Catalytic diastereo- and positionselective oxidative mono-cyclization of 1,5,9-trienes and polyenes†

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Ruthenium tetroxide (1 mol%) has been used as a catalyst for the oxidative mono-cyclization of 1,5,9-trienes and polyenes. The poly-unsaturated substrates underwent mono-cyclization with a high degree of diastereo- and positionselectivity to produce mono-tetrahydrofuran diols with a varying degree of unsaturation. Up to four new stereogenic centers were created in this single step transformation. The remarkable positionselectivity appears to be a result of relative electronic properties of the double bonds within the polyolefinic substrates in conjunction with conformational constraints.

Introduction

Selective transformations at specific sites of a polyfunctional substrate represent a significant challenge of current organic chemistry. In particular, the discrimination of similar or identical functional groups in a comparable chemical environment is a non-trivial synthetic task. For example, the selective oxidation of specific double bond(s) of a polyene substrate is generally difficult to achieve, especially in the absence of other directing functionality.[1] Different types of selectivity, such as stereo-, position-, and chemoselectivity have to be addressed simultaneously.

A number of terpenoid natural products consist of a tetrahydrofuran (THF) ring system along with a varying degree of unsaturation within the side chain (Fig. 1).[2]

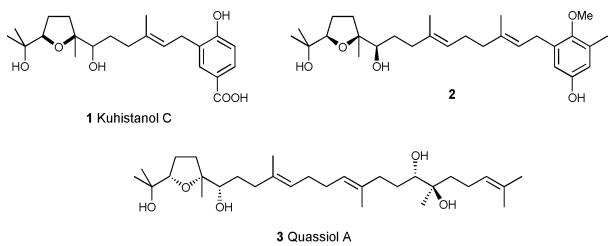
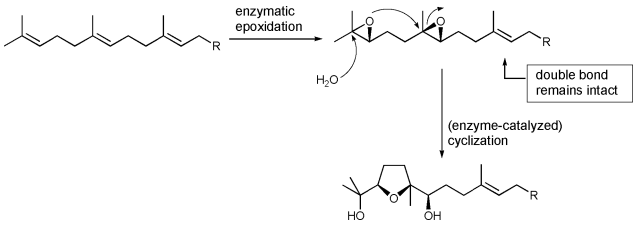


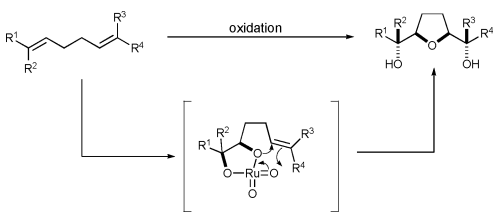
Fig. 1 Terpenoid mono-THF natural products.

Biogenetically, such compounds are believed to be derived from an appropriate 1,5,9-triene (or polyene) precursor.[3–5] In a key step of the biosynthesis, this triene (or polyene) is enzymatically epoxidized to yield a diepoxide with a high degree of selectivity (Scheme 1). A final spontaneous, or again enzyme catalyzed, cyclization furnishes the natural product (Scheme 1). Other mechanisms may be conceivable,[3] however, the diepoxide pathway appears most likely.[4,5]

Whereas nature's complex enzyme machinery is capable of achieving a high degree of selectivity, simple catalyst systems often fail.[1] Therefore, a biomimetic approach is anticipated to be difficult primarily due to low positionselectivity both for the epoxidation as well as for the hydrolytic epoxide opening–cyclization step, particularly for higher polyene substrates. An alternative chemical pathway to THF-diols is the direct oxidative cyclization of 1,5-dienes. Such unique cyclization reactions have been achieved using various d^0-metal-oxo-reagents (Scheme 2).[6] Applications to polyene substrates, especially attempts to achieve mono-cyclizations, have rarely been reported.[7,8]



Scheme 1 Proposed biosynthetic pathway to terpenoid mono-THF natural products.



Scheme 2 Direct oxidative cyclization of 1,5-dienes.

We recently described a method for the catalytic oxidative cyclization of 1,5-dienes to furnish tetrahydrofurans[9] and 1,6-dienes to yield tetrahydropyrans.[10] In continuation of this work, we were attracted to extend the scope of this methodology to 1,5,9-trienes and polyenes. The aim of the present study was to develop a protocol for the selective mono-cyclization of polyene substrates. In order to obtain synthetically useful amounts of mono-cyclization product, high levels of control over both position- and diastereoselectivity have to be achieved. Moreover, other oxidatively sensitive functionality within the

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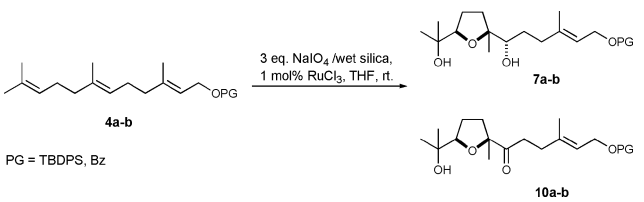
product (including other double bonds) need to be sufficiently stable under the reaction conditions.

Results and discussion

Initial experiments using conditions similar to those recently developed for simple 1,5-dienes showed that the desired mono-cyclization product of farnesol derivatives was formed, albeit in low yield. For these experiments, 0.2 mol% ruthenium tetroxide[11] (generated by *in situ* oxidation of ruthenium(III) chloride) was used as a catalyst and sodium periodate on wet silica[12] was employed as the terminal oxidant.[9] As solvent, a mixture of THF–CH_2Cl_2 (9 : 1) was used.[9] Under these conditions, the cyclization reaction of the 1,5,9-trienes did not go to completion and the majority of the starting material was recovered untouched. Moreover, a varying amount of undesired overoxidation product, ketol **10** (Scheme 3), was detected.

Therefore, optimization of several reaction parameters was necessary to achieve complete conversion of the starting material and to suppress the formation of unwanted overoxidation product (*cf.* Scheme 3). For the optimization process, farnesol derivatives **4a** and **4b** (Scheme 3) were chosen as substrates to allow facile UV-detection during the course of the reaction. It proved to be important to change the solvent mixture (THF–CH_2Cl_2 9 : 1) to THF only in order to achieve complete conversion within

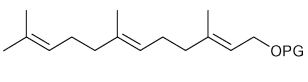
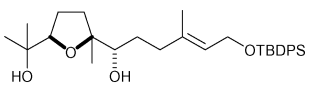
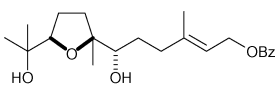
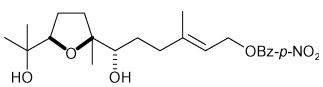
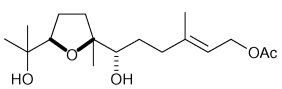
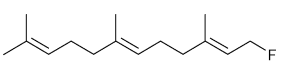
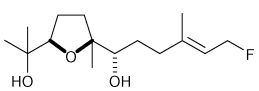
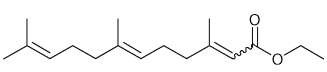
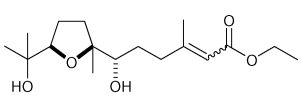


Scheme 3 Optimized reaction conditions for the mono-cyclization of 1,5,9-triene substrates.

24 h. A more polar solvent is generally believed to facilitate hydrolysis of ruthenium-ester intermediates and thus improve reaction rates.[13] Increasing the amount of pre-catalyst from 0.2 to 1 mol% ruthenium(III) chloride and the amount of $NaIO_4$ on wet silica from 2.2 to 3 equivalents shortened the reaction time to only 4–6 h (depending on substrate) at 0 °C. Performing the reaction at ambient temperature allowed complete conversion of starting trienes within 1–4 h, without any loss of selectivity regarding positionselectivity as well as the diol–ketol ratio (**7** : **10**, *cf.* Scheme 3). Moreover, the three stereogenic centres of these products were established with high diastereoselectivity (>95 : 5 dr), and other isomers such as *trans*-THFs were generally not detectable.[9]

Several farnesol derivatives were subjected to this optimized protocol (Table 1). Pleasingly, a range of protecting groups and functional groups were compatible with these conditions. Thus,

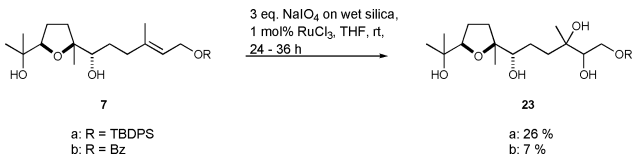
Table 1 Oxidative mono-cyclization of farnesol derived substrates

Entry	Substrate	Product	Reaction time	Yield (%)[a]
1	 PG = TBDPS, Bz, *p*-NO_2-Bz, Ac **4a-d**	 **7a**	4 h	46 (58)
2		 **7b**	1 h	67 (83)
3		 **7c**	2.5 h[b]	58 (75)
4		 **7d**	1 h	44 (60)
5	 **5**	 **8**	24 h	53 (64)
6	 **6**	 **9**	10 min.	69 (85)[c]

[a] All yields are isolated yields; yields in parentheses include the overoxidation product. [b] Reaction was incomplete and therefore quenched as no further conversion was detected by TLC. [c] *E*–*Z* 6 : 1 for the substrate as well as for the product.

farnesol with different protecting groups gave the mono-THF products in good yields. The best result in this series (Table 1, entry 1–4) was obtained using a simple benzoate protecting group. Notably, even farnesyl fluoride could be used as a substrate providing the fluorinated mono-THF **8** in good yield (53/64%). The best yield (69/85%) as well as the highest reaction rate was observed using ethyl farnesoate **6** as a substrate (Table 1, entry 6). In the case of farnesyl acetone, a complex mixture of products was obtained (data not shown). Generally, the cyclization reaction occurred involving the two double bonds with higher electron density leaving the olefin with a neighboring electron-withdrawing substituent unreacted. Cyclization involving the two other double bonds was not observed in any case, clearly demonstrating that for olefins bearing (slightly) different electronic properties a high degree of positionselectivity can be achieved.

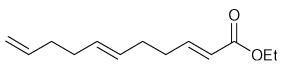
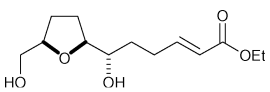
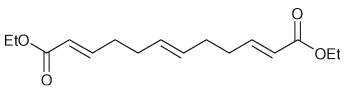
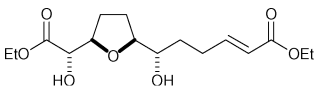
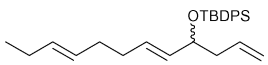
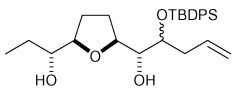
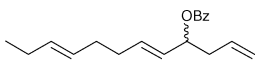
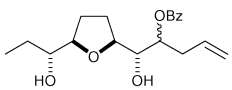
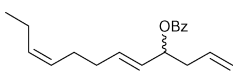
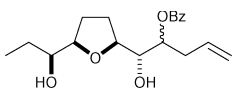
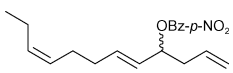
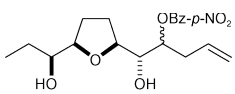
The remarkably low reactivity of the remaining olefin of the mono-cyclization products towards the strong oxidant, ruthenium tetroxide, prompted us to investigate the fate of oxidizable functionality within the primary cyclization products. We therefore resubmitted THF-diols **7a** and **7b** to the cyclization reaction conditions (Scheme 4). Interestingly, both the olefin and the secondary alcohol remained intact for several hours at room temperature. Only at extended reaction times (>24 h) were small amounts of dihydroxylation products **23a** and **23b** detectable (Scheme 4). Taking into account that ruthenium tetroxide catalyzed transformations are highly pH-dependent, the low propensity of oxidative side reactions appears to be a result of the essentially neutral reaction medium.[14] Alcohol oxidations would require high pH-values[15] whereas (flash)-dihydroxylations[16] or ketohydroxylations[17] are efficient only under strongly acidic conditions.



Scheme 4 Oxidative side reaction at extended reaction time.

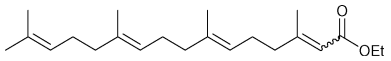
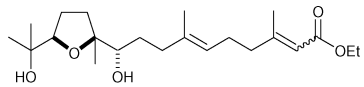
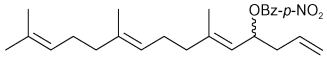
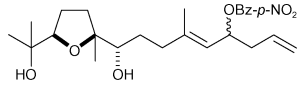
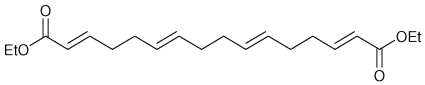
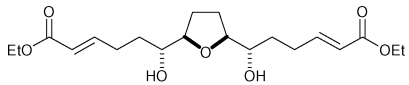
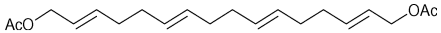
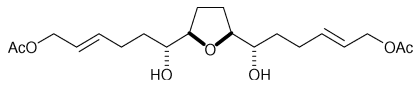
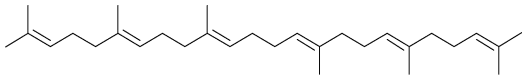
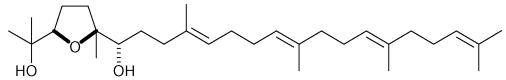
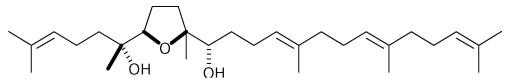
The high levels of selectivity achieved for the oxidative cyclization of oligo-prenyl triene derivatives prompted us to investigate other non-terpenoid trienes. The results of this investigation are summarized in Table 2. As expected, in the case of these mono- and disubstituted alkene substrates, somewhat lower yields were obtained.[18] Similar to ethyl farnesoate, ester and diester substrates underwent rapid conversion providing the corresponding THF-diols in good yield (Table 2, entry 1 and 2). Products **19–22** were

Table 2 Oxidative mono-cyclization of non-terpenoid 1,5,9-trienes

Entry	Substrate	Product	Reaction time	Yield (%)[a]
1	 **11**	 **17**	5 min.	36
2	 **12**	 **18**	5 min.	42
3	 **13**	 **19**	1 h[b]	21
4	 **14**	 **20**	3 h	36
5	 **15**	 **21**	3 h	24
6	 **16**	 **22**	2.5 h[b]	33

[a] All yields are isolated yields. [b] Reaction was incomplete and therefore quenched as no further conversion was detected by TLC.

Table 3 Oxidative mono-cyclization of polyene substrates

Entry	Substrate	Product	Reaction time	Yield (%)[a]
1	 **24**	 **29**	30 min.	19[b]
2	 **25**	 **30**	45 min.	51 (65)[c]
3	 **26**	 **31**	30 min.	43 (59)
4	 **27**	 **32**	1 h	32 (45)[c]
5	 **28**	 **33**	2 h	16 (22)[c]
6		 **34**		5(9)[c]

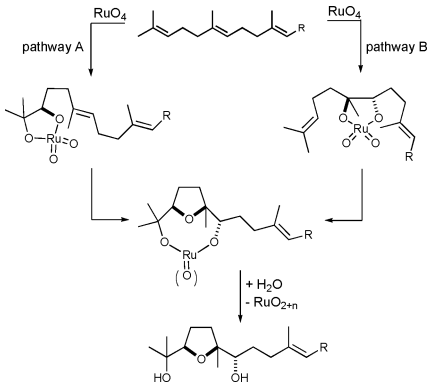
[a] All yields are isolated yields; yields in parenthesis include the overoxidation product. [b] In this case only the ketol could be isolated; [c] Reaction was incomplete and therefore quenched as no further conversion was detected by TLC.

obtained as a 1 : 1 mixture of diastereoisomers concerning the protected alcohol stereogenic center. However, in the case of the benzoate protected alcohols (**20** and **21**), the two diastereoisomers could be separated by column chromatography providing diastereomerically pure material. For all trienes shown in Table 2 no overoxidation product was isolated.

It was also possible to apply our reaction conditions to polyene substrates. As shown in Table 3, tetraenes **24–27** underwent smooth mono-cyclization in good yields. For these tetraenes as well as for the trienes (*cf.* Table 1 and 2), no poly-cyclization products were observed and only a single regioisomer was formed. Interestingly, attachment of suitable acceptor substituents (CO_2Et and CH_2OAc) to the terminal olefin allowed us to reverse the positionselectivity to the two internal double bonds. Thus, synthetically useful C_s-symmetric THF-diols **31** and **32** were accessible in good yields (Table 3, entry 3 and 4). We also investigated the oxidative cyclization of commercially available and inexpensive hexaene, squalene (**28**). For this triterpene, the reaction always stopped after about 30 minutes reaction time leaving most of the starting material unreacted. However, despite the presence of six competing trisubstituted olefins in this substrate, only two constitutional isomers (easily distinguished and assigned by their different MS-fragmentation patterns) were detectable. The mono-THF-diol products **33** and **34**, again accompanied by some ketol product, were isolated in 31% combined yield. It is also noteworthy that cyclization product **33** represents a dideoxy-derivative of quassiol A (**3**) (*cf.* Fig. 1).

Mechanism and rationale for the observed positionselectivity

Mechanistically, we suppose a similar pathway as has been previously suggested for the oxidative cyclization of simple 1,5-dienes.[19] Accordingly, THF-formation results from two consecutive [3 + 2] cycloaddition events between the unsaturated substrate and ruthenium in high oxidation states (+VIII and +VI; *cf.* Scheme 2 and 5). The excellent diastereoselectivity of this transformation is believed to result from the second highly ordered intramolecular addition event. Therefore the reaction leads to the exclusive formation of 2,5-*cis*-substituted THF-products. The positionselectivity observed for the oxidation of these polyunsaturated substrates appears to be primarily controlled by (marginal) electronic differences of the double bonds; with the initial attack to one of the electron rich olefins.[20] At least for higher polyenes, a second element of control has to be taken into consideration in order to account for the experimental findings. Thus, a certain degree of self-coiling of higher hydrocarbons in the polar reaction medium[21] would lead to effective shielding of the internal double bond(s) from oxidative attack and at the same time expose the terminal position for reaction (pathway A in Scheme 5). This "conformational-steric effect" may also be operative for trienes such as farnesol derivatives again leading to preferential attack at the terminal isopropylidene unit. Alternative reaction of the internal double bond (pathway B in Scheme 5) would produce a regioisomeric ruthenium(VI) diester. The subsequent electronically driven cyclization step, however, would render the two possible pathways (A and B in Scheme 5) indistinguishable by formation of identical THF-products. After cyclization, rapid hydrolysis of the ruthenium ester intermediate has to occur to prevent intramolecular oxidative side reactions. Taken together, the initial



Scheme 5 Mechanistic proposal for the oxidative mono-cyclization of polyenes and rationale for the observed positionselectivity.

[3 + 2] cycloaddition to the most electron rich *and* most accessible olefin dictates the positionselectivity of the process. Despite the presence of the strong oxidant ruthenium tetroxide, oxidation of remaining olefins (and other functionality) within the products was slow and easily controlled resulting in a highly chemoselective and practical oxidation procedure.

Conclusions

In summary, we have presented a general and efficient procedure for the oxidative mono-cyclization of 1,5,9-trienes and polyenes. As a result of conformational constraints and relative electronic density within the polyolefin substrates, a high degree of positionselectivity was observed. In addition, the hydroxy-flanked mono-THF products were obtained as single diastereoisomers. This oxidation reaction has been applied to compounds with three, four, and six double bonds to produce mono-cyclized THF-diols with a varying degree of unsaturation. Our current work in this area is focused on synthetic applications of this mono-cyclization methodolgy. The progress of these investigations will be reported in due course.

Experimental

General remarks

All reagents were used as purchased from commercial suppliers. Solvents were purified by conventional methods prior to use. Column chromatography: Merck silica gel 60, 0.040–0.063 mm (230–400 mesh). TLC: pre-coated aluminium sheets, Merck silica gel 60, F_{254}; detection by UV or by cerium/molybdenum solution [phosphomolybdic acid (25 g), $Ce(SO_4)_2 \cdot H_2O$ (10 g), concd H_2SO_4 (60 ml), H_2O (940 ml)]. ^1H and ^{13}C NMR spectra were recorded at room temperature in $CDCl_3$ on a Bruker AC 500 spectrometer. Chemical shifts δ are given relative to TMS as internal standard or relative to the resonance of the solvent (^1H: $CDCl_3$, $\delta = 7.24$ ppm; ^{13}C: $CDCl_3$, $\delta = 77.0$ ppm). Coupling constants are measured in hertz. Mass spectra were recorded with a Varian MAT 771, MAT 112 S. FT-IR spectra were recorded with a Nicolet 5 SXC with DTGS detector. Elemental analyses were recorded on a Perkin-Elmer 2400 CHN elemental analyzer. All substrates were prepared according to standard procedures.

General procedure for the oxidative mono-cyclization of 1,5,9-trienes and polyenes

To a solution of 0.5 mmol of the polyene substrate in 10 ml THF, 2.33 g (3 eq.) $NaIO_4$ on wet silica[12] are added. Then 0.1 ml of a 0.05 M solution of $RuCl_3$ in water are added and the reaction is stirred at room temperature until either complete consumption of the starting material or no further reaction progress is detected by TLC. The reaction is quenched by addition of 1 ml (excess) of i-propanol. After filtration, the solvent is evaporated under reduced pressure. The crude product is purified by silica gel chromatography using a mixture of hexane–ethyl acetate as eluent.

Benzoic acid 6-hydroxy-6-[5-(1-hydroxy-1-methyl-ethyl)-2-methyl-tetrahydro-furan-2-yl]-3-methyl-hex-2-enyl ester (7b). IR (KBr): ν_{max} 3420, 2973, 2930, 2875, 1717, 1451, 1379, 1315, 1273, 1070, 714; NMR: δ_H 1.05 (3 H, s, C(2)–CH_3), 1.14 (3 H, s, C(5)–C(OH)(CH_3)$_2$), 1.21 (3 H, s, C(5)–C(OH)(CH_3)$_2$), 1.53 (2 H, m, C(2)–CH(OH)CH_2), 1.63 (1 H, m, C(3)–H^a), 1.75 (3 H, s, $CH_2C(CH_3)$=CH), 1.86 (3 H, m, C(4)–H_2 and C(3)–H^b), 2.10 (1 H, C(2)–CH(OH)CH_2CH^a), 2.34 (1 H, C(2)–CH(OH)-CH_2CH^b), 3.38 (1 H, m, C(2)–CH(OH)), 3.83 (1 H, m, C(5)–H), 4.82 (2 H, d, J 7.0, CH_2OBz), 5.48 (1 H, m, $CH_2C(CH_3)$=C$H$$CH_2$), 7.41 (2 H, m, Ar), 7.52 (1 H, m, Ar), 8.02 (2 H, m, Ar); δ_C 16.6 ($CH_2C(CH_3)$=CHCH_2), 20.9 (C(5)–C(OH)(CH_3)$_2$), 24.8 (C(2)–CH_3), 26.6 (C(4)), 27.3 (C(5)–C(OH)(CH_3)$_2$), 30.0 (C(2)–CH(OH)CH_2), 35.2 (C(3)), 36.3 (C(2)–CH(OH)CH_2CH_2), 61.8 (CH_2OBz), 71.6 (C(5)–COH(CH_3)$_2$), 77.0 (C(2)–COHCH_2), 85.2 (C(5)), 85.8 (C(2)), 118.6 ($CH_2C(CH_3)$=$CH$$CH_2$), 128.3 (2 × Ar), 129.6 (2 × Ar), 132.8 (Ar), 142.3 ($CH_2C(CH_3)$=CHCH_2), 166.6 (OC(=O)Ar); MS (EI) m/z 377 ([MH]$^+$, 1%), 359 ([M–H_2O]$^+$, 1), 333 ([MH–C_3H_7]$^+$, 1) 318 ([MH–C(CH_3)$_2$OH]$^+$, 1), 275 (1), 251 (2), 239 (2), 233 ([M–(CH_3)$_2$(OH)C–THF–CH_3]$^+$, 1), 227 ([M–BzO–CH_2CH_2]$^+$, 6), 209 ([227-H_2O]$^+$, 3), 143 ([(CH_3)$_2$(OH)–THF–CH_3]$^+$, 100), 125 ([143-H_2O]+, 28) 105 ([PhCO]$^+$, 55), 71 ([THF–H]$^+$, 34), 59 ([C(CH_3)$_2$OH]$^+$, 14), 43 ([C_3H_7]$^+$, 72); HRMS (EI) m/z 377.2342 ([MH]$^+$, $C_{22}H_{33}O_5$ requires 377.2328).

Benzoic acid 6-[5-(1-hydroxy-1-methyl-ethyl)-2-methyl-tetrahydro-furan-2-yl]-3-methyl-6-oxo-hex-2-enyl ester (10b). EA: Found C, 70.1; H, 8.0; $C_{22}H_{30}O_5$ requires C, 70.0; H, 7.8%; IR (KBr): ν_{max} 3441, 2976, 1778, 1717, 1602, 1451, 1381, 1274, 1113, 714; NMR: δ_H 1.04 (3 H, s, C(5)–C(OH)(CH_3)$_2$), 1.23 (3 H, s, C(5)–C(OH)(CH_3)$_2$), 1.34 (3 H, s, C(2)–CH_3), 1.71 (3 H, s, CH_2C-(CH_3)=CH), 1.75 (3 H, m, C(4)–H_2 and C(3)–H^a), 2.17 (1 H, m, C(3)–H^b), 2.27 (2 H, m, C(2)–CH(=O)CH_2), 2.67 (2 H, m, C(2)–CH(OH)CH_2CH_2), 3.18 (1 H, br s, OH), 3.84 (1 H, m, C(5)–H), 4.77 (2 H, d, J 7.0, CH_2OBz), 5.41 (1 H, tq, J 7.0 and 1.2, CH_2C-(CH_3)=C$H$$CH_2$), 7.36 (2 H, m, Ar), 7.47 (1 H, m, Ar), 7.96 (2 H, m, Ar); δ_C 16.6 ($CH_2C(CH_3)$=CHCH_2), 23.7 (C(2)–CH_3), 24.8 (C(5)–C(OH)(CH_3)$_2$), 25.7 (C(4)), 27.5 (C(5)–C(OH)(CH_3)$_2$), 32.8 (C(2)–C(=O)CH_2), 35.1 (C(3)), 35.9 (C(2)–CH(OH)CH_2CH_2), 61.4 (CH_2OBz), 70.5 (C(5)–C(OH)(CH_3)$_2$), 86.6 (C(5)), 88.0 (C(2)), 118.8 ($CH_2C(CH_3)$=$CH$$CH_2$), 128.1 (2 × Ar), 129.4 (3 × Ar), 132.6 (Ar), 140.9 ($CH_2C(CH_3)$=CHCH_2), 166.3 (OC(=O)-Ar), 212.0 (C(2)–C(=O)CH_2); MS (EI) m/z 374 ([M]$^+$, 1%), 252 ([M–PhCO$_2$H]$^+$, 1), 237 ([M–CH_3–PhCO$_2$H]$^+$, 2), 194 ([M–(CH_3)$_2$C(OH)–PhCO$_2$]$^+$, 3), 143 ([(CH_3)$_2$C(OH)–THF–CH_3]$^+$, 100), 125 ([143-H_2O]$^+$, 17), 105 ([PhCO]$^+$, 33).

6-Hydroxy-6-[5-(1-hydroxy-1-methyl-ethyl)-2-methyl-tetrahydro-furan-2-yl]-3-methyl-hex-2-enoic acid ethyl ester (9). EA: Found C, 64.60; H, 10.22; $C_{17}H_{30}O_5$ requires C, 64.94; H, 9.62%; IR (KBr): ν_{max} 3406, 2975, 2934, 2873, 1715, 1647, 1447, 1378, 1225, 1147; NMR: δ_H 1.07 (3 H, s, C(2)–CH_3), 1.11 (3 H, s, C(5)–C(OH)(CH_3)$_2$), 1.19 (3 H, s, C(5)–C(OH)(CH_3)$_2$), 1.22 (3 H, t, J 7.2, C(=O)OCH_2CH_3), 1.53 (2 H, m, C(2)–CHOHCH_2), 1.60 (1 H, m, C(3)–H^a), 1.84 (3 H, m, C(4)–H_2 and C(3)–H^b), 2.11 (3 H, d, J 1.2, CH_2C(CH_3)=CHCO$_2$Et), 2.14 (1 H, C(2)–CH(OH)CH_2CH^a), 2.41 (1 H, C(2)–CH(OH)CH_2CH^b), 3.31 (1 H, m, C(2)–CHOH), 3.80 (1 H, m, C(5)–H), 4.08 (2 H, q, J 7.2, C(=O)OCH_2CH$_3$), 5.64 (1 H, q, J 1.2, $CH_2C(CH_3)$=CH-CO$_2$Et); δ_C 14.2 (C(=O)OCH_2CH$_3$), 18.8 ($CH_2C(CH_3)$=CHCH_2), 21.2 (C(5)–COH(CH_3)$_2$), 24.9 (C(2)–CH_3), 26.6 (C(4)), 27.3 (C(5)–COH(CH_3)$_2$), 29.8 (C(2)–CH(OH)CH_2), 35.2 (C(3)), 37.7 (C(2)–CH(OH)CH_2CH_2), 59.4/59.8 (C(=O)OCH_2CH$_3$), 71.6 (C(5)–C(OH)(CH$_3$)$_2$), 76.7 (C(2)–COHCH$_2$), 85.2 (C(5)), 85.6 (C(2)), 115.6/116.8 ($CH_2C(CH_3)$=CHC(=O)), 159.8 (CH_2C-(CH_3)=CHC(=O)), 166.8 (CHC(=O)OEt); MS (EI) m/z 314 ([M]$^+$, 1%), 299 ([M–CH_3]$^+$, 1), 296 ([M–H_2O]$^+$, 1), 281 ([M–CH_3–H_2O]$^+$, 2), 251 ([M–H_2O–OEt]$^+$, 5), 235 ([296–EtOH]$^+$, 1), 191 (4), 171 ([M–(CH_3)$_2$(OH)C–THF–CH_3]$^+$, 19), 143 ([(CH_3)$_2$(OH)C–THF–CH_3]$^+$, 100), 125 ([143–H_2O]$^+$, 36), 71 ([THF–H]$^+$, 35), 59 ([(CH_3)$_2$COH]$^+$, 19), 43 ([C_3H_7]$^+$, 75); HRMS (EI) m/z 314.2086 ([M]$^+$, $C_{17}H_{30}O_5$ requires 314.2093).

6-[5-(1-Hydroxy-1-methyl-ethyl)-2-methyl-tetrahydro-furan-2-yl]-3-methyl-6-oxo-hex-2-enoic acid ethyl ester (ketol corresponding to compound 9). EA: Found C, 65.00; H, 9.18; $C_{17}H_{28}O_5$ requires C, 65.36; H, 9.03; IR (KBr): ν_{max} 3453, 2977, 2934, 1713, 1649, 1448, 1369, 1226, 1148, 1050; NMR: δ_H 1.07/1.08 (3 H, s, Me), 1.22/1.24 (3 H, t, J 7.2, C(=O)OCH_2CH_3), 1.27/1.28 (3 H, s, Me), 1.38/1.39 (3 H, s, Me), 1.78 (4 H, m, C(3)–H_2 and C(4)–H_2), 2.12 (3 H, d, J 1.3, C(CH_3)=CHCO$_2$Et), 2.22 (1 H, m, C(2)–C(=O)CH_2CH^a), 2.37 (1 H, C(2)–C(=O)CH_2CH^b), 2.72/2.74 (2 H, m, C(2)–C(=O)CH_2), 2.83 (1 H, br s, OH), 3.88 (1 H, m, C(5)–H), 4.09/4.11 (2 H, q, J 7.2, C(=O)OCH_2CH$_3$), 5.62/5.66 (1 H, dt, J 3.7 and 1.3, $CH_2C(CH_3)$=CHCO$_2$Et); δ_C 14.2 (C(=O)-OCH_2CH$_3$), 18.9 ($CH_2C(CH_3)$=CHCH_2), 23.9 (C(5)–COH-(CH_3)$_2$), 24.9 (C(2)–CH_3), 25.9 (C(4)), 27.7/27.8 (C(5)–COH-(CH_3)$_2$), 34.3 (C(2)–C(=O)CH_2), 34.8/35.4 (C(3)), 35.9/36.1 (C(2)–C(=O)CH_2CH_2), 59.6 (C(=O)OCH_2CH$_3$), 70.8 (C(5)–COH-(CH$_3$)$_2$), 86.8 (C(5)), 88.2 (C(2)), 116.0/116.9 ($CH_2C(CH_3)$-=CHC(=O)), 158.0 ($CH_2C(CH_3)$=CHC(=O)), 166.6 (CHC(=O)-OEt), 212.0 (THF–C(=O)CH_2); MS (EI) m/z 312 ([M]$^+$, 1%), 297 ([M–CH_3]$^+$, 1), 267 ([M–OEt]$^+$, 4), 251 ([M–EtOH–CH_3]$^+$, 3), 143 ([(CH_3)$_2$(OH)C–THF–CH_3]$^+$, 100), 125 ([143–H_2O]$^+$, 19), 43 ([C_3H_7]$^+$, 47.6); HRMS (EI) m/z 312.1946 ([M]$^+$, $C_{17}H_{28}O_5$ requires 312.1937).

6-Hydroxy-6-(5-hydroxymethyl-tetrahydro-furan-2-yl)-hex-2-enoic acid ethyl ester (17). IR (KBr): ν_{max} 3416, 2978, 2939, 2876, 1719, 1653, 1369, 1272, 1199, 1044; NMR: δ_H 1.24 (3 H, t, J 7.2, C(=O)OCH_2CH$_3$), 1.55 (2 H, m, C(2)–CH(OH)CH_2), 1.76 (C(4)–H_2), 1.89 (C(3)–H_2), 2.26 (1 H, m, C(2)–CH(OH)CH_2CH^a), 2.39 (1 H, m, C(2)–CH(OH)CH_2CH^b), 3.40 (1 H, m, C(5)–CH(OH)), 3.47 (1 H, dd, J 11.5 and 4.8, C(2)–C(OH)H^a), 3.71 (1 H, dd, J 11.5 and 2.9, C(2)–C(OH)H^b), 3.79 (1 H, m, C(2)–H), 4.04 (C(5)–H), 4.13 (2 H, q, J 7.2, C(=O)OCH_2CH$_3$),

5.80 (1 H, dd, *J* 15.5 and 1.5, CH=C*H*CO_2Et), 6.93 (1 H, dt, *J* 15.5 and 7.0, C*H*=$CHCO_2$Et); δ_C 14.2 (C(=O)OCH_2CH_3), 27.0 (*C*(3)), 28.1 (*C*(4)), 28.3 (C(2)–CH(OH)CH_2CH_2), 32.2 (C(2)–CH(OH)CH_2), 60.2 (C(=O)OCH_2CH_3), 64.9 (C(5)–CH_2OH), 73.3 (C(2)–CH(OH)CH_2CH_2), 80.0 (*C*(5)), 82.9 (*C*(2)), 121.5 (CH=*C*HC(=O)OEt), 148.7 (*C*H=CHC(=O)OEt), 166.7 (*C*(=O)OEt); MS (EI) *m/z* 258 ([M]+, 1%), 240 ([M–H_2O]$^+$, 1), 227 ([M–CH_2OH]$^+$, 4), 213 ([M–OEt]$^+$, 4), 158 ([EtOC(=O)CH=CH-$(CH_2)_2$CH(OH) + H]$^+$, 34), 111 ([158–EtOH]$^+$, 41), 101 ([CH_2OH–THF]$^+$, 76), 57 ([CH–CO_2]$^+$, 100), 29 ([CH_3CH_2]$^+$, 54); HRMS (EI) *m/z* 240.1362 ([M–H_2O]$^+$, $C_{13}H_{20}O_4$ requires 240.1358).

6-[5-(Ethoxycarbonyl-hydroxy-methyl)-tetrahydro-furan-2-yl]-6-hydroxy-hex-2-enoic acid ethyl ester (18). IR (KBr): ν_{max} 3445, 2982, 1736, 1447, 1371, 1271, 1199, 1129, 1043, 863; NMR: δ_H 1.22 (3 H, t, *J* 7.2, CH=CHC(=O)OCH_2CH_3), 1.25 (3 H, t, *J* 7.2, CH(OH)C(=O)OCH_2CH_3), 1.55 (2 H, 2 × m, C(2)–CH-(OH)CH_2), 1.92 (2 H, m, C(3)–H_2), 1.96 (1 H, m, C(4)–H^a), 2.08 (1 H, m, C(4)–H^b), 2.23 (1 H, m, C(2)–CH(OH)CH_2CH^a), 2.36 (1 H, m, C(2)–CH(OH)CH_2CH^b), 3.39 (1 H, m, C(2)–C*H*-(OH)CH_2), 3.79 (1 H, m, C(2)–*H*), 4.06 (1 H, d, *J* 2.0, C(5)–C*H*(OH)CO_2Et), 4.12 (2 H, q, *J* 7.2, CH=CHC(=O)OCH_2CH_3), 4.21 (2 H, m, C(5)–CH(OH)C(=O)OCH_2CH_3), 4.31 (1 H, m, C(5)–*H*), 5.78 (1 H, td, *J* 15.7 and 1.5, CH=C*H*CO_2Et), 6.96 (1 H, dt, *J* 15.7 and 7.0, C*H*=$CHCO_2$Et); δ_C 14.1/14.2 (2 × C-(=O)OCH_2CH_3), 27.5 (*C*(3)), 28.2 (*C*(4)), 28.3 (C(2)–CH(OH)-CH_2CH_2), 32.6 (C(2)–CH(OH)CH_2), 60.1 (CH=CHC(=O)-OCH_2CH_3), 61.8 (C(5)–CH(OH)C(=O)OCH_2CH_3), 72.7 (C(5)–CH(OH)CO_2Et), 73.0 (C(2)–CH(OH)CH_2), 79.8 (*C*(5)), 82.8 (*C*(2)), 121.5 (CH=CHCO_2Et), 148.7 (*C*H=CHCO_2Et), 166.6 (CH=CH*C*(=O)OEt), 173.1 (C(5)–CH(OH)*C*(=O)OEt); MS (EI) *m/z* 330 ([M]$^+$, 1%), 328 ([M–H_2]$^+$, 1), 302 ([M + H–CH_3-CH_2]$^+$, 3), 285 ([M–OEt]$^+$, 11), 239 ([M–CO_2Et–H_2O]$^+$, 12), 227 ([M–CH(OH)CO_2Et]$^+$, 24), 173 ([M–CH(OH)$(CH_2)_2$CH=CH–CO_2Et]$^+$, 41), 158 ([EtOC(=O)CH=CH$(CH_2)_2$CH(OH) + H]$^+$, 53), 111 ([173–OEt–OH]$^+$, 68), 99 ([CH=CHCH_2Et]$^+$, 79), 71 ([THF + H]$^+$, 100); HRMS (EI) *m/z* 330.1669 ([M]$^+$, $C_{16}H_{26}O_7$ requires 330.1679).

Benzoic acid 1-{hydroxy-[5-(1-hydroxy-propyl)-tetrahydro-furan-2-yl]-methyl}-but-3-enyl ester (20). *Complete data for the first diastereoisomer of compound* ***20*****.** IR (KBr): ν_{max} 3418, 2964, 2935, 2878, 1718, 1451, 1275, 1112, 1071, 1027, 970, 917, 713; NMR: δ_H 0.93 (3 H, t, *J* 7.5, C(5)–CH(OH)CH_2CH_3), 1.50 (2 H, m, C(5)–CH(OH)CH_2CH_3), 1.87 (2 H, m, C(4)–H_2), 1.96 (2 H, m, C(3)–H_2), 2.60 (1 H, m, CH_2=CHCH^a), 2.70 (1 H, m, CH_2=CH-CH^b), 3.36 (1 H, m, C(5)–C*H*(OH)CH_2CH_3), 3.67 (1 H, dd, *J* 6.6 and 2.9, C(2)–C*H*(OH)), 3.83 (1 H, dt, *J* 7.0 and 4.0, C(5)–*H*), 4.09 (1 H, dt, *J* 7.0 and 2.9, C(2)–*H*), 5.04 (1 H, m, H_2C=CH-CH_2), 5.11 (1 H, ddd, *J* 17.0 and 3.2 and 1.5, H_2C=$CHCH_2$), 5.19 (1 H, ddd, *J* 7.6 and 6.6 and 3.9, C(2)–CH(OH)C*H*(OBz)CH_2), 5.83 (1 H, m, H_2C=C*H*CH_2), 7.41 (2 H, m, Ar), 7.53 (1 H, m, Ar), 8.02 (2 H, m, Ar); δ_C 10.2 (C(5)–CH(OH)CH_2CH_3), 27.2 (C(5)–CH(OH)CH_2CH_3), 28.1 (*C*(4)), 28.5 (*C*(3)), 34.9 (H_2C=CHCH_2), 74.2 (C(2)–CH(OH)), 74.9 (C(2)–CH(OH)CH(OBz)CH_2), 75.5 (C(5)–CH(OH)CH_2CH_3), 78.4 (*C*(2)), 82.1 (*C*(5)), 118.0 (H_2C=CH–CH_2), 128.3 (2 × Ar), 129.6 (2 × Ar), 133.0 (Ar), 133.6 (Ar), 166.1 (CHO*C*(=O)Ph); MS (EI) *m/z* 305 ([M–CH_3CH_2]$^+$, 1%), 275 ([M–CH_3CH_2CH(OH)]$^+$, 10), 205 ([H_2C=CHCH_2CH(OC-(=O)Ph)CH(OH)]$^+$, 15), 154 ([M–CH_2CH=CH_2–$PhCO_2$–H_2O]$^+$, 9), 129 ([M–205]$^+$, 31), 105 ([PhCO]$^+$, 100), 77 ([C_6H_5]$^+$, 26); HRMS (EI) *m/z* 305.1393 ([M–CH_3CH_2]$^+$, $C_{17}H_{21}O_5$ requires 305.1389).

NMR data for the second diastereoisomer of compound ***20****.* NMR: δ_H 0.88 (3 H, t, *J* 7.4, C(5)–CH(OH)CH_2CH_3), 1.39 (2 H, m, C(5)–CH(OH)CH_2CH_3), 1.78 (1 H, m, C(4)–H^a), 1.87 (2 H, m, C(4)–H^b, C(3)–H^a), 1.96 (1 H, m, C(3)–H^b), 2.57 (2 H, m, CH_2CH=CH_2), 3.30 (1 H, dt, *J* 8.3 and 4.6, C(5)–C*H*(OH)CH_2-CH_3), 3.60 (1 H, dd, *J* 4.0 and 4.0, C(2)–C*H*(OH)), 3.78 (1 H, dt, *J* 7.0 and 4.8, C(5)–*H*), 4.06 (1 H, dt, *J* 7.0 and 4.0, C(2)–*H*), 5.03 (1 H, m, H_2C=$CHCH_2$), 5.13 (1 H, ddd, *J* 17.0 and 3.2 and 1.4, H_2C=$CHCH_2$), 5.28 (1 H, ddd, *J* 7.6 and 5.0 and 4.2, C(2)–CH(OH)C*H*(OBz)CH_2), 5.79 (1 H, m, H_2C=C*H*CH_2), 7.40 (2 H, m, Ar), 7.52 (1 H, m, Ar), 8.03 (2 H, m, Ar); δ_C 10.1 (C(5)–CH-(OH)CH_2CH_3), 27.0 (C(5)–CH(OH)CH_2CH_3), 27.8 (*C*(4)), 28.5 (*C*(3)), 35.4 (H_2C=CHCH_2), 74.3 (C(2)–CH(OH)), 74.6 (C(2)–CH(OH)CH(OBz)CH_2), 75.4 (C(5)–CH(OH)CH_2CH_3), 79.5 (*C*(2)), 82.4 (*C*(5)), 118.2 (H_2C=CH–CH_2), 128.3 (2 × Ar), 129.7 (2 × Ar), 133.0 (Ar), 133.4 (Ar), 166.3 (CHO*C*(=O)Ph); IR and MS data are the same as for the first diastereoisomer.

4-Nitro-benzoic acid 1-{hydroxy-[5-(1-hydroxy-propyl)-tetrahydro-furan-2-yl]-methyl}-but-3-enyl ester (22). IR (KBr): ν_{max} 3402, 2965, 2940, 2879, 1724, 1608, 1528, 1348, 1272, 1104, 1015, 920, 874, 837, 784, 720; NMR: δ_H 0.91/0.94 (3 H, t, *J* 7.4, C(5)–CH(OH)CH_2CH_3), 1.35 (2 H, m, C(5)–CH(OH)CH_2CH_3), 1.75 (1 H, m, C(4)–H^a), 1.98 (3 H, m, C(4)–H^b, C(3)–H_2), 2.55 (2 H, m, CH_2CH=CH_2), 3.58/3.67 (2 H, m, C(2)–C*H*(OH)), 3.68/3.81 (1 H, m, C(5)–C*H*(OH)CH_2CH_3), 3.90 (1 H, m, C(5)–*H*), 4.09 (1 H, m, C(2)–*H*), 5.08 (1 H, m, H_2C=$CHCH_2$), 5.24/5.36 (1 H, m, C(2)–CH(OH)C*H*(OBzNO_2)CH_2), 5.79 (1 H, m, H_2C=C*H*CH_2), 8.22 (4 H, m, Ar); δ_C 10.3 (C(5)–CH(OH)CH_2CH_3), 24.0 (*C*(3)), 26.2/26.4 (C(5)–CH(OH)CH_2CH_3), 29.0 (*C*(4)), 35.0/35.4 (H_2C=CHCH_2), 74.0/74.2 (C(5)–CH(OH)CH_2CH_3), 74.4/74.8 (C(2)–CH(OH)), 75.8/76.0 (C(2)–CH(OH)CH(OBzNO_2)CH_2), 77.7/78.9 (*C*(2)), 82.6/82.8 (*C*(5)), 118.2/118.4 (H_2C=CH–CH_2), 123.4/123.5 (2 × Ar), 130.7/130.8 (2 × Ar), 150.5 (Ar–NO_2), 164.1/164.7 (CHO*C*(=O)Ph); MS (EI) *m/z* 338 ([M–CH_2CH=CH_2]$^+$, 5%), 320 ([M–CH_3CH_2CH(OH)]$^+$, 56), 251 ([320–THF + H]$^+$, 6), 150 (([O_2N–PhCO]$^+$, 100), 129 ([CH_3CH_2CH(OH)–THF]$^+$, 72), 104 ([C_6H_4–CO]$^+$, 35); HRMS (EI) *m/z* 338.1238 ([M–CH_2CH=CH_2]$^+$, $C_{16}H_{20}NO_7$ requires 338.1240).

2-(*tert*-Butyl-diphenyl-silanyloxy)-1-[5-(1-hydroxy-propyl)-tetrahydro-furan-2-yl]-pent-4-en-1-ol (19). IR (KBr): ν_{max} 3366, 3072, 2961, 2931, 2857, 1640, 1589, 1428, 1111, 911, 822, 740, 702, 611, 506; NMR: δ_H 0.95 (3 H, 2 × t, *J* 7.4, C(5)–CH(OH)CH_2-CH_3), 1.05 (9 H, 2 × s, $SiC(CH_3)_3$), 1.43 (2 H, m, C(5)–CH(OH)-CH_2CH_3), 1.72 (4 H, m, C(3)–H_2 and C(4)–H_2), 2.20 (1 H, m, H_2-C=CHCH_2), 2.39 (1 H, m, H_2C=CHCH_2), 3.21/3.26 (1 H, 2 × m, C(2)–CH(OH)C*H*(OR)CH_2), 3.42 (1 H, m, C(2)–C*H*(OH)), 3.71/3.80 (1 H, m, C(5)–C*H*(OH)CH_2CH_3), 3.84 (1 H, m, C(5)–*H*), 4.03/4.10 (1 H, 2 × m, C(2)–*H*), 5.67/5.79 (1 H, 2 × dddd, *J* 16.9 and 10.3 and 7.6 and 6.6/*J* 17.2 and 10.3 and 7.4 and 6.9, H_2C=$CHCH_2$), 7.41 (6 H, m, Ar), 7.70 (4 H, m, Ar); δ_C 10.1/10.3 (C(5)–CH(OH)CH_2CH_3), 19.4 ($SiC(CH_3)_3$, 27.1 ($SiC(CH_3)_3$), 27.0/27.2 C(5)–CH(OH)CH_2CH_3), 27.9/28.0 (*C*(4)), 28.0/28.1 (*C*(3)), 37.1/37.7 (H_2C=CHCH_2), 73.9/74.0 (*C*(2)), 75.0/75.5 (C(2)–CH(OH)), 75.6/75.7 (C(2)–CH(OH)CH-(OR)CH_2), 77.8/78.8 (*C*(5)), 82.0/82.2 (C(5)–CH(OH)),

117.2/117.6 (H_2C=$CHCH_2$), 127.4/127.5 (2 × Ar), 127.6/127.8 (2 × Ar), 129.7 (Ar), 129.8/129.9 (Ar), 133.4/133.6 (Ar), 133.7/133.9 (Ar), 134.0/134.8 (H_2C=$CHCH_2$), 135.8/136.0 (2 × Ar), 136.0 (2 × Ar); MS (EI) *m/z* 411 ($[M–C_4H_9]^+$, 8%), 333 ($[M–C_4H_9–C_6H_6]^+$, 28), 285 ($[333–CH_2CH=CH_2–CH_3CH_2]^+$, 17), 199 ($[Ph_2SiOH]^+$, 100), 135 ($[M–^tBuPh_2SiOH–CH_2CH=CH_2–2H_2O]^+$, 53), 71 ($[THF + H]^+$, 46), 57 ($[C_4H_9]^+$, 55); HRMS (EI) *m/z* 411.1988 ($[M–C_4H_9]^+$, $C_{24}H_{31}O_4Si$ requires 411.1992).

4-Nitro-benzoic acid 1-allyl-6-hydroxy-6-[5-(1-hydroxy-1-methyl-ethyl)-2-methyl-tetrahydro-furan-2-yl]-3-methyl-hex-2-enyl ester (30). EA: Found C, 65.15; H, 7.84, N, 2.95; $C_{25}H_{35}NO_7$ requires C, 65.06; H, 7.64; N, 3.03%; IR (KBr): ν_{max} 3433, 2972, 2932, 2971, 1721, 1608, 1528, 1273, 784, 720; NMR: δ_H 1.05/1.08 (3 H, 2 × s, Me), 1.12 (3 H, 2 × s, Me), 1.18/1.20 (3 H, 2 × s, Me), 1.49 (2 H, m, C(2)–C(OH)CH_2), 1.60 (1 H, m, C(3)–H^a), 1.77 (3 H, t, *J* 1.5, C(2)–CH_3), 1.84 (3 H, m, C(3)–H^b and C(4)–H_2), 2.07 (1 H, m, C(2)–C(OH)CH$_2$CH^a), 2.29 (1 H, m, C(2)–C(OH)CH$_2$CH^b), 2.44 (1 H, m, CH_2CH=CH$_2$), 2.50 (1 H, m, CH_2-CH=CH$_2$), 3.33 (1 H, m, C(2)–CH(OH)), 3.81 (1 H, m, C(5)–H), 5.05 (1 H, m, CH$_2$CH=CH_2), 5.10 (1 H, m, CH$_2$CH=CH_2), 5.27 (1 H, dq, *J* 9.1 and 1.2, CH$_2$C(CH$_3$)=CHCH(OR)CH$_2$-CH=CH$_2$), 5.75 (2 H, m, CH(OR)CH$_2$CH=CH$_2$), 8.16 (2 H, m, Ar), 8.22 (2 H, dt, *J* 8.9 and 2.0, Ar); δ_C 16.9/17.0 (CH$_2$C-(CH$_3$)=CH), 20.8/21.0 (Me), 24.9 (Me), 26.6 (*C*(4)), 27.3 (Me), 29.9/30.0 (C(2)–C(OH)CH$_2$), 35.1 (*C*(3)), 36.3 (C(2)–C(OH)-CH$_2$$CH_2$), 39.3/39.4 ($CH_2$CH=CH$_2$), 71.5 (C(5)–$C$(OH)(CH$_3$)$_2$), 72.5/72.6 ($C$H(OR)CH$_2$CH=CH$_2$), 76.7 (C(2)–$C$H(OH), 85.1 (*C*(2)), 85.7 (*C*(5)), 118.1 (CH$_2$CH=CH$_2$), 122.4/122.5 (CH$_2$-C(CH$_3$)=CH), 123.4 (2 × Ar), 130.6 (2 × Ar), 133.0 (CH$_2$-CH=CH$_2$), 136.1 (Ar), 140.6/141.7 (CH$_2$$C$(CH$_3$)=CH), 150.4 (Ar), 164.0 (O$_2$N–Ph–C(=O)OR); MS (EI) *m/z* 462 ($[MH]^+$, 1%), 443 ($[M–H_2O]^+$, 1), 294 ($[M–O_2N–Ph–CO_2H]^+$, 2), 279 ([294–Me]$^+$, 9), 235 ($[M–O_2N–PhCO–C(CH_3)_2OH]^+$, 12), 167 ($[O_2N–Ph–CO_2H]^+$, 58), 143 ($[(CH_3)_2(OH)C–THF–CH_3]^+$, 100), 125 ([143–H$_2$O]$^+$, 64); HRMS (EI) *m/z* 443.2311 ($[M–H_2O]^+$, $C_{25}H_{33}NO_6$ requires 443.2308).

4-Nitro-benzoic acid 1-allyl-6-[5-(1-hydroxy-1-methyl-ethyl)-2-methyl-tetrahydro-furan-2-yl]-3-methyl-6-oxo-hex-2-enyl ester (ketol corresponding to compound 30). IR (KBr): ν_{max} 3445, 2976, 2930, 1718, 1608, 1529, 1348, 1275, 1117, 1102, 721; NMR: δ_H 1.04/1.07 (3 H, s, Me), 1.26 (3 H, s, Me), 1.37 (3 H, s, Me), 1.70 (1 H, m, C(3)–H^a), 1.77 (3 H, s, Me), 1.78 (2 H, m, C(2)–C-(=O)CH_2), 2.19 (1 H, m, C(3)–H^b), 2.28 (2 H, m, C(4)–H_2), 2.44 (1 H, m, C(2)–C(=O)CH$_2$CH^a), 2.50 (1 H, m, C(2)–C(=O)-CH$_2$CH^b), 2.65 (2 H, m, CH_2CH=CH$_2$), 3.05 (1 H, br s, OH), 3.87 (1 H, m, C(5)–H), 5.06 (1 H, m, CH$_2$CH=CH_2), 5.09 (1 H, m, CH$_2$CH=CH_2), 5.24 (1 H, m, CH$_2$C(CH$_3$)=CHCH(OR)), 5.74 (2 H, m, CH(OR)CH$_2$CH=CH$_2$), 8.16 (2 H, dt, *J* 9.0 and 2.1, Ar), 8.24 (2 H, dt, *J* 9.0 and 2.1, Ar); δ_C 17.1 (CH$_2$-C(CH$_3$)=CH), 23.9 (Me), 24.8 (Me), 25.8 (*C*(4)), 27.8 (Me), 33.0 (C(2)–C(=O)CH$_2$), 35.3 (*C*(3)), 36.1 (C(2)–C(=O)CH$_2$$CH_2$), 39.3 ($CH_2$CH=CH$_2$), 70.7 (C(5)–$C$(OH)(CH$_3$)$_2$), 72.2 ($C$H(OR)-CH$_2$CH=CH$_2$), 86.8 (*C*(5)), 88.2 (*C*(2)), 118.3 (CH$_2$CH=CH$_2$), 122.8 (CH$_2$C(CH$_3$)=CH), 123.4 (2 × Ar), 130.6 (2 × Ar), 132.8 CH$_2$$C$H=CH$_2$), 136.0 (Ar), 140.5 (CH$_2$$C$(CH$_3$)=CH), 150.4 (Ar), 163.9 (O$_2$N–Ph–C(=O)OR); MS (EI) *m/z* 460 ($[M + H]^+$, 1%), 400 ($[M–(CH_3)_2(OH)C]^+$, 1), 277 ($[M–O_2N–Ph–CO–H_2O–CH_3]^+$, 4), 234 ($[M–O_2N–Ph–CO_2–H_2O–CH_2CH=CH_2]^+$, 5), 178 ($[M–O_2N–Ph–(CH_3)_2(OH)C–THF–CH_3–O]^+$, 6), 167 ($[M + H–O_2N–Ph–CO–(CH_3)_2(OH)C–THF–CH_3]^+$, 6), 143 ($[(CH_3)_2(OH)C–THF–CH_3]^+$, 100), 125 ([143–H$_2$O]$^+$, 25); HRMS (EI) *m/z* 400.1766 ($[M–C(CH_3)_2OH]^+$, $C_{22}H_{26}O_6N$ requires 400.1760).

6-[5-(5-Ethoxycarbonyl-1-hydroxy-pent-4-enyl)-tetrahydro-furan-2-yl]-6-hydroxy-hex-2-enoic acid ethyl ester (31). IR (KBr): ν_{max} 3431, 2978, 2937, 2875, 1713, 1653, 1446, 1369, 1044, 981, 922, 854, 714; NMR: δ_H 1.22 (6 H, t, *J* 7.2, CO$_2$CH$_2$-CH_3), 1.54 (2 H, m, C(2)–CH(OH)CH_2), 1.60 (2 H, m, C(2)–CH-(OH)CH_2), 1.72 (2 H, m, C(3)–H^a), 1.88 (2 H, m, C(3)–H^b), 2.26 (2 H, m, C(2)–CH(OH)CH$_2$CH_2), 2.37 (2 H, m, C(2)–CH-(OH)CH$_2$CH_2), 3.38 (2 H, m, (C(2)–CH(OH)CH$_2$), 3.77 (2 H, m, C(2)–H), 4.11 (4 H, q, *J* 7.2, CO$_2$CH_2CH$_3$), 5.79 (2 H, dt, *J* 15.5 and 1.5, CH=CHCO$_2$Et), 6.91 (2 H, dt, *J* 15.5 and 6.9, CH=CHCO$_2$Et); δ_C 14.1 (CO$_2$CH$_2$$CH_3$), 27.9 (*C*(3)), 28.3 (C(2)–CH(OH)CH$_2$$CH_2$), 32.3 (C(2)–CH(OH)$CH_2$), 60.1 (CO$_2$$CH_2$-CH$_3$), 73.1 (C(2)–$C$H(OH)), 82.5 (*C*(2)), 121.5 (CH=CHCO$_2$Et), 148.7 (CH=CHCO$_2$Et), 166.6 (CO$_2$Et); MS (EI) *m/z* 384 ($[M]^+$, 1%), 366 ($[M–H_2O]^+$, 1), 339 ($[M–OEt]^+$, 7), 293 ($[M–OEt–EtOH]^+$, 25), 258 ($[MH–(CH_2)_2CH=CHC(=O)OEt]^+$, 10) 228 ($[EtOC(=O)CH=CH–(CH_2)_2CH(OH)–THF + H]^+$, 51), 181 ($[EtOC(=O)CH=CH–(CH_2)_2CH(OH)THF–EtOH]^+$, 84), 157 ([M–228]$^+$, 100), 135 ($[EtOC(=O)CH=CH(CH_2)_2CH(OH)THF–EtOH–CO–H_2O]^+$, 38), 111 ([157–EtOH]$^+$, 76); HRMS (EI) *m/z* 384.2144 ($[M]^+$, $C_{20}H_{32}O_7$ requires 384.2148).

6-[5-(5-Ethoxycarbonyl-1-hydroxy-pent-4-enyl)-tetrahydro-furan-2-yl]-6-oxo-hex-2-enoic acid ethyl ester (ketol corresponding to compound 31). IR (KBr): ν_{max} 3437, 2981, 2939, 1717, 1654, 1368, 1271, 1198, 1043, 979, 855; NMR: δ_H 1.21 (6 H, 2 × t, *J* 7.2, C(=O)OCH$_2$CH_3), 1.55 (1 H, m, C(5)–CH(OH)CH_2), 1.70 (2 H, m, C(5)–CH(OH)CH_2 and C(4)–H^a), 1.92 (2 H, m, C(4)–H^b and C(3)–H^a), 2.20 (1 H, m, C(3)–H^b), 2.27 (1 H, m, C(5)–CH(OH)CH$_2$CH^a), 2.42 (3 H, m, C(5)–CH(OH)CH$_2$CH^b and C(2)–C(=O)CH$_2$CH_2), 2.59 (2 H, m, C(2)–C(=O)CH_2), 3.38 (1 H, m, C(5)–CH(OH)CH$_2$), 3.43 (1 H, br s, OH), 3.90 (1 H, m, C(5)–H), 4.10 (4 H, 2 × q, *J* 7.2, C(=O)OCH_2CH$_3$), 4.44 (1 H, dd, *J* 8.9 and 4.7, C(2)–H), 5.78 (2 H, m, CH=CHCO$_2$Et), 6.83 (1 H, ddd, *J* 15.4 and 6.7 and 6.7, CH=CHCO$_2$Et), 6.92 (1 H, ddd, *J* 15.4 and 6.5 and 6.5, CH=CHCO$_2$Et); δ_C 14.1 (2 C, C(=O)OCH$_2$$CH_3$), 25.4 (C(2)–C(=O)CH$_2$$CH_2$), 26.7 (*C*(4)), 28.4 (C(5)–CH(OH)CH$_2$$CH_2$), 29.2 (*C*(3)), 32.9 (C(5)–CH(OH)CH$_2$), 36.6 (C(2)–C(=O)CH$_2$), 60.0 (C(=O)OCH$_2$CH$_3$), 60.2 (C(=O)OCH$_2$CH$_3$), 71.4 (C(5)–CH(OH)CH$_2$), 82.6 (*C*(5)), 83.9 (*C*(2)), 121.5 (CH(OH)(CH$_2$)$_2$CH=CH), 122.2 (C(=O)-(CH$_2$)$_2$CH=CH), 146.5 (C(=O)(CH$_2$)$_2$$C$H=CH), 148.6 (CH-(OH)CH$_2CH_2$ CH=CH), 166.2 (*C*(=O)OEt), 166.5 (*C*(=O)OEt), 210.2 (C(2)–*C*(=O)CH$_2$); MS (EI) *m/z* 382 ($[M]^+$, 5%), 354 ($[M–Et + H]^+$, 3), 337 ($[M–OEt]^+$, 11), 291 ($[M–CO_2Et–H_2O]^+$, 11), 227 ($[M–C(=O)(CH_2)_2CH=CHCO_2Et]^+$, 79), 181 ([227–EtOH]$^+$, 100), 135 ($[227–CO_2Et–H_2O]^+$, 51), 99 ([EtOC(=O)CH=CH]$^+$, 80), 71 ([THF + H]$^+$, 77), 29 ([CH$_2$CH$_3$]$^+$, 71); HRMS (EI) *m/z* 381.1894 ($[M–H]^+$, $C_{20}H_{29}O_7$ requires 381.1913).

1-[5-(1-Hydroxy-1,5-dimethyl-hex-4-enyl)-2-methyl-tetrahydro-furan-2-yl]-5,9,13-trimethyl-tetradeca-4,8,12-trien-1-ol (34). IR (KBr): ν_{max} 3404, 2967, 2925, 2856, 1449, 1376, 1076; NMR: δ_H 1.05 (3 H, s, Me), 1.11 (3 H, s, Me), 1.45 (3 H, m, C(2)–CH(OH)CH_2) and C(5)–C(CH$_3$)(OH)CH^a), 1.57 (6 H, s, 2 × Me), 1.58 (1 H, m,

C(5)–CH(CH$_3$)(OH)CH^b), 1.59 (3 H, s, Me), 1.60 (3 H, s, Me), 1.65 (6 H, s, 2 × Me), 1.86 (3 H, m, C(3)–H_2 and C(4)–H^a), 1.94 and 2.03 (12 H, 2 × m, 5 × CH$_2$ and C(4)–H^b and C(2)–CH-(OH)CH$_2$CH^a), 2.22 (1 H, m, C(2)–CH(OH)CH$_2$CH^b), 3.37 (1 H, dd, J 9.8 and 2.3, C(2)–CH(OH)CH$_2$), 3.86 (1 H, m, C(5)–H), 5.09 (4 H, m, 4 × C=CH); δ_C 15.9 (Me), 16.0 (Me), 17.6 (2 × Me), 20.8 (Me), 21.8 (Me), 22.4 (CH$_2$), 24.9 (CH$_2$), 25.6 (2 × Me), 26.4 (C(4)), 26.6 (CH$_2$), 26.7 (CH$_2$), 32.2 (C(2)–CH(OH)CH$_2$), 35.0 (C(3)), 39.7 (2 × CH$_2$), 40.1 (C(5)–C(CH$_3$)(OH)CH$_2$), 73.2 (C(5)–C(CH$_3$)(OH)CH$_2$), 77.1 (C(2)–CH(OH)CH$_2$), 83.8 (C(5)), 85.6 (C(2)), 124.0 (C=CH), 124.2 (C=CH), 124.4 (C=CH), 124.6 (C=CH), 131.2 ((CH$_3$)$_2$$C$=CH), 131.5 ((CH$_3$)$_2$$C$=CH), 134.9 (CH$_2$$C$(CH$_3$)=CH), 135.7 (CH$_2$$C$(CH$_3$)=CH); MS (EI) m/z 460 ([M]$^+$, 2%), 442 ([M–H$_2$O]$^+$, 6), 373 ([M–H$_2$O–(CH$_3$)$_2$-C=CHCH$_2$]$^+$, 12), 360 ([M–(CH$_3$)$_2$C=CH(CH$_2$)$_2$–OH]$^+$, 10), 278 ([360–(CH$_3$)$_2$C=CHCH]$^+$, 23), 247 ([C(=O)(CH$_2$)$_2$CH=C(CH$_3$)-(CH$_2$)$_2$CH=C(CH$_3$)(CH$_2$)$_2$CH=C(CH$_3$)$_2$]$^+$, 22), 227 ([(CH$_2$)$_2$C-(CH$_3$)(OH)–THF(CH$_3$)–CH(OH)(CH$_2$)$_2$CH]$^+$, 16), 211 ([(CH$_3$)$_2$)-C=CH(CH$_2$)$_2$C(CH$_3$)–(OH)–THF–CH$_3$]$^+$, 62), 135 ([247–(CH$_3$)$_2$-C=CHCH$_2$–C=O–CH$_3$]$^+$, 35), 69 ([(CH$_3$)$_2$C=CHCH$_2$]$^+$, 100).

1-[5-(1-Hydroxy-1-methyl-ethyl)-2-methyl-tetrahydro-furan-2-yl]-4,9,13,17-tetramethyl-octadeca-4,8,12,16-tetraen-1-ol (33). IR (KBr): ν_{max} 3416, 2968, 2926, 1448, 1376, 1080, 951; NMR: δ_H 1.09 (3 H, s, Me), 1.13 (3 H, s, Me), 1.20 (3 H, s, Me), 1.48 (2 H, m, C(2)–CH(OH)CH_2), 1.56 (6 H, s, 2 × Me), 1.58 (3 H, s, Me), 1.59 (1 H, m, C(3)–H^a), 1.64 (6 H, s, 2 × Me), 1.86 (3 H, m, C(3)–H^b and C(4)–H_2), 1.98 (13 H, m, 6 × CH_2 and C(2)–CH(OH)CH$_2$CH^a), 2.23 (1 H, m, C(2)–CH(OH)CH$_2$CH^b), 3.36 (1 H, m, C(2)–CH(OH)CH$_2$), 3.82 (1 H, m, C(5)–H), 5.08 (3 H, m, 3 × C=CH), 5.17 (1 H, m, C=CH); δ_C 15.9 (2 × Me), 16.0 (Me), 21.0 (Me), 24.8 (Me), 25.6 (2 × Me), 26.7 (C(4)), 27.3 (Me), 28.2 (2 × CH$_2$), 30.3 (C(2)–CH(OH)CH$_2$), 35.1 (C(3)), 36.6 (C(2)–CH-(OH)CH$_2$$CH_2$), 39.7 (2 × CH$_2$), 71.5 (C(5)–$C$(OH)(CH$_3$)$_2$), 77.2 (C(2)–$C$H(OH)CH$_2$), 85.2 ($C$(5)), 85.8 ($C$(2)), 124.1 (C=$C$H), 124.2 (C=$C$H), 124.3 (C=$C$H), 124.6 (C=$C$H), 131.1 ((CH$_3$)$_2$-$C$=CH), 134.8 (CH$_2$$C$(CH$_3$)=CH), 135.0 (CH$_2$$C$(CH$_3$)=CH), 135.1 (CH$_2$$C$(CH$_3$)=CH); MS (EI) m/z 460 ([M]$^+$, 5%), 442 ([M–H$_2$O]$^+$, 6), 425 ([M–H$_2$O–OH]$^+$, 3), 373 ([M–H$_2$O–(CH$_3$)$_2$-C=CHCH$_2$]$^+$, 2), 227 ([(CH$_3$)$_2$(OH)C–THF(CH$_3$)CH(OH)-(CH$_2$)$_2$)C(CH$_3$)–H]$^+$, 14), 143 ([(CH$_3$)$_2$(OH)C–THF–CH$_3$]$^+$, 100), 125 ([143–H$_2$O]$^+$, 18), 69 ([(CH$_3$)$_2$C=CHCH$_2$]$^+$, 69); HRMS (EI) m/z 460.3921 ([M]$^+$, $C_{30}H_{52}O_3$ requires 460.3916).

1-[5-(1-Hydroxy-1,5-dimethyl-hex-4-enyl)-2-methyl-tetrahydro-furan-2-yl]-5,9,13-trimethyl-tetradeca-4,8,12-trien-1-one (ketol corresponding to compound 34). IR (KBr): ν_{max} 3435, 2973, 2933, 1713, 1452, 1377, 1154, 1108, 1063; NMR: δ_H 1.01 (3 H, s, Me), 1.19 (3 H, s, Me), 1.37 (3 H, s, Me), 1.51 (1 H, m, C(5)–C(CH$_3$)(OH)CH^a), 1.55 (3 H, s, Me), 1.56 (3 H, s, Me), 1.58 (3 H, s, Me), 1.64 (6 H, s, 2 × Me), 1.66 (1 H, m, C(5)–C(CH$_3$)(OH)CH^b), 1.76 (3 H, m, C(4)–H_2 and C(3)–H^a), 1.98 (10 H, m, 5 × CH_2), 2.23 (3 H, m, C(3)–H^b and C(2)–C(=O)CH$_2$CH_2), 2.51 (2 H, m, C(2)–C(=O)CH_2), 3.22 (1 H, br s, OH), 3.91 (1 H, m, C(5)–H), 5.05 (3 H, m, 3 × C=CH), 5.10 (1 H, m, C=CH); δ_C 15.9 (Me), 16.0 (Me), 17.6 (2 × Me), 21.6 (Me), 22.3 (C(2)–C(=O)CH$_2$$CH_2$), 22.6 ($CH_2$), 23.8 (Me), 25.5 (C(4)), 25.6 (2 × Me), 26.5 (CH$_2$), 26.7 (CH$_2$), 29.4 (CH$_2$), 35.9 (C(3)), 37.2 (C(2)–C(=O)CH$_2$), 39.6 (CH$_2$), 39.7 (CH$_2$), 40.5 (C(5)–C(CH$_3$)(OH)CH$_2$), 72.3 (C(5)–C(CH$_3$)(OH)CH$_2$), 85.5 (C(5)), 88.0 (C(2)), 122.5 (C=CH), 124.0 (C=CH), 124.3 (C=CH), 124.7 (C=CH), 131.2 (C=CH), 135.0 (2 × C=CH), 136.6 (C=CH); MS (EI) m/z 458 ([M]$^+$, 2%), 440 ([M–H$_2$O]$^+$, 2), 371 ([M–H$_2$O–(CH$_3$)$_2$C=CHCH$_2$]$^+$, 1), 332 ([M–(CH$_3$)$_2$C=CH(CH$_2$)$_2$–C(OH)(CH$_3$) + H]$^+$, 2), 211 ([(CH$_3$)$_2$C=CH-(CH$_2$)$_2$C(OH)(CH$_3$)–THF–CH$_3$]$^+$, 63), 193 ([211–H$_2$O]$^+$, 19), 69 ([(CH$_3$)$_2$C=CHCH$_2$]$^+$, 100), 43 ([C$_3$H$_7$]$^+$, 64).

1-[5-(1-Hydroxy-1-methyl-ethyl)-2-methyl-tetrahydro-furan-2-yl]-4,9,13,17-tetramethyl-octadeca-4,8,12,16-tetraen-1-one (ketol corresponding to compound 33). IR (KBr): ν_{max} 3437, 2974, 2932, 1715, 1453, 1379; NMR: δ_H 1.06 (3 H, s, Me), 1.26 (3 H, s, Me), 1.38 (3 H, s, Me), 1.56 (12 H, s, 4 × Me), 1.64 (3 H, s, Me), 1.75 (3 H, m, C(3)–H^a and C(4)–H_2), 1.99 (12 H, m, (CH$_3$)$_2$C=CH-(CH_2)$_2$C(CH$_3$)=CH(CH_2)$_2$C(CH$_3$)C=CH(CH_2)$_2$), 2.20 (3 H, m, C(2)–C(=O)CH_2 and C(3)–H^b), 2.60 (2 H, m, C(2)–C(=O)CH$_2$-CH_2), 3.20 (1 H, br s, OH), 3.87 (1 H, m, C(5)–H), 5.07 (4 H, m, (CH$_3$)$_2$C=CH(CH$_2$)$_2$C(CH$_3$)=CH(CH$_2$)$_2$C(CH$_3$)C=CH-(CH$_2$)$_2$CH=C(CH$_3$)CH$_2$); δ_C 15.9 (Me), 16.0 (Me), 16.1 (Me), 17.6 (Me), 23.9 (Me), 24.2 (Me), 25.6 (Me), 25.8 (C(3)), 26.6 (CH$_2$), 26.7 (CH$_2$), 27.8 (CH$_2$), 28.0 (Me), 28.2 (CH$_2$), 33.3 (C(2)–C(=O)CH$_2$), 35.9 (C(2)–C(=O)CH$_2$$CH_2$), 36.1 ($C$(4)), 39.7 (2 × CH$_2$), 70.5 ((CH$_3$)$_2$C(OH)), 86.8 (C(5)), 88.2 (C(2)), 124.0 (CH=C), 124.2 (CH=C), 124.3 (CH=C), 125.0 (CH=C), 131.1 (CH=C), 133.7 (CH=C), 134.8 (CH=C), 135.2 (CH=C), 213.0 (C(2)–C(=O)CH$_2$); (EI) m/z 458 ([M]$^+$, 1%), 389 ([M–(CH$_3$)$_2$C=CHCH$_2$]$^+$, 1), 225 ([(CH$_3$)$_2$(OH)C–THF(CH$_3$)–C(=O)-(CH$_2$)$_2$C(CH$_3$)–H]$^+$, 5), 143 ([(CH$_3$)$_2$(OH)C–THF–CH$_3$]$^+$, 100), 125 ([M–H$_2$O]$^+$, 32), 69 ([(CH$_3$)$_2$C=CHCH$_2$]$^+$, 100); HRMS (EI) m/z 458.3754 ([M]$^+$, $C_{30}H_{50}O_3$ requires 458.3760).

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