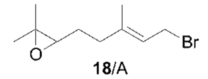
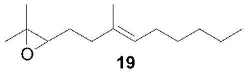
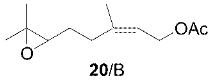
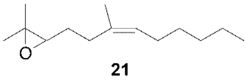
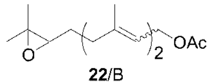
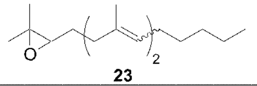
Scheme 3. Synthesis of substrates for epoxypolyen cyclization utilizing organolithium or Grignard reagents.

We investigated the ability of the highly reactive epoxygeranyl bromide (**18**) to retard the anticipated epoxide opening and used Bu_2CuLi to increase the range of nucleophiles to alkyl groups. The desired **19** was obtained in good yield (75%) and with high diastereoselectivity. No allylic isomer was observed. This finding was even surpassed when the stable and readily available epoxygeranyl acetate (**6**) was employed as the substrate. Epoxy olefin **19** was obtained in 79% yield as essentially a single isomer (*dr* > 98:2) with no products arising from epoxide opening. Thus, even relatively unreactive allylic acetates are more reactive towards cuprates than epoxides. Gratifyingly, the Li_2CuCl_4-catalyzed (4–5 mol-%) substitution reaction of BuMgBr also gave the desired **19** in good yield and high diastereoselectivity. This result is even more surprising as in the presence of copper salts, Grignard reagents open epoxides even more swiftly than dialkylcuprates.[14] The reaction also gave satisfactory results on a larger scale (10 mmol). With **20** a 79% yield of **21** as a single isomer was obtained, while epoxyfarnesyl acetate (**22**) gave an almost quantitative yield of the coupling product. These results are summarized in Table 2.

From a practical point of view Li_2CuCl_4 catalysis is more convenient as no large excess of the organometallic reagent has to be used and Grignard reagents are easier to prepare than the corresponding organolithium compounds.

Using these reaction conditions we synthesized a number of epoxy olefins containing different and functionalized alkyl and benzyl substituents from **6** and **22**, as shown in Table 3.

Table 2. Products and yields from the synthesis of compounds **19**, **21**, and **23** from cuprates and Grignard reagents.

Substrate/method[a]	Product	Yield
 **18**/A	 **19**	75 %
6/A	**19**	79 %
6/B	**19**	72 %
 **20**/B	 **21**	79 %
 **22**/B	 **23**	90 %

[a] See the Exp. Sect. for Methods A and B.

Table 3. Li_2CuCl_4-catalyzed transfer of alkyl and benzyl Grignard reagents to **6** and **22**.

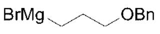
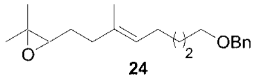
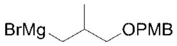
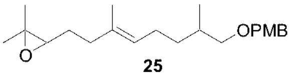
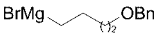
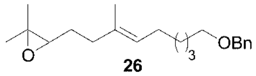
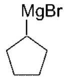
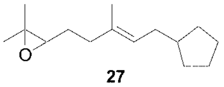
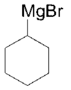
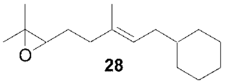
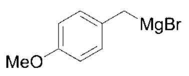
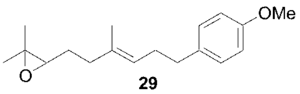
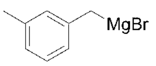
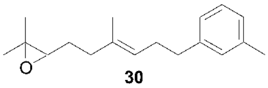
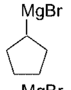
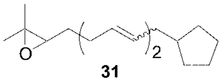
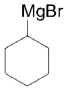
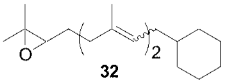
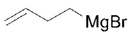
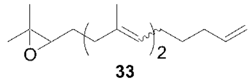
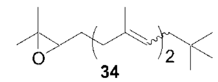
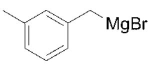
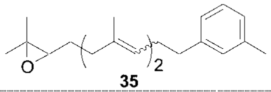
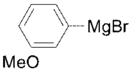
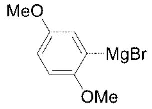
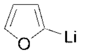
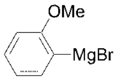
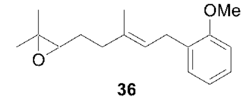
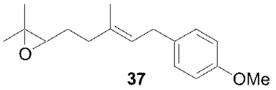
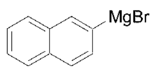
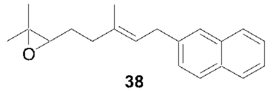
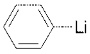
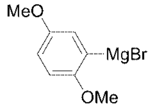
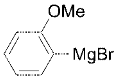
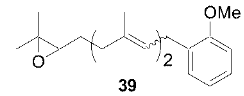
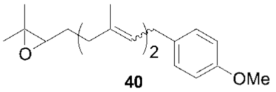
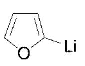
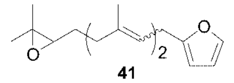
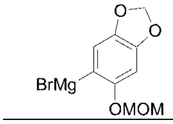
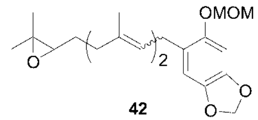
Grignard reagent	Product	Yield
	 **24**	70 %
	 **25**	74 %
	 **26**	73 %
	 **27**	61 %
	 **28**	63 %
	 **29**	68 %
	 **30**	54 %
	 **31**	65 %
	 **32**	66 %
	 **33**	62 %
	 **34**	79 %
	 **35**	48 %

Table 4. Copper-mediated or Li_2CuCl_4-catalyzed transfer of aryl groups to **6** and **22** from cuprates and Grignard reagents.

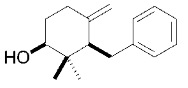
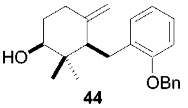
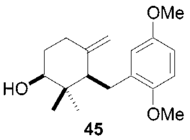
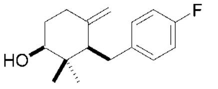
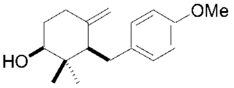
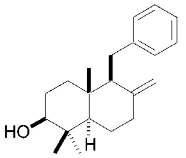
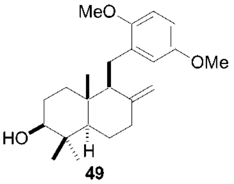
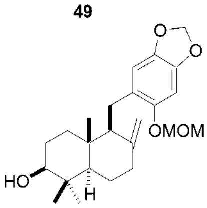
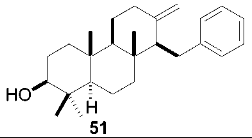
Grignard reagent	Product	Yield
	**8**	83 %
	**12**	68 %
	**14**	68 %[a]
	 **36**	69 %
	 **37**	68 %
	 **38**	76 %
	**15**	47 %[a]
	**16**	66 %
	 **39**	61 %
	 **40**	59 %
	 **41**	62 %[a]
	 **42**	60 %

[a] Method A was used, see Exp. Sect.

The reaction proceeded smoothly in all cases. Only during the synthesis of **24** were small amounts of the allylic isomer observed which could be removed by column chromatography. The ether-substituted products are valuable intermediates for the synthesis of spirodihydrofuranolactams from *Stachybotry chartarum*,[17] for example, stachybotrylactam.[18]

Finally, the transfer of aryl groups was also investigated (Table 4). It turned out that the reaction of **6** with PhMgBr catalyzed by Li_2CuCl_4 (4–5 mol-%) gave **8** in a yield and diastereoselectivity (83%, *dr* > 97:3) very similar to the Stille reaction without producing toxic stannane waste.

Table 5. Cp_2TiCl-catalyzed cyclization of epoxypolyenes (see Exp. Sect. for details).

Epoxide	Product	Yield
8	 **43**	50 %
10	 **44**	48 %
12	 **45**	43 %
13	 **46**	42 %
37	 **47**	60 %
15	 **48**	40 %
16	 **49**	46 %
42	 **50**	41 %
17	 **51**	35 %

This is a general observation, as similar or better yields were obtained with Li_2CuCl_4 in all cases. This protocol is therefore more practical. Moreover, the stannanes necessary for the Stille coupling reaction are usually prepared from either organolithium compounds or Grignard reagents in an additional step.[5c] However, owing to the mildness of the Stille protocol, no basic organometallic reagents are used during coupling, and therefore we recommend its use in the coupling reactions of epoxypolyene carbonates containing sensitive groups, such as alcohols or carbonyl groups.

Titanocene-Catalyzed Epoxypolyene Cyclization Reactions

Titanocene(III)-catalyzed cyclization reactions of epoxypolyenes have recently been developed as a unique tool in natural product synthesis, taking advantage of the particular behavior of the radical intermediates involved.[2d]

We found that a substoichiometric quantity of commercial Cp_2TiCl_2 (20 mol-%), Mn dust, and Me_3SiCl/2,4,6-collidine in dry THF at room temperature are the best reaction conditions for carrying out epoxypolyene cyclization reactions yielding the corresponding terpenoid carbocycles. One of the main features of this transformation is the termination of the process by the regioselective formation of an exocyclic olefin through a β-hydride elimination process. This clearly has advantages over the cationic reactions in which mixtures of olefins are usually obtained. Moreover, these cyclization reactions proceed with high stereoselectivity giving only one of the many possible stereoisomers. A number of pertinent examples of titanocene-catalyzed epoxypolyene cyclization reactions are summarized in Table 5.

Another important feature of the application of the titanocene-catalyzed protocol to natural product synthesis is related to the inertness of aromatic rings as radical traps under our conditions. Thus, as opposed to cationic processes, the arenes, including strongly activated aromatic compounds, remain intact after the radical cyclization. Therefore, the cyclization products can be converted into valuable key intermediates for natural product synthesis under very mild conditions, as exemplified below.

Total and Formal Syntheses of Natural Products

Exocyclic olefins are present in a number of pertinent natural products. Thus, some of the cyclization products can readily be further elaborated into natural products or key intermediates for their synthesis. This specific advantage results in overall sequences much shorter than syntheses reported to date.

As pointed out above, the epoxide's stereocenter is an essential and highly beneficial control element for the highly stereoselective formation of all the other stereocenters of the cyclization products. Gratifyingly, the resulting hydroxy group is also present in a large number of natural products. Besides this obvious usefulness, our cyclization products can, after deoxygenation, be readily employed in the preparation of a large number of natural compounds containing the reduced decalin structure.

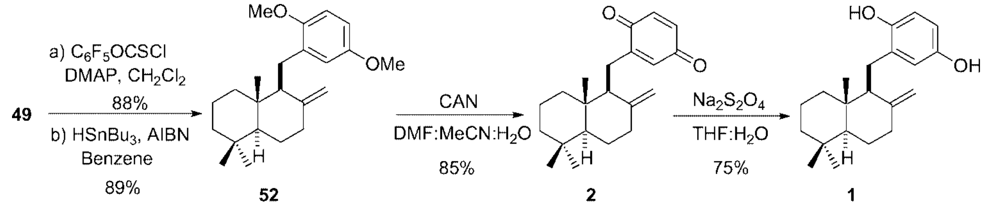
Both of these points are demonstrated by the very short preparation of zonarone (**2**) and zonarol (**1**) from **49**, as depicted in Scheme 4. Both natural products possess interesting antifungal properties.[10]

After the high-yielding Barton–McCombie deoxygenation[19] of **49** (79% over two steps) zonarone (**2**) was obtained by oxidation of the arene with CAN in 85% yield. Reduction of **2** by $Na_2S_2O_4$ yields zonarol (**1**) in 75% yield. Thus, starting from epoxyfarnesyl acetate (**22**), zonarone (**2**) and zonarol (**1**) can be prepared in just four or five steps, respectively. The previously described syntheses require significantly more steps.[20] Direct demethylation of **52** with acids or Lewis acids was not attempted to avoid suspected benzodihydropyran formation.

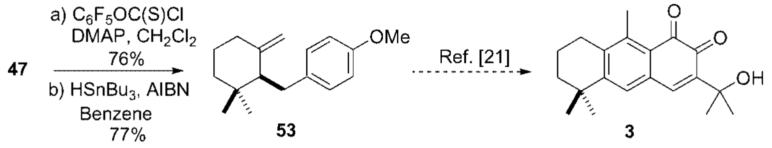
A very short synthesis of the key intermediate **53** in the synthesis of umbrosone (**3**) by Ghatak[21] can be accomplished in an overall yield of 35% by the titanocene-catalyzed epoxypolyene cyclization of **37** followed by deoxygenation according to the Barton–McCombie protocol, as depicted in Scheme 5. As the configuration of the only stereocenter remaining in **53** is controlled by the absolute configuration of **47**, our method offers a straightforward approach to enantiomerically pure **3** from enantiomerically pure epoxygeranyl acetate (**6**).

The presence of the exocyclic olefin in the cyclization products is also of paramount interest for the further functionalization of the epoxypolyene cyclization products. In this respect the formation of cyclic ethers, such as benzodihydropyrans, by the addition of phenolic hydroxy groups to the double bond is of special relevance. This heterocyclic element is present in a number of important natural products, such as taondiol, K-76, kampanol A, puupehedione, and its unnatural 8-epimer, and is therefore of some interest.[5c]

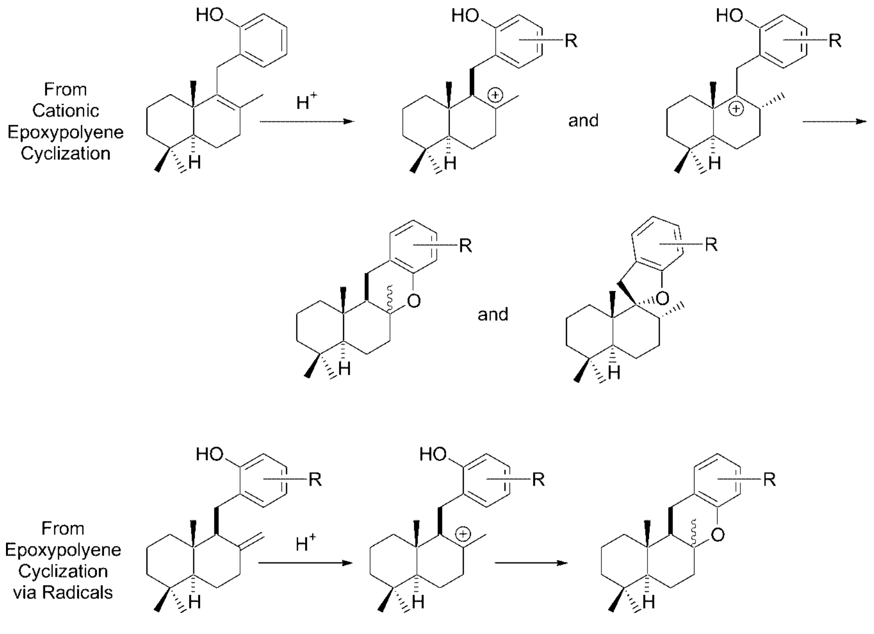
Our epoxypolyene cyclization approach offers a straightforward solution to the existing problems of the regio- and



Scheme 4. Preparation of zonarone (**2**) and zonarol (**1**) from **49**.



Scheme 5. Preparation of the key intermediate **53** in Ghatak's synthesis of umbrosone (**3**).



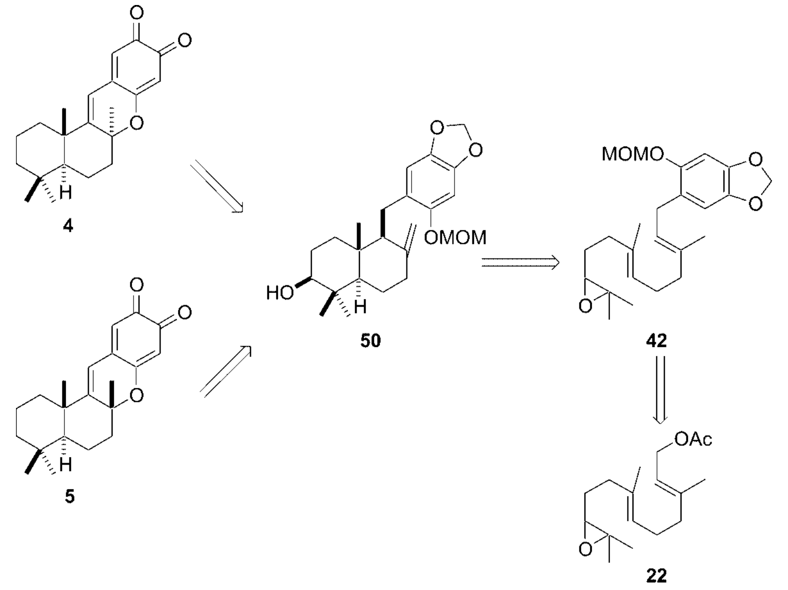
Scheme 6. Regioselective benzodihydropyran synthesis from epoxypolyene cyclization products.

stereoselectivity of benzodihydropyran synthesis. With the endocyclic olefins obtained from cationic cyclization reactions or natural sources, selective generation of the desired tertiary cation is difficult to achieve and thus mixtures of benzodihydropyrans and furans are usually obtained. With our compounds, upon addition of a proton or other electrophiles, only the tertiary cation is generated, and thus ether synthesis is expected to occur with high regioselectivity, as shown in Scheme 6.

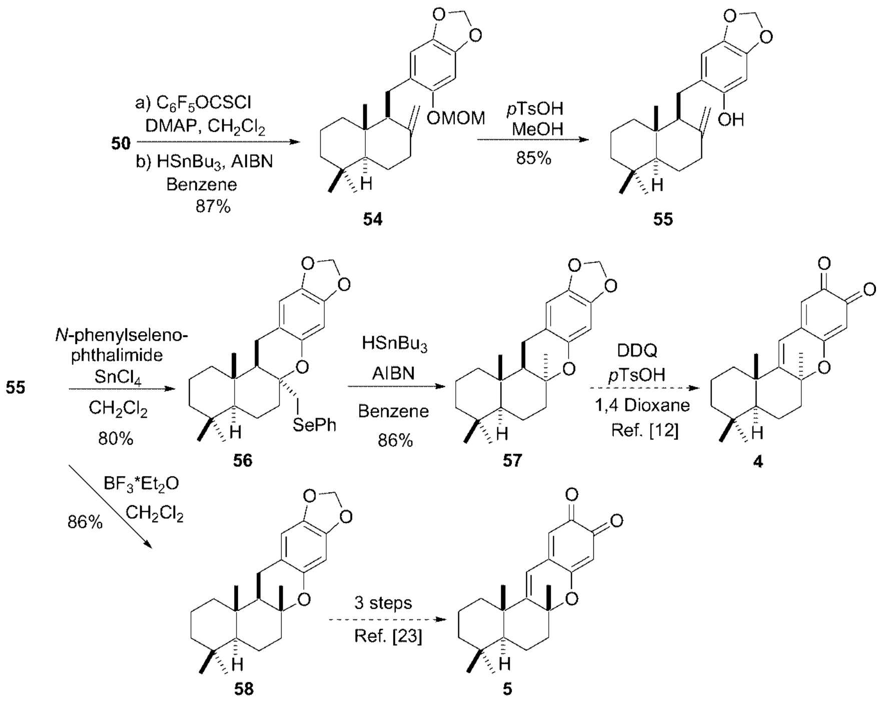
We have chosen puupehedione (**4**) and its 8-epimer (**5**) to demonstrate the validity of our approach. Both **4** and **5** are pertinent for their antitumor, antiviral, and antibiotic activity.[12] Interestingly, the unnatural **5** is the more potent compound and is therefore an interesting target for synthetic studies.

The key feature of our synthetic approach is the use of the cyclization product **50** as a common intermediate for the preparation of both **4** and **5**, as shown in Scheme 7.

To this end, **50** was deoxygenated in two steps using the Barton–McCombie conditions[19] described above to give **54** in high yield. Cleavage of the OMOM group proceeded smoothly using *p*TsOH in MeOH. Phenol **55** thus obtained was then selectively converted into either of the epimeric benzodihydropyrans, as shown in Scheme 8, by varying the



Scheme 7. Retrosynthetic strategy for the preparation of puupehedione (**4**) and its 8-epimer **5** from **50**.



Scheme 8. Completion of the formal syntheses of **4** and **5**.

electrophilic reagent for attack on the exocyclic double bond.

It turned out that the protocol described by Katoh and co-workers[22] for the synthesis of kampanol A [*N*-(phenylseleno)phthalimide, $SnCl_4$, followed by reduction of the selenide with Bu_3SnH] yielded **57** in good overall yield (69%), completing the formal synthesis of puupehedione (**4**). From a 1:3 mixture of **57** and **58**, **4** was obtained by Barrero et al. by oxidation with DDQ and *p*TsOH in 1,4-dioxane.[12b]

From a mixture of isomers of **58** (*dr* = 73:27), 8-*epi*-puupehedione (**5**) was synthesized by Yamamoto and co-workers in three steps [DDQ, 1,4-dioxane; $B(C_6F_5)_3$, Et_3SiH; DDQ, 1,4-dioxane, H_2O] and an overall yield of 91%.[23]

Conclusions

We have devised a short and efficient approach to a number of natural products and biologically active substances containing sesquiterpenes linked to arenes, especially phenols. Our strategy relies on allylic substitution reactions employing stannanes, Grignard reagents, or cuprates and titanocene-catalyzed epoxypolyene cyclization reactions as the key transformations. These reactions proceed under mild conditions and with high stereo- and chemoselectivity. The products obtained by this route are valuable intermediates for organic synthesis, as demonstrated by short and efficient syntheses and formal syntheses of a number of natural products.

Experimental Section

General Remarks: All reactions were performed in oven-dried (100 °C) glassware under Ar. THF was freshly distilled from K, Et_2O from Na/K, while CH_2Cl_2, MeOH, and benzene were freshly distilled from CaH_2. The products were purified by flash chromatography on Merck silica gel 50 (eluents are given in parentheses, EA refers to ethyl acetate, CH to cyclohexane). Yields refer to analytically pure samples. Isomer ratios were determined by suitable ^1H NMR integrals of cleanly separated signals. NMR: Bruker AMX 300 and AM 400 spectrometers. ^1H NMR: $CHCl_3$ (δ = 7.26 ppm) in the indicated solvent as internal standard in the same solvent. ^{13}C NMR: $CDCl_3$ (δ =77.16 ppm) as internal standard in the same solvent; integrals in agreement with assignments, coupling constants are measured in Hz and are always given as *J*(H,H) coupling constants. An asterisk (*) indicates the signal of the (*Z*,*E*) isomer. IR spectra: Perkin-Elmer 1600 series FTIR spectrometer as neat films on KBr plates. Farnesol was bought from Aldrich in the form of a mixture of stereoisomers containing 50% of the all-(*E*) isomer (GC-MS analysis with an authentic sample as standard).[5b,24] Geranylgeraniol was obtained from the plant *Bellardia trixago*[5b] as an (*E*,*E*,*E*) isomer. The epoxy acetates **6**,[5b] **7**,[5c] **20**,[5b] and **22**[5b] were prepared according to known procedures. Compounds **8**–**13**, **15**–**17**, **43**–**46**, **48**, **49**, and **51** have been described previously.[5c]

General Procedure for Cu-Catalyzed Coupling. Method A: The lithiated compound (2–4 mmol) was added to a solution of CuI (1–2 mmol) in Et_2O at –30 °C and the mixture was stirred at this temperature for 30 min. Then a solution of epoxypolyene (0.5–1 mmol) was added and the new mixture was stirred at room temp. overnight. Satd. aq. NH_4Cl was added and the mixture was extracted with EtOAc, the extract dried with $MgSO_4$, and the solvent removed. The residue was purified by flash chromatography (mixtures of CH/EA) to yield the coupling product. **Method B:** A 0.1 M solution of Li_2CuCl_4 in THF (0.04 mmol) was added dropwise to a solution of epoxypolyene (1 mmol) in THF (9 mL) at 0 °C. Then a solution of Grignard reagent (2–4 mmol) was added dropwise over 20 min. The mixture was stirred at 0 °C for 3 h and then at room temp. overnight. Satd. aq. NH_4Cl was added and the mixture was extracted with EtOAc, the extract dried with $MgSO_4$, and the solvent removed. The residue was purified by flash chromatography (mixtures of CH/EA) to yield the coupling product.

Compound 14: Yield 110 mg, 68% from **6** (0.74 mmol) by Method A; CH/EA, 9:1; colorless oil. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.22 (d, *J* = 1.2 Hz, 1 H), 6.27 (dd, *J* = 3.1, 1.2 Hz, 1 H), 5.96 (dd, *J* = 3.1, 0.9 Hz, 1 H), 5.38 (tq, *J* = 7.1, 1.2 Hz, 1 H), 3.35 (d, *J* = 7.1 Hz, 2 H), 2.70 (t, *J* = 6.2 Hz, 1 H), 2.28–2.19 (m, 2 H), 1.70 (s, 3 H), 1.69–1.63 (m, 2 H), 1.28 (s, 3 H), 1.25 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.14 (C), 141.08 (CH), 136.76 (C), 120.14 (CH), 110.29 (CH), 104.86 (CH), 64.19 (CH), 58.44 (C), 36.39 (CH_2), 27.45 (CH_2), 27.14 (CH_2), 24.96 (CH_3), 18.86 (CH_3), 16.22 (CH_3) ppm. HRMS (70 eV): calcd. for $C_{14}H_{20}O_2$ $[M]^+$ 220.1463; found 220.1460. IR (neat): $\tilde{\nu}$ = 3379, 2924, 1719, 1455, 1377, 1257, 1012, 883 cm^{-1}.

Compound 19: Yield 119 mg, 75% from **18** (0.75 mmol) and 670 mg, 79% from **6** (4.0 mmol) by Method A; 1520 mg, 72% from **6** (10 mmol) by Method B; CH/EA, 97:3; colorless oil. ^1H NMR (400 MHz, $CDCl_3$): δ = 5.17 (t, *J* = 7.0 Hz, 1 H), 2.69 (t, *J* = 6.3 Hz, 1 H), 2.04–2.19 (m, 2 H), 1.97 (q, *J* = 7.0 Hz, 2 H), 1.70–1.54 (m, 2 H), 1.60 (s, 3 H), 1.25–1.36 (m, 6 H), 1.29 (s, 3 H), 1.25 (s, 3 H), 0.88 (t, *J* = 6.9 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 133.93 (C), 125.65 (CH), 64.38 (CH), 58.41 (C), 36.57 (CH_2), 31.72 (CH_2), 29.64 (CH_2), 28.02 (CH_2), 27.69 (CH_2), 25.05 (CH_3), 22.73 (CH_2), 18.92 (CH_3), 16.11 (CH_3), 14.28 (CH_3) ppm. HRMS (70 eV): calcd. for $C_{14}H_{26}O$ $[M]^+$ 210.1984; found 210.1986. IR (neat): $\tilde{\nu}$ = 2925, 1460, 1375, 1120 cm^{-1}.

Compound 21: Yield 78 mg, 79% from **20** (0.47 mmol) by Method B; CH/EA, 97:3; colorless oil. ^1H NMR (400 MHz, $CDCl_3$): δ = 5.16 (t, *J* = 7.1 Hz, 1 H), 2.70 (t, *J* = 6.4 Hz, 1 H), 2.20–2.05 (m, 2 H), 1.97 (q, *J* = 6.9 Hz, 2 H), 1.69 (s, 3 H), 1.50–1.65 (m, 2 H), 1.25–1.34 (m, 6 H), 1.29 (s, 3 H), 1.26 (s, 3 H), 0.81 (t, *J* = 6.9 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 133.97 (C), 126.46 (CH), 64.25 (CH), 58.43 (C), 31.74 (CH_2), 29.84 (CH_2), 28.61 (CH_2), 27.95 (CH_2), 27.58 (CH_2), 25.03 (CH_3), 23.44 (CH_3), 22.74 (CH_2), 18.82 (CH_3), 14.17 (CH_3) ppm. HRMS (70 eV): calcd. for $C_{14}H_{26}O$ $[M]^+$ 210.1984; found 210.1985. IR (neat): $\tilde{\nu}$ = 2960, 2925, 2855, 1460, 1375, 1120, 865 cm^{-1}.

Compound 23: Yield 92 mg, 90% from **22** (0.35 mmol) by Method B as a 1:1 mixture of (*E*,*E*) and (*Z*,*E*) isomers; CH/EA, 97:3; colorless oil. ^1H NMR (400 MHz, $CDCl_3$): δ = 5.20–5.05 (m, 2 H), 2.69 (dd, *J* = 12.4, 6.2 Hz, 1 H), 2.68 (t, *J* = 6.2 Hz, 1 H), 2.20–2.00 (m, 4 H), 1.96 (quintuplet, *J* = 6.7 Hz, 4 H), 1.68 (m, 2 H), 1.60 (s, 6 H), 1.58 (s, 6 H), 1.35–1.20 (m, 6 H), 1.29* (s, 3 H), 1.28 (s, 3 H), 1.26* (s, 3 H), 1.24 (s, 3 H), 0.87 (t, *J* = 7.0 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 134.65 (C), 134.58 (C), 134.09 (C), 134.06 (C), 125.90 (CH), 125.87 (CH), 125.17 (CH), 125.07 (CH), 64.29 (CH), 64.22 (CH), 58.36 (C), 58.34 (C), 40.03 (CH_2), 39.78 (CH_2), 36.44 (CH_2), 31.98 (CH_2), 31.68 (CH_2), 31.65 (CH_2), 29.67 (CH_2), 29.65 (CH_2), 28.01 (CH_2), 27.99 (CH_2), 27.62 (CH_2), 27.58 (CH_2), 26.74 (CH_2), 26.62 (CH_2), 25.03 (CH_3), 25.00 (CH_3), 23.49

(CH$_3$), 23.42 (CH$_3$), 22.74 (CH$_2$), 22.72 (CH$_2$), 18.85 (CH$_3$), 18.81 (CH$_3$), 16.11 (CH$_3$), 16.06 (CH$_3$), 14.19 (CH$_3$), 14.18 (CH$_3$) ppm. HRMS (70 eV): calcd. for $C_{19}H_{34}O$ [M]$^+$ 278.2610; found 278.2600. IR (neat): $\tilde{\nu}$ = 2923, 1458, 1378, 1248, 1120, 864 cm^{-1}.

Compound 24: Yield 123 mg, 70% from **6** (0.72 mmol); CH/EA, 95:5; colorless oil. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 7.34–7.30 (m, 4 H), 7.29–7.21 (m, 1 H), 5.16 (tq, J = 7.1, 1.2 Hz, 1 H), 4.48 (s, 2 H), 3.45 (t, J = 6.6 Hz, 2 H), 2.68 (t, J = 6.2 Hz, 1 H), 2.20–2.05 (m, 2 H), 1.99 (dd, J = 14.7, 7.4 Hz, 2 H), 1.73–1.60 (m, 3 H), 1.59 (s, 3 H), 1.47–1.35 (m, 3 H), 1.28 (s, 3 H), 1.24 (s, 3 H) ppm. ^{13}C NMR (75 MHz, CDCl$_3$): δ = 138.81 (C), 134.32 (C), 128.42 (CH), 127.68 (CH), 127.55 (CH), 125.15 (CH), 72.98 (CH$_2$), 70.47 (CH$_2$), 64.27 (CH), 58.35 (C), 36.45 (CH$_2$), 29.51 (CH$_2$), 27.81 (CH$_2$), 27.56 (CH$_2$), 26.46 (CH$_2$), 24.99 (CH$_3$), 18.85 (CH$_3$), 16.08 (CH$_3$) ppm. HRMS (70 eV): calcd. for $C_{20}H_{30}O_2$ [M]$^+$ 302.2246; found 302.2249. IR (neat): $\tilde{\nu}$ = 1613, 1586, 1513, 1462, 1377, 1301, 1247, 1172, 1094, 1036, 820 cm^{-1}. $C_{20}H_{30}O_2$ (302.22): calcd. C 79.42, H 10.00; found C 79.21, H 10.09.

Compound 25: Yield 93 mg, 74% from **6** (0.37 mmol); CH/EA, 96:4; colorless oil. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.23 (d, J = 8.7 Hz, 2 H), 6.85 (d, J = 8.7 Hz, 2 H), 5.15 (tq, J = 7.0, 1.1 Hz, 1 H), 4.40 (s, 2 H), 3.78 (s, 3 H), 3.28 (dd, J = 9.1, 6.7 Hz, 1 H), 3.20 (dd, J = 9.1, 6.7 Hz, 1 H), 2.68 (t, J = 6.2 Hz, 1 H), 2.19–1.80 (m, 4 H), 1.80–1.60 (m, 3 H), 1.59 (s, 3 H), 1.50–1.42 (m, 1 H), 1.28 (s, 3 H), 1.24 (s, 3 H), 1.19–1.15 (m, 1 H), 0.91 (d, J = 6.7 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ = 159.19 (C), 134.03 (C), 131.04 (C), 129.18 (CH), 125.33 (CH), 113.84 (CH), 75.73 (CH$_2$), 72.75 (CH$_2$), 64.28 (CH), 58.37 (C), 55.35 (CH$_3$), 36.44 (CH$_2$), 33.82 (CH$_2$), 33.23 (CH), 27.57 (CH$_2$), 25.47 (CH$_2$), 24.98 (CH$_3$), 18.86 (CH$_3$), 17.22 (CH$_3$), 16.06 (CH$_3$) ppm. HRMS (70 eV): calcd. for $C_{22}H_{34}O_2$ [M]$^+$ 346.2508; found 346.2525. IR (neat): $\tilde{\nu}$ = 2957, 1613, 1513, 1462, 1377, 1301, 1247, 1172, 1095, 820 cm^{-1}.

Compound 26: Yield 119 mg, 73% from **6** (0.52 mmol); CH/EA, 95:5; colorless oil. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.33–7.30 (m, 4 H), 7.28–7.23 (m, 1 H), 5.16 (tq, J = 7.1, 1.2 Hz, 1 H), 4.48 (s, 2 H), 3.45 (t, J = 6.6 Hz, 2 H), 2.68 (t, J = 6.2 Hz, 1 H), 2.19–2.03 (m, 2 H), 1.98 (dd, J = 13.4, 6.7 Hz, 2 H), 1.72–1.61 (m, 4 H), 1.74 (s, 3 H), 1.38–1.33 (m, 4 H), 1.28 (s, 3 H), 1.24 (s, 3 H) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ = 138.82 (C), 134.10 (C), 128.40 (CH), 127.67 (CH), 127.53 (CH), 125.32 (CH), 72.95 (CH$_2$), 70.54 (CH$_2$), 64.26 (CH), 58.34 (C), 36.44 (CH$_2$), 29.79 (CH$_2$), 29.73 (CH$_2$), 27.97 (CH$_2$), 27.55 (CH$_2$), 25.99 (CH$_2$), 24.98 (CH$_3$), 18.84 (CH$_3$), 16.05 (CH$_3$) ppm. HRMS (70 eV): calcd. for $C_{21}H_{32}O_2$ [M]$^+$ 316.2402; found 316.2401. IR (neat): $\tilde{\nu}$ = 1495, 1454, 1377, 1249, 1204, 1104, 1027, 901, 873, 735, 697 cm^{-1}.

Compound 27: Yield 67 mg, 61% from **6** (0.50 mmol); CH/EA, 92:8; colorless oil. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 5.38 (tq, J = 7.2, 1.3 Hz, 1 H), 2.70 (t, J = 6.2 Hz, 1 H), 2.23–2.09 (m, 2 H), 1.99 (t, J = 6.9 Hz, 2 H), 1.88–1.63 (m, 5 H), 1.61 (s, 3 H), 1.59–1.42 (m, 4 H), 1.29 (s, 3 H), 1.26 (s, 3 H), 1.20–1.08 (m, 2 H) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ = 134.08 (C), 124.95 (CH), 64.35 (CH), 58.44 (C), 40.63 (CH), 36.60 (CH$_2$), 34.21 (CH$_2$), 32.48 (CH$_2$), 32.46 (CH$_2$), 27.64 (CH$_2$), 25.28 (CH$_2$), 25.05 (CH$_3$), 18.89 (CH$_3$), 16.23 (CH$_3$) ppm. HRMS (70 eV): calcd. for $C_{15}H_{26}O$ [M]$^+$ 222.1984; found 222.1985. IR (neat): $\tilde{\nu}$ = 2951, 1451, 1377, 1121, 872 cm^{-1}.

Compound 28: Yield 68 mg, 63% from **6** (0.46 mmol); CH/EA, 9:1; colorless oil. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 5.20 (tq, J = 7.3, 1.2 Hz, 1 H), 2.70 (t, J = 6.3 Hz, 1 H), 2.21–1.98 (m, 2 H), 1.87 (t, J = 6.9 Hz, 2 H), 1.75–1.61 (m, 6 H), 1.60 (s, 3 H), 1.29 (s, 3 H), 1.26 (s, 3 H), 1.25–0.85 (m, 7 H) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ = 134.54 (C), 124.18 (CH), 64.37 (CH), 58.44 (C), 43.64 (CH), 36.65 (CH$_2$), 35.94 (CH$_2$), 33.38 (CH$_2$), 30.35 (CH$_2$), 27.66 (CH$_2$), 27.07 (CH$_2$), 26.80 (CH$_2$), 26.57 (CH$_2$), 25.04 (CH$_3$), 18.90 (CH$_3$), 16.23 (CH$_3$) ppm. HRMS (70 eV): calcd. for $C_{16}H_{28}O$ [M]$^+$ 236.2140; found 236.2145. IR (neat): $\tilde{\nu}$ = 2921, 2849, 1447, 1375, 1124, 880 cm^{-1}.

Compound 29: Yield 124 mg, 68% from **6** (0.67 mmol); CH/EA, 97:3; colorless oil. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.10 (d, J = 8.8 Hz, 2 H), 6.81 (d, J = 8.8 Hz, 2 H), 5.22 (t, J = 7.0 Hz, 1 H), 3.78 (s, 3 H), 2.69 (t, J = 6.2 Hz, 1 H), 2.60 (d, J = 7.3 Hz, 1 H), 2.58 (d, J = 6.9 Hz, 1 H), 2.28 (q, J = 7.7 Hz, 2 H), 2.20–2.00 (m, 2 H), 1.68–1.59 (m, 2 H), 1.57 (s, 3 H), 1.30 (s, 3 H), 1.26 (s, 3 H) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ = 157.88 (C), 134.91 (C), 134.50 (C), 129.44 (CH), 124.45 (CH), 113.82 (CH), 64.27 (CH), 58.40 (C), 55.38 (CH$_3$), 36.44 (CH$_2$), 35.24 (CH$_2$), 30.27 (CH$_2$), 27.60 (CH$_2$), 25.02 (CH$_3$), 18.87 (CH$_3$), 16.11 (CH$_3$) ppm. HRMS (70 eV): calcd. for $C_{18}H_{26}O_2$ [M]$^+$ 274.1933; found 274.1935. IR (neat): $\tilde{\nu}$ = 2922, 1456, 1377, 782 cm^{-1}. $C_{18}H_{26}O_2$ (274.19): calcd. C 78.79, H 9.55; found C 78.64, H 9.57.

Compound 30: Yield 125 mg, 54% from **6** (0.9 mmol); CH/EA, 97:3; colorless oil. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 7.20–6.90 (m, 4 H), 5.24 (t, J = 7.1 Hz, 1 H), 2.69 (t, J = 6.2 Hz, 1 H), 2.60 (dd, J = 8.3, 7.5 Hz, 2 H), 2.33, (s, 3 H), 2.30–2.00 (m, 4 H), 1.73–1.61 (m, 2 H), 1.59, (s, 3 H), 1.30 (s, 3 H), 1.26 (s, 3 H) ppm. ^{13}C NMR (75 MHz, CDCl$_3$): δ = 142.34 (C), 137.88 (C), 134.93 (C), 129.40 (CH), 128.28 (CH), 126.59 (CH), 125.57 (CH), 124.50 (CH), 64.29 (CH), 58.41 (C), 36.46 (CH$_2$), 36.12 (CH$_2$), 30.10 (CH$_2$), 27.63 (CH$_2$), 25.03 (CH$_3$), 21.54 (CH$_3$), 18.88 (CH$_3$), 16.12 (CH$_3$) ppm. HRMS (70 eV): calcd. for $C_{18}H_{26}O$ [M]$^+$ 258.1984; found 258.1984. IR (neat): $\tilde{\nu}$ = 2922, 1377, 780 cm^{-1}. $C_{18}H_{26}O$ (258.19): calcd. C 83.62, H 10.14; found C 83.15, H 10.05.

Compound 31: Yield 95 mg, 65% from **22** (0.50 mmol) as a 1:1 mixture of (*E*,*E*) and (*Z*,*E*) isomers; CH/EA, 96:4; colorless oil. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 5.33–5.21 (m, 2 H), 2.55 (t, J = 6.2 Hz, 1 H), 2.22–2.00 (m, 10 H), 1.85–1.62 (m, 6 H), 1.60* (s, 3 H), 1.59 (s, 3 H), 1.55* (s, 3 H), 1.54 (s, 3 H), 1.52–1.44 (m, 2 H), 1.14 (s, 3 H), 1.11* (s, 3 H), 1.10 (s, 3 H) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ = 134.98 (C), 134.78 (C), 134.27 (C), 134.07 (C), 125.93 (CH), 125.08 (CH), 124.49 (CH), 124.40 (CH), 64.31 (CH), 64.24 (CH), 58.41 (C), 58.36 (C), 46.46 (CH$_2$), 40.70 (CH), 40.65 (CH), 40.12 (CH$_2$), 39.87 (CH$_2$), 34.16 (CH$_2$), 34.13 (CH$_2$), 32.43 (CH$_2$), 32.41 (CH$_2$), 32.06 (CH$_2$), 31.94 (CH$_2$), 27.63 (CH$_2$), 27.59 (CH$_2$), 26.75 (CH$_2$), 26.63 (CH$_2$), 25.49 (CH$_2$), 25.27 (CH$_2$), 25.04 (CH$_3$), 25.02 (CH$_3$), 23.56 (CH$_3$), 23.44 (CH$_3$), 18.86 (CH$_3$), 18.83 (CH$_3$), 16.21 (CH$_3$), 16.15 (CH$_3$) ppm. HRMS (70 eV): calcd. for $C_{20}H_{34}O$ [M]$^+$ 290.2610; found 290.2618. IR (neat): $\tilde{\nu}$ = 2951, 1449, 1377, 1247, 1211, 871, 680 cm^{-1}.

Compound 32: Yield 92 mg, 66% from **22** (0.46 mmol) as a 1:1 mixture of (*E*,*E*) and (*Z*,*E*) isomers; CH/EA, 9:1; colorless oil. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 5.21–5.09 (m, 2 H), 2.70* (t, J = 6.4 Hz, 1 H), 2.69 (t, J = 6.4 Hz, 1 H), 2.21–1.97 (m, 6 H), 1.69* (s, 3 H), 1.68 (s, 3 H) 1.66–1.64 (m, 2 H), 1.63* (s, 3 H), 1.61 (s, 3 H), 1.59–1.54 (m, 2 H), 1.30* (s, 3 H), 1.29 (s, 3 H), 1.27* (s, 3 H), 1.25 (s, 3 H), 1.23–0.82 (m, 11 H) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ = 135.24 (C), 135.14 (C), 134.11 (C), 134.08 (C), 125.11 (CH), 125.08 (CH), 123.75 (CH), 123.64 (CH), 64.33 (CH), 64.25 (CH), 58.43 (C), 58.37 (C), 43.62 (CH), 40.17 (CH$_2$), 39.92 (CH$_2$), 38.77 (CH), 36.45 (CH$_2$), 35.93 (CH$_2$), 35.91 (CH$_2$), 35.81 (CH$_2$), 33.46 (CH$_2$), 33.38 (CH$_2$), 33.37 (CH$_2$), 30.34 (CH$_2$), 28.68 (CH$_2$), 27.64 (CH$_2$), 27.60 (CH$_2$), 27.06 (CH$_2$), 27.04 (CH$_2$), 26.82 (CH$_2$), 26.80 (CH$_2$), 26.76 (CH$_2$), 26.68 (CH$_2$), 26.60 (CH$_2$), 25.04 (CH$_3$), 25.03 (CH$_3$), 23.59 (CH$_3$), 23.44 (CH$_3$), 18.89 (CH$_3$), 18.83 (CH$_3$), 16.23 (CH$_3$), 16.16 (CH$_3$) ppm. HRMS (70 eV): calcd. for $C_{21}H_{36}O$ [M]$^+$ 304.2766; found 304.2772. IR (neat): $\tilde{\nu}$ = 2921, 2849, 1447, 1376, 1121, 873 cm^{-1}. $C_{21}H_{36}O_2$ (304.27): calcd. C 82.83, H 11.92; found C 83.22, H 11.80.

Compound 33: Yield 60 mg, 62% from **22** (0.35 mmol) as a 1:1 mixture of (*E*,*E*) and (*Z*,*E*) isomers; CH/EA, 97:3; colorless oil. ^1H NMR (400 MHz, $CDCl_3$): δ = 5.74 (m, 1 H), 5.15–5.00 (m, 2 H), 4.92 (ddd, *J* = 17.0, 3.7, 1.8 Hz, 1 H), 4.86 (ddt, *J* = 10.3, 2.2, 1.1 Hz, 1 H), 2.68* (t, *J* = 6.2 Hz, 1 H), 2.63 (dd, *J* = 12.4, 6.2 Hz, 1 H), 2.10–1.85 (m, 10 H), 1.62 (q, *J* = 1.4 Hz, 2 H), 1.54* (s, 3 H), 1.52 (s, 3 H), 1.40–1.30 (m, 2 H), 1.23* (s, 3 H), 1.23 (s, 3 H), 1.22 (s, 3 H), 1.20* (s, 3 H), 1.19* (s, 3 H), 1.18 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 139.12 (CH), 139.11 (CH), 135.14 (C), 135.06 (C), 134.17 (C), 134.13 (C), 125.86 (CH), 125.02 (CH), 124.68 (CH), 124.59 (CH), 114.42 (CH_2), 114.41 (CH_2), 64.30 (CH), 64.22 (CH), 58.42 (C), 58.37 (C), 40.04 (CH_2), 39.79 (CH_2), 36.45 (CH_2), 33.48 (CH_2), 33.46 (CH_2), 29.22 (CH_2), 29.21 (CH_2), 28.67 (CH_2), 27.62 (CH_2), 27.58 (CH_2), 27.48 (CH_2), 27.46 (CH_2), 26.73 (CH_2), 26.60 (CH_2), 25.04 (CH_3), 25.02 (CH_3), 23.51 (CH_3), 23.44 (CH_3), 18.87 (CH_3), 18.83 (CH_3), 16.13 (CH_3), 16.11 (CH_3) ppm. HRMS (70 eV): calcd. for $C_{19}H_{32}O$ $[M]^+$ 276.2453; found 276.2445. IR (neat): $\tilde{\nu}$ = 2923, 1451, 1378, 1248, 1121, 908 cm^{-1}.

Compound 34: Yield 77 mg, 79% from **22** (0.35 mmol) as a 1:1 mixture of (*E*,*E*) and (*Z*,*E*) isomers; CH/EA, 97:3; colorless oil. ^1H NMR (400 MHz, $CDCl_3$): δ = 5.25–5.15 (m, 2 H), 2.69* (t, *J* = 6.2 Hz, 1 H), 2.68 (t, *J* = 6.2 Hz, 1 H), 2.20–2.0 (m, 6 H), 1.86 (d, *J* = 7.7 Hz, 2 H), 1.70 (dq, *J* = 9.7, 1.1 Hz, 2 H), 1.62 (s, 3 H), 1.58 (s, 3 H), 1.30* (s, 3 H), 1.29 (s, 3 H), 1.25* (s, 3 H), 1.25 (s, 3 H), 0.87 (s, 9 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 136.11 (C), 136.04 (C), 134.11 (C), 134.09 (C), 125.09 (CH), 125.08 (CH), 122.25 (CH), 122.12 (CH), 64.33 (CH), 64.31 (CH), 58.42 (C), 58.36 (C), 42.02 (CH_2), 41.86 (CH_2), 40.41 (CH_2), 40.15 (CH_2), 36.47 (CH_2), 36.45 (CH_2), 31.95 (C), 31.82 (C), 29.47 (CH_3), 29.41 (CH_3), 27.63 (CH_2), 27.58 (CH_2), 27.06 (CH_2), 26.76 (CH_2), 25.05 (CH_3), 25.03 (CH_3), 23.76 (CH_3), 23.46 (CH_3), 18.88 (CH_3), 18.83 (CH_3), 16.18 (CH_3), 16.16 (CH_3) ppm. HRMS (70 eV): calcd. for $C_{19}H_{34}O$ $[M]^+$ 278.2610; found 278.2603. IR (neat): $\tilde{\nu}$ = 2956, 1460, 1377, 1245, 1122, 871, 681 cm^{-1}.

Compound 35: Yield 111 mg, 48% from **22** (0.7 mmol) as a 1:1 mixture of (*E*,*E*) and (*Z*,*E*) isomers; CH/EA, 97:3; colorless oil. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.18 (dd, *J* = 7.6, 1.3 Hz, 1 H), 7.02 (s, 1 H), 7.01 (d, *J* = 7.6 Hz, 2 H), 5.25–5.15 (m, 2 H), 2.76–2.69 (m, 1 H), 2.65–2.59 (m, 2 H), 2.35 (s, 3 H), 2.40–2.00 (m, 7 H), 1.74–1.57 (m, 3 H), 1.65 (s, 3 H), 1.59 (s, 3 H), 1.33* (s, 3 H), 1.32 (s, 3 H), 1.29* (s, 3 H), 1.28 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.42 (C), 142.40 (C), 137.83 (C), 137.78 (C), 135.71 (C), 135.62 (C), 134.18 (C), 134.15 (C), 129.37 (CH), 129.34 (CH), 128.26 (CH), 128.22 (CH), 126.56 (CH), 126.51 (CH), 125.55 (CH), 125.51 (CH), 125.00 (CH), 124.91 (CH), 124.03 (CH), 123.95 (CH), 64.27 (CH), 64.25 (CH), 58.39 (C), 58.35 (C), 39.99 (CH_2), 39.75 (CH_2), 36.47 (CH_2), 36.42 (CH_2), 36.19 (CH_2), 36.17 (CH_2), 30.10 (CH_2), 30.08 (CH_2), 27.62 (CH_2), 27.58 (CH_2), 26.77 (CH_2), 26.61 (CH_2), 25.01 (CH_3), 24.99 (CH_3), 23.49 (CH_3), 22.43 (CH_3), 21.50 (CH_3), 18.87 (CH_3), 17.86 (CH_3), 16.10 (CH_3), 16.09 (CH_3) ppm. HRMS (70 eV): calcd. for $C_{23}H_{34}O$ $[M]^+$ 326.2610; found 326.2608. IR (neat): $\tilde{\nu}$ = 2945, 1386, 787 cm^{-1}.

Compound 36: Yield 68 mg, 69% from **6** (0.40 mmol);CH/EA, 92:8; colorless oil. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.17 (td, *J* = 7.4, 1.5 Hz, 1 H), 7.12 (dd, *J* = 7.4, 1.5 Hz, 1 H), 6.87 (td, *J* = 7.4, 1.1 Hz, 1 H), 6.77 (br. d, 1 H), 5.36 (tq, *J* = 7.3, 1.2 Hz, 1 H), 3.82 (s, 3 H), 3.34 (d, *J* = 7.3 Hz, 2 H), 2.70 (t, *J* = 6.2 Hz, 1 H), 2.31–2.05 (m, 2 H), 1.73 (s, 3 H), 1.71–1.57 (m, 2 H), 1.26 (s, 3 H), 1.24 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.45 (C), 135.14 (C), 130.02 (C), 129.45 (CH), 127.08 (CH), 123.35 (CH), 120.58 (CH), 110.39 (CH), 64.36 (CH), 58.50 (C), 55.46 (CH_3), 36.53 (CH_2), 28.52 (CH_2), 27.57 (CH_2), 24.97 (CH_3), 18.88 (CH_3), 16.21 (CH_3) ppm. HRMS (70 eV): calcd. for $C_{17}H_{24}O_2$ $[M]^+$ 260.1776; found 260.1782. IR (neat): $\tilde{\nu}$ = 2966, 2930, 1721, 1599, 1490, 1461, 1379, 1289, 1245, 1027, 753 cm^{-1}.

Compound 37: Yield 75 mg, 68% from **6** (0.45 mmol); CH/EA, 92:8; colorless oil. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.09 (d, *J* = 8.8 Hz, 2 H), 6.82 (d, *J* = 8.8 Hz, 2 H), 5.38 (tq, *J* = 7.3, 1.3 Hz, 1 H), 3.78 (s, 3 H), 3.31 (d, *J* = 7.3 Hz, 2 H), 2.71 (t, *J* = 6.2 Hz, 1 H), 2.26–2.11 (m, 2 H), 1.74 (s, 3 H), 1.71–1.56 (m, 2 H), 1.28 (s, 3 H), 1.26 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.93 (C), 135.02 (C), 133.73 (C), 129.27 (CH), 124.27 (CH), 113.96 (CH), 64.24 (CH), 58.40 (C), 55.38 (CH_3), 36.48 (CH_2), 33.44 (CH_2), 27.55 (CH_2), 24.97 (CH_3), 18.86 (CH_3), 16.24 (CH_3) ppm. HRMS (70 eV): calcd. for $C_{17}H_{24}O_2$ $[M]^+$ 260.1776; found 260.1781. IR (neat): $\tilde{\nu}$ = 3372, 2959, 1607, 1511, 1460, 1378, 1246, 1175, 1109, 1035, 970, 819 cm^{-1}.

Compound 38: Yield 725 mg, 76% from **6** (3.00 mmol); CH/EA, 96:4; colorless oil. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.81–7.76 (m, 3 H), 7.62 (s, 1 H), 7.48–7.40 (m, 2 H), 7.33 (td, *J* = 8.6, 1.3 Hz, 1 H), 5.50 (t, *J* = 7.3 Hz, 1 H), 3.50 (d, *J* = 7.2 Hz, 2 H), 2.74 (t, *J* = 6.2 Hz, 1 H), 2.31–2.17 (m, 2 H), 1.81 (s, 3 H), 1.76–1.65 (m, 2 H), 1.29 (s, 3 H), 1.28 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 139.17 (C), 135.71 (C), 133.82 (C), 132.15 (C), 128.04 (CH), 127.72 (CH), 127.54 (CH), 127.44 (CH), 126.25 (CH), 126.00 (CH), 125.23 (CH), 123.68 (CH), 64.22 (CH), 58.39 (CH_3), 36.54 (CH_2), 34.55 (CH_2), 27.57 (CH_2), 24.98 (CH_3), 18.88 (CH_3), 16.37 (CH_3) ppm. HRMS (70 eV): calcd. for $C_{20}H_{24}O$ $[M]^+$ 280.1827; found 280.1820. IR (neat): $\tilde{\nu}$ = 3050, 2960, 2920, 1630, 1600, 1440, 1375, 1120, 855, 810, 770, 745, 680 cm^{-1}.

Compound 39: Yield 58 mg, 61% from **22** (0.30 mmol) as a 1:1 mixture of (*E*,*E*) and (*Z*,*E*) isomers; CH/EA, 95:5; colorless oil. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.16 (t, *J* = 7.7 Hz, 1 H), 7.13 (d, *J* = 7.7 Hz, 1 H), 6.88 (td, *J* = 7.7, 1.0 Hz, 1 H), 6.84 (dd, *J* = 7.7, 1.0 Hz, 1 H), 5.32 (t, *J* = 7.3 Hz, 1 H), 5.17 (t, *J* = 6.9 Hz, 1 H), 3.83 (s, 3 H), 3.33 (d, *J* = 7.3 Hz, 2 H), 2.69 (t, *J* = 6.2 Hz, 1 H), 2.68* (t, *J* = 6.2 Hz, 1 H), 2.20–2.03 (m, 8 H), 1.74* (s, 3 H), 1.70 (s, 3 H), 1.63* (s, 3 H), 1.61 (s, 3 H), 1.60–1.50 (m, 4 H), 1.30* (s, 3 H), 1.29 (s, 3 H), 1.26* (s, 3 H), 1.25 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.47 (C), 157.41 (C), 136.13 (C), 136.07 (C), 134.27 (C), 134.23 (C), 130.24 (C), 130.21 (C), 129.46 (CH), 129.37 (CH), 127.02 (CH), 126.97 (CH), 125.03 (CH), 125.01 (CH), 122.77 (CH), 122.67 (CH), 120.58 (CH), 120.56 (CH), 110.35 (CH), 110.34 (CH), 64.36 (CH), 64.27 (CH), 58.44 (C), 58.43 (C), 55.47 (CH_3), 55.44 (CH_3), 40.09 (CH_2), 39.85 (CH_2), 36.46 (CH_2), 32.01 (CH_2), 28.33 (CH_2), 28.31 (CH_2), 27.63 (CH_2), 27.60 (CH_2), 26.74 (CH_2), 26.70 (CH_2), 25.06 (CH_3), 25.04 (CH_3), 23.63 (CH_3), 23.47 (CH_3), 18.90 (CH_3), 18.84 (CH_3), 16.19 (CH_3), 16.17 (CH_3) ppm. HRMS (70 eV): calcd. for $C_{22}H_{32}O_2$ $[M]^+$ 328.2402; found 328.2401. IR (neat): $\tilde{\nu}$ = 3350, 2959, 2924, 1596, 1490, 1457, 1377, 1243, 1111, 1030, 871, 753 cm^{-1}.

Compound 40: Yield 75 mg, 59% from **22** (0.40 mmol) as a 1:1 mixture of (*E*,*E*) and (*Z*,*E*) isomers; CH/EA, 97:3; colorless oil. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.08 (d, *J* = 8.5 Hz, 2 H), 6.82 (d, *J* = 8.5 Hz, 2 H), 5.32 (t, *J* = 7.3 Hz, 1 H), 5.17 (t, *J* = 6.9 Hz, 1 H), 3.78 (s, 3 H), 3.30 (d, *J* = 7.3 Hz, 2 H), 2.62* (t, *J* = 6.2 Hz, 1 H), 2.61 (t, *J* = 6.2 Hz, 1 H), 2.13–1.95 (m, 7 H), 1.74* (s, 3 H), 1.70 (s, 3 H), 1.63* (s, 3 H), 1.62 (s, 3 H), 1.60–1.52 (m, 4 H), 1.30* (s, 3 H), 1.29 (s, 3 H), 1.26* (s, 3 H), 1.25 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.12 (C), 158.11 (C), 136.14 (C), 136.08 (C), 134.57 (C), 134.53 (C), 134.20 (C), 134.19 (C), 129.51 (CH), 129.50 (CH), 125.98 (CH), 125.13 (CH), 124.01 (CH), 123.92 (CH), 113.98 (CH), 113.96 (CH), 64.35 (CH), 64.27 (CH), 58.48 (C), 58.44 (C), 55.44 (CH$_3$), 40.02 (CH$_2$), 39.78 (CH$_2$), 36.48 (CH$_2$), 36.46 (CH$_2$), 33.43 (CH$_2$), 33.34 (CH$_2$), 27.63 (CH$_2$), 27.60 (CH$_2$), 26.71 (CH$_2$), 26.54 (CH$_2$), 25.07 (CH$_3$), 25.05 (CH$_3$), 23.58 (CH$_3$), 23.48 (CH$_3$), 18.90 (CH$_3$), 18.86 (CH$_3$), 16.26 (CH$_3$), 16.19 (CH$_3$) ppm. HRMS (70 eV): calcd. for $C_{22}H_{32}O_2$ [M]$^+$ 328.2402; found 328.2401. IR (neat): $\tilde{\nu}$ = 3352, 2925, 1608, 1510, 1457, 1378, 1245, 1175, 1115, 1034, 822 cm^{-1}.

Compound 41: Yield 131 mg, 62% from **22** (0.74 mmol) as a 1:1 mixture of (*E*,*E*) and (*Z*,*E*) isomers; CH/EA, 9:1; colorless oil. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.29 (br. s, 1 H), 6.19 (br. s, 1 H), 5.88 (br. s, 1 H), 5.33 (t, J = 7.4 Hz, 1 H), 5.22–5.13 (m, 1 H), 3.34 (d, J = 7.4 Hz, 2 H), 2.69 (t, J = 6.1 Hz, 1 H), 2.22–2.03 (m, 10 H), 1.76–1.74 (m, 2 H), 1.69* (s, 3 H), 1.68 (s, 3 H), 1.62* (s, 3 H), 1.62 (s, 3 H), 1.29 (s, 3 H), 1.26* (s, 3 H), 1.25 (s, 3 H) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ = 155.45 (C), 155.44 (C), 141.07 (CH), 137.59 (C), 137.51 (C), 134.47 (C), 134.44 (C), 124.79 (CH), 124.67 (CH), 119.63 (CH), 119.55 (CH), 110.31 (CH), 110.28 (CH), 104.81 (CH), 104.80 (CH), 64.34 (CH), 64.25 (CH), 58.48 (C), 58.43 (C), 39.90 (CH$_2$), 39.66 (CH$_2$), 36.47 (CH$_2$), 28.70 (CH$_2$), 27.62 (CH$_2$), 27.59 (CH$_2$), 27.15 (CH$_2$), 27.06 (CH$_2$), 26.60 (CH$_2$), 26.46 (CH$_2$), 25.06 (CH$_3$), 25.04 (CH$_3$), 23.54 (CH$_3$), 23.46 (CH$_3$), 18.90 (CH$_3$), 18.86 (CH$_3$), 16.25 (CH$_3$), 16.17 (CH$_3$) ppm. HRMS (70 eV): calcd. for $C_{19}H_{28}O_2$ [M]$^+$ 288.2089; found 288.2079. IR (neat): $\tilde{\nu}$ = 3330, 2958, 1593, 1457, 1378, 1250, 1119, 1009, 803, 732, 672 cm^{-1}.

Compound 42: Yield 920 mg, 60% from **22** (3.8 mmol) as a 1:1 mixture of (*E*,*E*) and (*Z*,*E*) isomers; CH/EA, 95:5; colorless oil. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 6.70 (s, 1 H), 6.63 (s, 1 H), 5.87 (s, 3 H), 5.86* (s, 3 H), 5.29–5.23 (m, 1 H), 5.22–5.13 (m, 1 H), 5.08 (s, 3 H), 3.48 (s, 3 H), 3.47* (s, 3 H), 3.26 (d, J = 7.2 Hz, 2 H), 2.73–2.67 (m, 1 H), 2.20–2.00 (m, 5 H), 1.73 (q, J = 1.2 Hz, 1 H), 1.70* (s, 3 H), 1.69 (s, 3 H), 1.62* (s, 3 H), 1.61 (s, 3 H), 1.30 (s, 3 H), 1.29* (s, 3 H), 1.26* (s, 3 H), 1.25 (s, 3 H) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ = 149.51 (C), 149.50 (C), 146.05 (C), 146.02 (C), 142.34 (C), 142.33 (C), 136.23 (C), 136.17 (C), 134.41 (C), 134.35 (C), 124.91 (CH), 124.85 (CH), 123.70 (C), 123.62 (C), 123.00 (CH), 122.89 (CH), 109.20 (CH), 109.14 (CH), 101.15 (CH$_2$), 98.71 (CH), 98.65 (CH), 95.94 (CH$_2$), 95.93 (CH$_2$), 64.34 (CH), 64.31 (CH), 58.47 (C), 58.41 (C), 56.13 (CH$_3$), 56.12 (CH$_3$), 40.04 (CH$_2$), 39.80 (CH$_2$), 36.46 (CH$_2$), 36.42 (CH$_2$), 28.69 (CH$_2$), 28.25 (CH$_2$), 27.60 (CH$_2$), 27.58 (CH$_2$), 26.67 (CH$_2$), 26.51 (CH$_2$), 25.05 (CH$_3$), 25.03 (CH$_3$), 23.59 (CH$_3$), 23.44 (CH$_3$), 18.87 (CH$_3$), 18.83 (CH$_3$), 16.16 (CH$_3$), 16.13 (CH$_3$) ppm. HRMS (70 eV): calcd. for $C_{24}H_{34}O_5$ [M]$^+$ 402.2406; found 402.2408. IR (neat): $\tilde{\nu}$ = 2924, 1504, 1484, 1436, 1210, 1152, 1042, 988, 938, 856 cm^{-1}.

General Procedure for Radical Cyclization: THF (15 mL) was added to a mixture of Cp$_2$TiCl$_2$ (0.2 mmol) and Mn dust (8 mmol) under Ar and the suspension was stirred at room temp. until it turned green (about 15 min). Then a solution of 2,4,6-collidine (7 mmol) and Me$_3$SiCl (4 mmol) in THF (5 mL) was added and the mixture was stirred for 5 min and a solution of epoxypolyene (1 mmol) in THF (5 mL) was finally added and the mixture was stirred at room temp. overnight. Then 2 N HCl was added, and the mixture was extracted with *t*BuOMe. The combined organic layers were dried with MgSO$_4$ and the solvent was removed. The residue was dissolved in THF and a 1 M solution of Bu$_4$NF in THF (1.2 mmol) was added. The new mixture was stirred for 30 min, diluted with *t*BuOMe, and washed with brine. The organic layer was dried with MgSO$_4$ and the solvent removed. The residue was purified by flash chromatography (CH/EA) to yield the cyclization compound.

Compound 47: Yield 210 mg, 60% from **37** (1.34 mmol); CH/EA, 92:8; colorless oil. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.08 (d, J = 8.3 Hz, 2 H), 6.80 (d, J = 8.3 Hz, 2 H), 4.81 (s, 1 H), 4.55 (s, 1 H), 3.77 (s, 3 H), 3.50 (dd, J = 9.5, 4.2 Hz, 1 H), 2.91 (dd, J = 14.9, 2.8 Hz, 1 H), 2.77 (dd, J = 14.9, 10.8 Hz, 1 H), 2.37 (dt, J = 13.3, 5.1 Hz, 1 H), 2.13 (dq, J = 10.8, 1.4 Hz, 1 H), 2.10–1.95 (m, 1 H), 1.88 (ddd, J = 12.7, 9.4, 4.9 Hz, 1 H), 1.60 (s, 1 H, OH), 1.62–1.50 (m, 1 H), 1.13 (s, 3 H), 0.87 (s, 3 H) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ = 157.56 (C), 146.72 (C), 134.33 (C), 129.55 (CH), 113.62 (CH), 110.12 (CH$_2$), 77.26 (CH), 55.33 (CH$_3$), 53.08 (CH), 40.76 (C), 32.73 (CH$_2$), 32.18 (CH$_2$), 31.29 (CH$_2$), 26.35 (CH$_3$), 16.21 (CH$_3$) ppm. HRMS (70 eV): calcd. for $C_{17}H_{24}O_2$ [M]$^+$ 260.1776; found 260.1780. IR (neat): $\tilde{\nu}$ = 3394, 2934, 1512, 1246, 1043 cm^{-1}. $C_{17}H_{24}O_2$ (260.17): calcd. C 78.42, H 9.29; found C 78.13, H 9.40.

Compound 50: Yield 141 mg, 41% from **42** (1.71 mmol); CH/EA, 9:1; colorless oil. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 6.68 (s, 1 H), 6.61 (s, 1 H), 5.85 (s, 2 H), 5.09 (s, 2 H), 4.79 (br. s, 1 H), 4.65 (br. s, 1 H), 3.49 (s, 3 H), 3.28 (dd, J = 11.5, 4.7 Hz, 1 H), 2.70 (d, J = 4.9 Hz, 1 H), 2.69 (s, 1 H), 2.38 (ddd, J = 12.8, 4.3, 2.5 Hz, 1 H), 2.09 (q, J = 4.3 Hz, 1 H), 2.05–1.85 (m, 2 H), 1.78 (sextuplet, J = 2.5 Hz, 1 H), 1.77–1.28 (m, 4 H), 1.17 (dd, J = 12.8, 2.5 Hz, 1 H), 1.01 (s, 3 H), 0.81 (s, 3 H), 0.80 (s, 3 H) ppm. ^{13}C NMR (75 MHz, CDCl$_3$): δ = 149.73 (C), 147.91 (C), 145.78 (C), 142.15 (C), 123.84 (C), 108.94 (CH), 108.22 (CH$_2$), 101.11 (CH$_2$), 98.30 (CH), 95.80 (CH$_2$), 79.09 (CH), 56.38 (CH$_3$), 56.28 (CH), 55.05 (CH), 39.94 (C), 39.32 (C), 38.21 (CH$_2$), 37.32 (CH$_2$), 28.54 (CH$_3$), 28.10 (CH$_2$), 24.11 (CH$_2$), 23.52 (CH$_2$), 15.65 (CH$_3$), 14.76 (CH$_3$) ppm. HRMS (70 eV): calcd. for $C_{24}H_{34}O_5$ [M]$^+$ 402.2406; found 402.2413. IR (neat): $\tilde{\nu}$ = 3444, 2938, 1505, 1484, 1209, 1151, 1042, 992, 937, 757 cm^{-1}.

Synthesis of 52: *O*-Pentafluorophenyl chlorothioformate (225 mg, 0.86 mmol) was added to a stirred solution of **49** (153 mg, 0.43 mmol) and DMAP (156 mg, 1.29 mmol) in CH$_2$Cl$_2$ (3 mL) at 0 °C and the solution was stirred at room temp. for 4 h. Then AcOEt was added and the mixture was washed with water, the organic layer was dried with MgSO$_4$, and the solvent removed. The residue was purified by flash chromatography (CH/EA, 97:3) to yield the xanthate (218 mg, 88%) as a colorless oil. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 6.76–6.62 (m, 3 H), 5.03 (dd, J = 11.9, 4.3 Hz, 1 H), 4.81 (br. s, 1 H), 4.70 (br. s, 1 H), 3.81 (s, 3 H), 3.74 (s, 3 H), 2.80–2.73 (m, 2 H), 2.45–2.36 (m, 1 H), 2.23 (t, J = 6.8 Hz, 1 H), 2.13–1.96 (m, 3 H), 1.94–1.68 (m, 3 H), 1.52–1.33 (m, 3 H), 1.04 (s, 3 H), 0.99 (s, 3 H), 0.90 (s, 3 H) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ = 191.88 (C), 153.50 (C), 151.86 (C), 147.33 (C), 131.62 (C), 116.53 (CH), 111.10 (CH), 110.22 (CH), 108.68 (CH$_2$), 95.28 (CH), 56.03 (CH$_3$), 55.73 (CH$_3$), 55.68 (CH), 54.99 (CH), 39.72 (CH$_2$), 39.08 (CH$_2$), 38.62 (C), 38.01 (CH$_2$), 36.89 (C), 36.74 (CH$_2$), 28.20 (CH$_3$), 23.13 (CH$_2$), 17.01 (CH$_3$), 14.76 (CH$_3$) ppm (some signals were not observed). HRMS (70 eV): calcd. for $C_{30}H_{33}F_5O_4S$ [M]$^+$ 584.2020; found 584.2026. IR (neat): $\tilde{\nu}$ = 2947, 1523, 1377, 1306, 1220, 1129, 997, 791, 727 cm^{-1}. The xanthate (240 mg, 0.41 mmol) was dissolved in benzene (45 mL), and then AIBN (14 mg, 0.08 mmol) and HSnBu$_3$ (347 mg, 1.23 mmol) were added, and the mixture was stirred at reflux for 4 h. Then, the solvent was removed. The residue was purified by flash chromatography (CH/EA, 99:1) to yield **52** (125 mg, 89%) as a colorless oil. Its ^{1}H and ^{13}C NMR data match with those previously reported.[20e]

Synthesis of Zonarone (2): 2,6-Dicarboxypyridine *N*-oxide (416 mg), H$_2$O (13.7 mL) and a 1 M aq. solution of CAN (3.75 mL, 4.5 mmol) were added to a solution of **52** (125 mg, 0.37 mmol) in a mixture of MeCN/DMF (1:1, 35 mL). The mixture was stirred at room temp. for 8 min. Then, water was added, the mixture was extracted with *t*BuOMe, the combined organic layers were dried with $MgSO_4$, and the solvent was removed. The residue was purified by flash chromatography (CH/EA, 95:5) to yield **2** (95 mg, 85%) as a yellow oil. Its ^1H and ^{13}C NMR data match with those previously reported.[20d]

Synthesis of Zonarol (1): $Na_2S_2O_4$ (635 mg, 3.6 mmol) was added to a solution of **2** (95 mg, 0.3 mmol) in THF/H_2O (3:2, 40 mL), and the mixture was heated at reflux for 30 min. Then, water was added, the mixture was extracted with AcOEt, the combined organic layers were dried with $MgSO_4$, and the was solvent removed. The residue was purified by flash chromatography (CH/EA, 8:2) to afford **1** (72 mg, 75%) as a colorless oil. Its ^1H and ^{13}C NMR data match with those previously reported.[10]

Preparation of Compound 53: DMAP (280 mg, 2.28 mmol) and *O*-pentafluorophenyl chlorothioformate (0.244 mL, 1.52 mmol) were added to a solution of alcohol **47** (200 mg, 0.76 mmol) in CH_2Cl_2 (8 mL) at 0 °C and the mixture was stirred at room temp. for 2 h. Then water was added and the mixture was extracted with AcOEt, the extract dried with $MgSO_4$, and the solvent removed. The residue was purified by flash chromatography (CH/EA, 97:3) to afford the xanthate (280 mg, 76%) as a colorless oil. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.05 (d, J = 8.6 Hz, 2 H), 6.80 (d, J = 8.6 Hz, 2 H), 5.22 (dd, J = 7.9, 3.8 Hz, 1 H), 4.83 (s, 1 H), 4.52 (s, 1 H), 3.78 (s, 3 H), 2.93 (dd, J = 14.6, 2.9 Hz, 1 H), 2.74 (dd, J = 14.6, 10.9 Hz, 1 H), 2.50–2.35 (m, 1 H), 2.21 (dd, J = 10.9, 2.9 Hz, 1 H), 2.18–2.03 (m, 2 H), 1.98–1.83 (m, 1 H), 1.14 (s, 3 H), 1.06 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 191.69 (C), 157.80 (C), 145.05 (C), 133.67 (C), 129.70 (CH), 113.70 (CH), 111.88 (CH_2), 92.68 (CH), 55.33 (CH_3), 53.98 (CH), 40.12 (C), 31.97 (CH_2), 30.45 (CH_2), 27.26 (CH_2), 26.58 (CH_3), 19.12 (CH_3) ppm (some signals were not observed). HRMS (70 eV): calcd. for $C_{24}H_{23}O_3F_5S$ $[M]^+$ 486.1288; found 486.1291. IR (neat): $\tilde{\nu}$ = 2950, 1521, 1377, 1305, 1247, 1145, 1038, 998, 948 cm^{-1}. $HSnBu_3$ (0.21 mL, 0.78 mmol) and AIBN (9 mg, 0.055 mmol) were slowly added to a solution of the xanthate (130 mg, 0.26 mmol) in benzene (2 mL) and the mixture was refluxed for 1 h. Then the solvent was removed. The residue was purified by flash chromatography (CH/EA, 98:2) to yield **53** (52 mg, 77%) as a colorless oil. Its ^1H and ^{13}C NMR data match with those previously reported.[21]

Synthesis of Compound 54: DMAP (109 mg, 0.89 mmol) and *O*-pentafluorophenyl chlorothioformate (0.1 mL, 0.58 mmol) were added to a solution of alcohol **50** (120 mg, 0.29 mmol) in CH_2Cl_2 (3 mL) at 0 °C. Then the mixture was stirred at room temp. for 2 h. The reaction was quenched with water, the mixture extracted with AcOEt, the extract dried with $MgSO_4$, and the solvent removed. The residue was purified by flash chromatography (CH/EA, 95:5) to yield the xanthate derivative (170 mg, 94%) as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$): δ = 6.69 (s, 1 H), 6.61 (s, 1 H), 5.86 (s, 2 H), 5.11 (s, 2 H), 5.01 (dd, J = 11.9, 4.4 Hz, 1 H), 4.83 (s, 1 H), 4.70 (s, 1 H), 3.50 (s, 3 H), 2.75 (dd, J = 15.3, 9.7 Hz, 1 H), 2.69 (dd, J = 15.3, 3.3 Hz, 1 H), 2.41 (ddd, J = 12.9, 4.0, 2.3 Hz, 1 H), 2.20–1.40 (m, 8 H), 1.35 (dd, J = 12.9, 2.3 Hz, 1 H), 1.03 (s, 3 H), 0.98 (s, 3 H), 0.88 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 191.93 (C), 149.72 (C), 147.44 (C), 145.87 (C), 142.25 (C), 123.53 (C), 108.91 (CH), 108.73 (CH_2), 101.16 (CH_2), 98.38 (CH), 95.89 (CH_2), 95.24 (CH), 56.22 (CH_3), 56.15 (CH), 55.11 (CH), 39.74 (C), 39.05 (C), 38.08 (CH_2), 36.89 (CH_2), 28.21 (CH_3), 23.82 (CH_2), 23.74 (CH_2), 23.11 (CH_2), 17.07 (CH_3), 14.83 (CH_3) ppm (some signals were not observed). HRMS (70 eV): calcd. for $C_{31}H_{33}O_6F_5S$ $[M]^+$ 628.1918; found 628.1918. IR (neat): $\tilde{\nu}$ = 2958, 1523, 1481, 1381, 1309, 1130, 1036, 996, 928, 852 cm^{-1}. A solution of the xanthate derivative (160 mg, 0.25 mmol) in benzene (2 mL) was slowly added to a mixture of $HSnBu_3$ (0.2 mL, 0.76 mmol) and AIBN (9 mg, 0.05 mmol) in benzene (1.5 mL) and the new mixture was refluxed for 1 h. Then the solvent was removed and the residue was purified by flash chromatography (CH/EA, 98:2) to yield **54** (89 mg, 93%) as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$): δ = 6.68 (s, 1 H), 6.63 (s, 1 H), 5.86 (s, 2 H), 5.10 (d, J = 0.7 Hz, 2 H), 4.77 (br. s, 1 H), 4.62 (br. s, 1 H), 3.50 (s, 3 H), 2.71 (d, J = 1.3 Hz, 1 H), 2.70 (s, 1 H), 2.36 (ddd, J = 12.8, 4.2, 2.5 Hz, 1 H), 2.13 (t, J = 6.6 Hz, 1 H), 1.99 (ddd, J = 12.9, 12.9, 5.2 Hz, 1 H), 1.87 (dd, J = 12.9, 1.3 Hz, 1 H), 1.75 (dquint, J = 12.9, 2.6 Hz, 1 H), 1.61 (dt, J = 13.6, 3.3 Hz, 1 H), 1.58–1.10 (m, 6 H), 0.90 (s, 3 H), 0.84 (s, 3 H), 0.81 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 149.73 (C), 148.61 (C), 145.67 (C), 142.13 (C), 124.30 (C), 109.06 (CH), 107.87 (CH_2), 101.09 (CH_2), 98.35 (CH), 95.93 (CH_2), 56.61 (CH_3), 56.24 (CH), 55.96 (CH), 42.41 (CH_2), 40.23 (C), 39.42 (CH_2), 38.47 (CH_2), 33.83 (CH_3), 33.81 (C), 24.61 (CH_2), 23.42 (CH_2), 21.97 (CH_3), 19.68 (CH_2), 14.72 (CH_3) ppm. HRMS (70 eV): calcd. for $C_{24}H_{34}O_4$ $[M]^+$ 386.2457; found 386.2455. IR (neat): $\tilde{\nu}$ = 2933, 1505, 1483, 1208, 1150, 1043, 993, 938, 858 cm^{-1}.

Preparation of Compound 55: *p*TsOH (4 mg, 0.021 mmol) was added to a solution of compound **54** (18 mg, 0.046 mmol) in MeOH (0.5 mL). The mixture was stirred at room temp. for 48 h. Then AcOEt was added and the mixture was washed with water. The organic layer was dried with $MgSO_4$ and the solvent removed. The residue was purified by flash chromatography (CH/EA, 95:5) to yield **55** (13 mg, 85%) as a colorless oil. Its ^1H and ^{13}C NMR data match with those previously reported.[12b]

Synthesis of Compound 56: *N*-(Phenylseleno)phthalimide (102 mg, 0.31 mmol) and a 0.19 M solution of $SnCl_4$ in CH_2Cl_2 (0.15 mL, 0.03 mmol) were added to a solution of **55** (100 mg, 0.29 mmol) in CH_2Cl_2 (4 mL) at 0 °C. After stirring for 30 min, the solution was diluted with satd. aq. $NaHCO_3$ and extracted with *t*BuOMe. The combined organic layers were washed with brine, dried with $MgSO_4$, and the solvent was removed. The residue was purified by flash chromatography (CH/EA, 95:5) to yield **56** (115 mg, 80%) as a colorless oil. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.46–7.40 (m, 3 H), 7.22–7.18 (m, 2 H), 6.42 (s, 1 H), 6.24 (s, 1 H), 5.83 (d, J = 7.3 Hz, 1 H), 5.80 (d, J = 7.3 Hz, 1 H), 3.13 (d, J = 12.1 Hz, 1 H), 3.05 (d, J = 12.1 Hz, 1 H), 2.69–2.58 (m, 2 H), 2.19 (dt, J = 13.7, 3.0 Hz, 1 H), 1.85–1.37 (m, 10 H), 1.17 (ddd, J = 13.7, 13.1, 4.0 Hz, 1 H), 0.90 (s, 3 H), 0.81 (s, 3 H), 0.73 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 148.32 (C), 146.35 (C), 141.56 (C), 133.13 (CH), 131.01 (C), 129.10 (CH), 127.04 (CH), 114.02 (C), 107.45 (CH), 100.83 (CH_2), 99.37 (CH), 77.94 (C), 55.19 (CH), 47.06 (CH), 42.03 (CH_2), 40.32 (CH_2), 38.65 (C), 38.37 (CH_2), 37.81 (CH_2), 33.82 (CH_3), 33.42 (C), 22.65 (CH_2), 22.04 (CH_3), 18.61 (CH_2), 18.27 (CH_2), 14.51 (CH_3) ppm. HRMS (70 eV): calcd. for $C_{28}H_{34}O_3Se$ $[M]^+$ 498.1673; found 498.1696. IR (neat): $\tilde{\nu}$ = 2929, 1477, 1437, 1181, 1150, 1039, 936, 855, 754 cm^{-1}.

Synthesis of Compound 57: A mixture of $HSnBu_3$ (0.07 mL, 0.25 mmol) and AIBN (14 mg, 0.085 mmol) in benzene (2 mL) was slowly added to a solution of **56** (85 mg, 0.17 mmol) in benzene (5 mL) and the mixture was refluxed for 1 h. Then the solvent was removed and the residue was purified by flash chromatography (CH/EA, 95:5) to yield compound **57** (50 mg, 86%) as a colorless oil. Its ^1H and ^{13}C NMR data match with those previously reported.[12b]

Synthesis of Compound 58: $BF_3{\cdot}Et_2O$ (101 mg, 0.71 mmol) was added to a solution of **55** (121 mg, 0.35 mmol) in CH_2Cl_2 (4 mL) and the mixture was stirred at room temp. for 1 h. Then water was added and the new mixture was extracted with Et_2O, the extract dried with $MgSO_4$, and the solvent removed. The residue was purified by flash chromatography (CH/EA, 97:3) to yield compound **55**

(104 mg, 86%) as a colorless oil. Its ^{1}H and ^{13}C NMR data match with those previously reported.[12b]

Acknowledgments

We are grateful to the Spanish Ministerio de Educación y Ciencia (project no. CTQ2005-08402/BQU) and to the University of Granada, the Ministerio de Educación y Ciencia, and the Fundación Ramón Areces for postdoctoral grants. Continuing generous financial support from the Fonds der Chemischen Industrie (Dozentenstipendium, Sachbeihilfen) is acknowledged.

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Received: May 3, 2006