Pergamon

Tetrahedron: *Asymmetry* 12 (2001) 3223–3234

TETRAHEDRON: *ASYMMETRY*

Novel chiral lipoxygenase substrates: design and synthesis. Part 2

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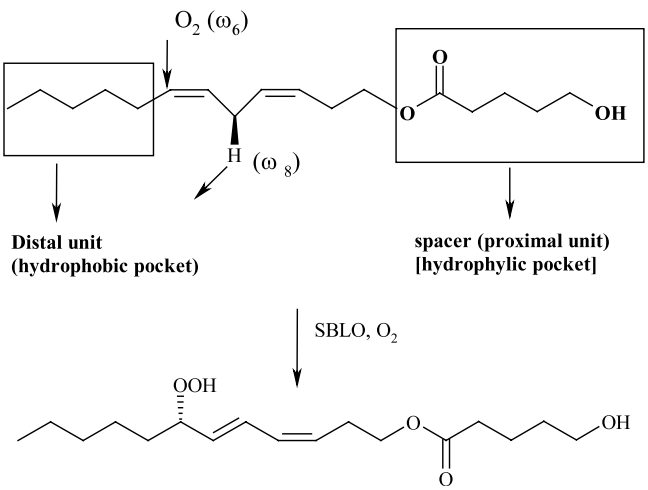
Received 5 October 2001; accepted 28 December 2001

Abstract—A series of novel lipoxygenase substrates carrying a spacing modifier with a non-ionic hydroxyl terminus have been synthesized in an enantioselective fashion. One of the methylene hydrogens (flanked by the *cis*,*cis*-pentadienyl moiety) is replaced by alkyl, aryl and hydroxyl groups. The key steps in the synthesis involved enzymatic transesterification of 1,3-propanediol derivatives and two consecutive *cis*-selective Wittig olefinations.

1. Introduction

The lipoxygenases constitute a family of lipid peroxidizing enzymes, which are involved in the biosynthesis of inflammatory mediators in cell differentiation and atherogenesis.[1] They catalyze the stereospecific and regiospecific incorporation of molecular oxygen into the (1*Z*,4*Z*)-pentadienyl moiety of polyunsaturated fatty acids.[2] Previous studies reveal that substrates with a single ω-6-(1*Z*,4*Z*)-pentadienyl moiety carrying spacing modifiers with a non-ionic hydroxyl terminus are well recognized by soybean lipoxygenase (Scheme 1).[3] The stereospecificity of lipoxygenase is characterized by the stereoselective removal of pro-(*S*) hydrogen from the prochiral methylene center.[4] In our earlier communication[5] we described the synthesis of some useful intermediates, which can lead to the total synthesis of novel lipoxygenase substrates where pro-(*R*) and pro-(*S*) hydrogens are replaced by a hydroxyl group. As a continuation of our previous study, we wish to report herein the asymmetric synthesis of some lipoxygenase substrates where the pro-(*R*) and pro-(*S*) hydrogens are replaced by several groups (Scheme 2). At the prochiral methylene center we introduced different alkyl, aryl and hydroxyl groups in an enantioselective fashion.



Scheme 1. Substrate recognition by SBLO.

2. Results and discussion

2.1. Retrosynthesis

Careful retrosynthetic analysis of **1a**–**i** reveals (Scheme 2) that (*Z*,*Z*)-dienols **9a**–**i** serve as very good intermediates and are in turn easily accessible from 2-substituted 1,3-propanediol derivatives. First of all our main aim is to construct the 2-substituted 1,3-propanediol derivatives in an asymmetric fashion. For this we adopted enzymatic transesterification of racemic 1,3-propanediol derivatives. Secondly, to construct the (*Z*,*Z*)-diene moiety we adopted a *cis*-selective Wittig olefination strategy. Finally the attachment of a hydroxy protected acid as a prosthetic modifier completes the synthesis.

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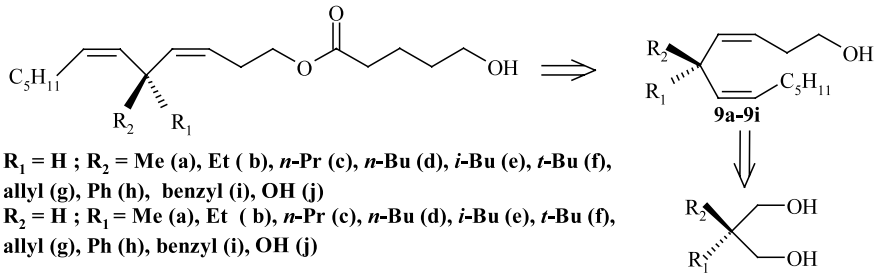


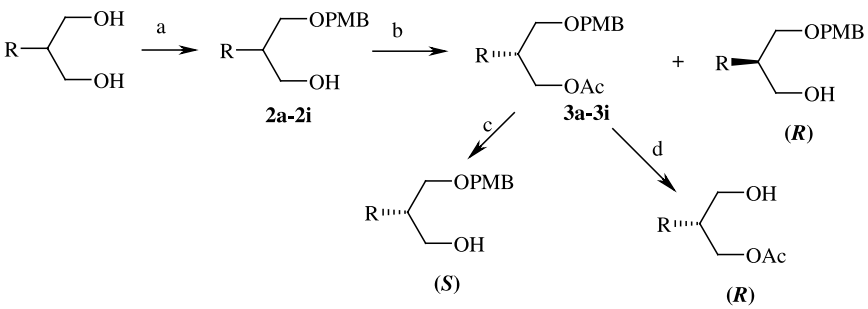
R_1 = H ; R_2 = Me (a), Et (b), *n*-Pr (c), *n*-Bu (d), *i*-Bu (e), *t*-Bu (f), allyl (g), Ph (h), benzyl (i), OH (j)
R_2 = H ; R_1 = Me (a), Et (b), *n*-Pr (c), *n*-Bu (d), *i*-Bu (e), *t*-Bu (f), allyl (g), Ph (h), benzyl (i), OH (j)

Scheme 2. Substrates **1a**–**j**.

2.2. Enzymatic transesterification of 2-substituted 1,3-propanediols

To introduce chirality at the 2-position we adopted an enzymatic transesterification of racemic 1,3-propanediol derivatives. The corresponding *meso*-1,3-diols were easily available from monoalkylated diethyl malonate derivatives. Enzymatic transesterification of 2-substituted *meso*-1,3-propanediol in organic solvents is well documented in the literature.[6] However, we have monoprotected the diols as their mono PMB ethers (4-methoxybenzyloxy). When these monoprotected diols were subjected to transesterification (Scheme 3) the acetates **3a**–**i** and the unreacted alcohols **2a**–**i** rich in the (*R*)-form were obtained. The corresponding (*S*)-isomers of **2a**–**i** can be obtained by hydrolysis of the acetates **3a**–**i**.

The transesterification of racemic 2-substituted 1,3-propanediol derivatives deserves some comment. It was already known that the (*S*)-isomer of the alcohol will undergo faster acetylation[7,8] to form the acetate than the corresponding (*R*)-isomer. Regarding the selection of lipases, CRL (lipase from *Candida rugosa*) gave better result when compared to PPL (lipase from porcine pancreas) and PSL (lipase from *Pseudomonas* species). The enantioselectivity of the acetate and the unreacted alcohols ranged from 70 to 95% (Table 1). The absolute configuration of the acetates and the alcohols were determined as follows: Deprotection of



R = Me (a), Et (b), *n*-Pr (c), *n*-Bu (d), *i*-Bu (e), *t*-Bu (f), allyl (g), Ph (h) benzyl (i)

Scheme 3. Desymmetrization of 2-substituted 1,3-propanediol derivatives. *Reagents and conditions*: (a) NaH, PMB-Br, rt; (b) CRL, vinyl acetate, MS (4 Å), rt; (c) K_2CO_3, MeOH, rt; (d) DDQ, DCM:H_2O (18:1), rt.

Table 1. Transesterification of **2a**–**i** with CRL and vinyl acetate

Entry	R	Time (h)	Conversion (*c*)	(*R*)-Acetate		(*R*)-Alcohol		E^b
				E.e.$_p$[a]	Yield (%)	E.e.$_s$	Yield (%)	
1	Me	10	48	96	48	90	40	145
2	Et	9	49	95	40	91	38	125
3	*n*-Pr	12	47	90	43	82	30	50
4	*n*-Bu	8	47	98	46	88	39	282
5	*i*-Bu	8	47.5	88	41	80	35	40
6	*t*-Bu	15	49.5	92	39	90	42	70
7	Allyl	7	47	96	42	85	44	134
8	Ph	8	52	70	43	75	31	14
9	$PhCH_2$	9	50	91	38	90	42	68

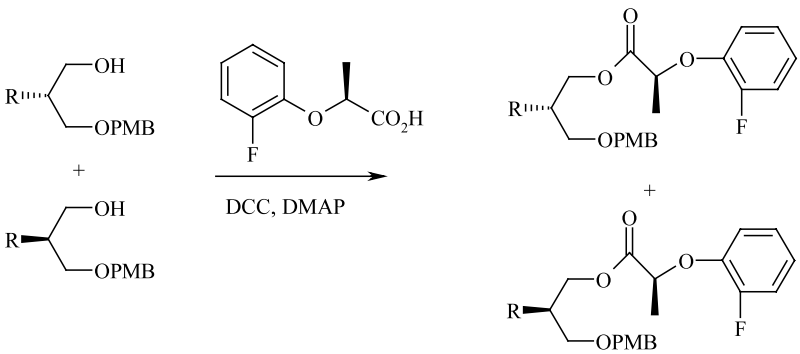
[a] E.e.s were calculated by chiral HPLC (Diacel, Chiral OD column, hexane-*iso*-propanol, 8.5:1).
[b] Enantioselectivities of the reaction (*E*)[13] were determined using the following equation: $E=\ln[1-c(1+\text{e.e.}_p)]/\ln[1-c(1-\text{e.e.}_p)]$, where e.e._p = pdt. e.e.; $c=\text{e.e.}_s/(\text{e.e.}_s+\text{e.e.}_p)$.

the PMB (4-methoxybenzyl) group with DDQ afforded the monoacetates, which have identical specific rotation values to those reported earlier.[7] The enantiomeric excess (e.e.) of each of the products was calculated by chiral HPLC and from NMR analysis by the Heunmann method (Scheme 4).[9] In this way the monoprotected diols were derivatized as their esters with (*S*)-FAC acid (fluoroaryllactic acid). As the esters are diastereomeric in nature, their ^{1}H NMR spectrum will be of different pattern. Mainly by comparing the integration of the Me-doublet signal (coming from FAC acid) at δ 1.6 ppm we can predict their relative ratios and hence the e.e.

Diisopropyl ether seems to be the best solvent to carry out the transesterification reaction. We have also conducted the same transesterification reaction in different organic solvents and the results are summarized in Table 2.

2.3. Synthesis of the (*Z*,*Z*)-diene moiety

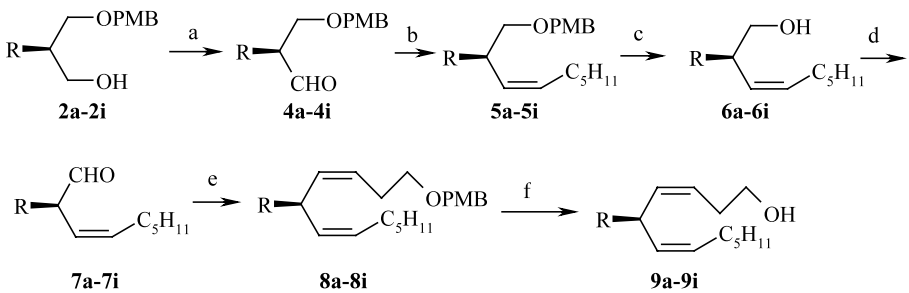
Our next target was to construct the (*Z*,*Z*)-diene moiety. It was evident that we need (*R*)-**2a**–**i** for synthesis of **1a**–**i** having pro-(*S*) hydrogen whereas (*S*)-**2a**–**i** will be the precursor for **1a**–**i** having pro-(*R*) hydrogen. Compounds (*R*)-**2a**–**i** were subjected to Swern oxidation[10] to give the aldehydes **4a**–**i**. Stereoselective *cis*-Wittig olefination of **4a**–**i** with *n*-hexyltriphenylphosphonium iodide in the presence of *t*-BuOK yielded the (*Z*)-olefins **5a**–**i** in 60% yield. Deprotection of the PMB ether functionality with DDQ[11] furnished the (*Z*)-alkenol **6a**–**i** in good yield. Oxidation of **6a**–**i** under Swern conditions afforded the aldehyde **7a**–**i**. A second Wittig olefination with $PMBO(CH_2)_3Ph_3P^+I^-$ in the presence of *t*-BuOK in THF yielded the (*Z*,*Z*)-diene **8a**–**i**. Subsequent removal of the PMB ether group furnished the (*Z*,*Z*)-dienol **9a**–**i** (Scheme 5).



Scheme 4. Synthesis of FAC esters.

Table 2. Transesterification of 2-methyl-monoprotected 1,3-propane diol **2a**

Entry	Solvent	Time (h)	Conversion	(*R*)-Acetate		(*R*)-Alcohol		*E*
				E.e.$_p$	Yield (%)	E.e.$_s$	Yield (%)	
1	Hexane	16	44	90	39	72	32	40
2	Et_2O	12	46	80	30	70	34	19
3	*i*-Pr_2O	10	48	96	48	90	48	145
4	*t*-BuOMe	14	48	85	28	80	25	30
5	THF	15	49	60	30	58	21	7
6	Cyclohexane	20	49	68	35	65	30	11
7	Toluene	18	49	72	31	70	28	13
8	Dioxan	22	49	78	32	75	30	18



Scheme 5. Synthesis of (*Z*,*Z*)-dienol. *Reagents and conditions*: (a) $Me_2S^+ClCl^-$, TEA, −78°C; (b) KO*t*-Bu, *n*-$C_6H_{13}PPh_3P^+I^-$, THF, 0°C; (c) DDQ, DCM:H_2O (18:1), rt; (d) same as (a); (e) KO*t*-Bu, $PMBO(CH_2)_3PPh_3P^+I^-$, THF; (f) same as (c).

2.4. Total synthesis of 1a–i

After successful construction of the (*Z*,*Z*)-diene moiety our next target was to attach the prosthetic modifier. The (*Z*,*Z*)-dienols **9a**–**i** were coupled with 5-(4-methoxybenzyloxy)pentanoic[3e] acid in the presence of DCC and DMAP to afford the esters **10a**–**i**. Removal of the PMB ether functionality furnished **1a**–**i** in good yield (Scheme 6). The enantiomers of **1a**–**i** having pro-(*R*) hydrogen were also prepared starting from (*S*)-**2a**–**i** by the same synthetic route.

2.5. Total synthesis of 1j

Our next target was compound **1j**, where one of the methylene hydrogens (flanked by the (*Z*,*Z*)-diene moiety) was replaced by a hydroxyl group. A logical retrosynthesis (Scheme 7) revealed that **1j** could be prepared from the bis-acetylenic diol **11** by attaching the prosthetic modifier. Compound **11** can be easily constructed from **12**, which is readily prepared by enzymatic transesterification.[5]

Starting the synthesis of **1j** from compound **12**, the acetate functionality was removed using K_2CO_3/MeOH. The secondary hydroxyl group was then protected as its PMB ether with PMB imidate[12] in the presence of catalytic CSA to yield **13**. Deprotection of the TBDPS group with TBAF afforded **11** and attachment of the prosthetic modifier yielded the coupled ester **14** in good yield. Removal of the PMB ether group in the presence of DDQ gave diacetylenic diol **15**. Controlled hydrogenation of **15** with Lindlar catalyst yielded **1j** in good yield (Scheme 8). The enantiomer of **1j** was also prepared starting from the enantiomer of **12** following the same synthetic route.

Our main intention was to study the effect of different groups present in **1a**–**j**, e.g. alkyl, aryl, hydroxyl in asymmetric hydroxylation with soybean lipoxygenase. In the first step of lipoxygenase-catalyzed asymmetric hydroxylation the pro-(*S*) hydrogen was removed to give a radical which undergoes resonance with the diene to form the conjugated double bond. The presence of different groups governs the course of the reaction, particularly phenyl and allyl because these groups can take part in conjugation with the generated radical (due to the presence of an extra double bond). Currently we are actively engaged in a detailed mechanistic investigation for the soybean lipoxygenase-catalyzed asymmetric hydroxylation of these novel substrates.

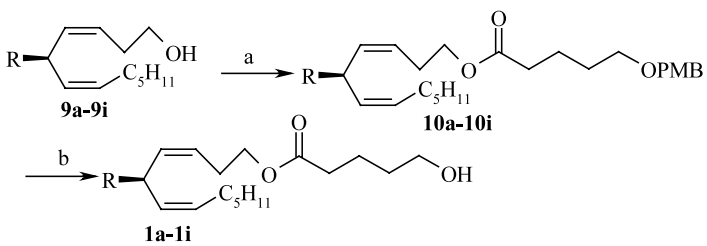
3. Conclusion

An efficient asymmetric synthesis of a series of novel lipoxygenase substrates has been described. Compounds where the pro-(*S*) hydrogen is present should act as substrates for lipoxygenase, whereas compounds lacking the pro-(*S*) hydrogen may act as suitable substrate analogue inhibitors of lipoxygenase, which are of tremendous biological interest.

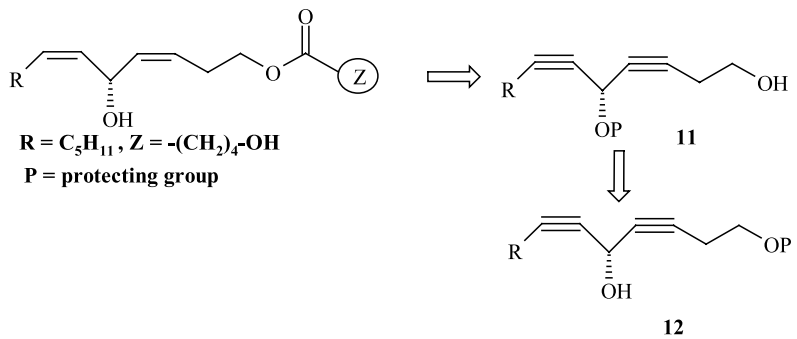
4. Experimental

4.1. General

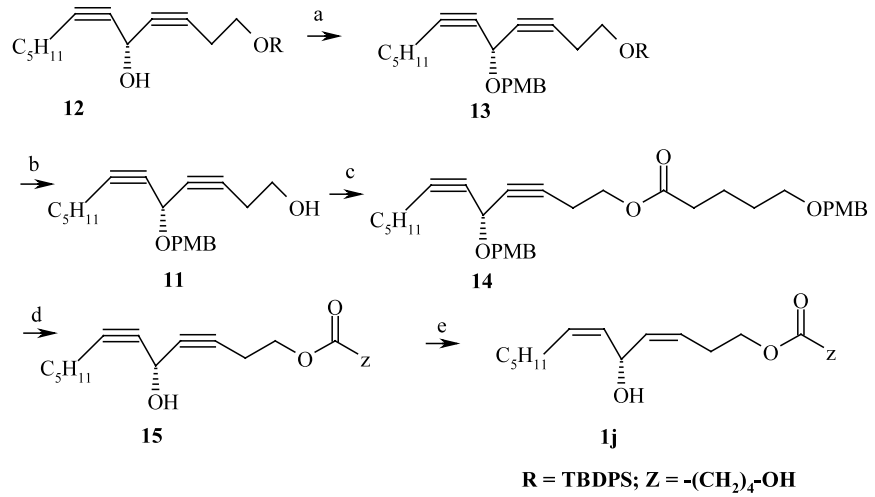
Unless otherwise stated, materials were obtained from commercial suppliers and used without further purification. THF and diethyl ether were distilled from sodium benzophenone ketyl. HMPA was distilled from BaO



Scheme 6. Total synthesis of **1a**–**i**. *Reagents and conditions*: (a) $PMBO(CH_2)_4CO_2H$, DCC, DMAP, rt; (b) DDQ, DCM:H_2O (18:1).



Scheme 7. Retrosynthetic analysis of **1j**.



Scheme 8. Total synthesis of **1j**. *Reagents and conditions*: (a) K_2CO_3, MeOH, PMBO(C=N)CCl_3, CSA, rt; (b) TBAF, THF, rt; (c) PMBO$(CH_2)_4CO_2H$, DCC, DMAP; (d) DDQ, DCM:H_2O (18:1), rt; (e) H_2, Lindlar catalyst.

and stored over 3 Å molecular sieves. Dichloromethane (DCM) was distilled from calcium hydride. Lipase (from *Candida rugosa*, type VII, 1440 units/mg of protein), lipase (from porcine pancreas, type II, 66 units/mg of protein) and lipase (from *Pseudomonas* species, type XIII, 60 units/mg of protein) were obtained from SIGMA Co. (USA) and used as obtained. Reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25 mm silica gel plates with UV light and 2.5% ethanolic anisaldehyde (with 1% AcOH and 3% conc. H_2SO_4) heat as developing agents. Silica gel 100–200 mesh was used for column chromatography. Yields refer to chromatographically and spectroscopically homogeneous materials unless otherwise stated. NMR spectra were recorded on 200 MHz spectrometers at rt in $CDCl_3$ using tetramethylsilane as internal standard and the chemical shifts are shown in δ. ^{13}C NMR spectra were recorded with a complete proton decoupling instrument. Infrared spectra were recorded on a Perkin–Elmer 1420 spectrometer. For enzymatic reactions the solvents employed were desiccated over 4 Å molecular sieve powder for 50 h prior to use. Optical rotations were measured on a JASCO Dip 360 digital polarimeter. The abbreviation TF denotes thin film.

4.2. 3-(4-Methoxybenzyloxy)-2-substituted-1-propanol 2a–i

The appropriate 2-substituted 1,3-propanediol (1 mmol) was dissolved in dry THF (5 mL) and NaH (60% dispersion in mineral oil, 1 mmol) was added to the solution portionwise at 0°C. The reaction mixture was stirred at 0°C for 1 h under a nitrogen atmosphere. Tetrabutylammonium iodide (catalytic) was added to the mixture, followed by the addition of 4-methoxybenzyl bromide (0.24 g, 1.2 mmol). The mixture was stirred for a further 2 h at rt. Water was added to the reaction mixture and extracted with EtOAc. The reaction mixture was then washed with brine and dried (Na_2SO_4). Purification by means of column chromatography gave the product in 80% yield.

^{1}H NMR data:

R = Me 2a: 0.95 (d, J = 6.5 Hz, 3H), 1.75 (m, 1H), 3.4–3.6 (m, 4H), 3.9 (s, 3H), 4.45 (s, 2H), 6.8 (d, J = 6.0 Hz, 2H), 7.2 (d, J = 6.0 Hz, 2H). EIMS (m/z): 210 (M^+).
R = Et 2b: 0.9 (t, J = 7.5 Hz, 3H), 1.3 (m, 2H), 1.75 (m, 1H), 3.3–3.7 (m, 4H), 3.9 (s, 3H), 4.45 (s, 2H), 6.8 (d, J = 6.0 Hz, 2H), 7.2 (d, J = 6.0 Hz, 2H). EIMS (m/z): 224 (M^+).
R = *n*-Pr 2c: 0.9 (t, J = 7.0 Hz, 3H), 1.3 (m, 4H), 1.8 (m, 1H), 2.5 (brs, 1H, -OH), 3.4 (m, 1H), 3.55 (m, 2H), 3.7 (m, 1H), 3.8 (s, 3H), 4.4 (ABq, J = 6.0 Hz, 2H), 6.8 (d, J = 6.0 Hz, 2H), 7.2 (d, J = 6.0 Hz, 2H). EIMS (m/z): 238 (M^+).
R = *n*-Bu 2d: 0.9 (t, J = 7.2 Hz, 3H), 1.2–1.4 (m, 6H), 1.8 (m, 1H), 3.4 (m, 1H), 3.6 (m, 2H), 3.7 (m, 1H), 3.8 (s, 3H), 4.45 (ABq, J = 6.0 Hz, 2H), 6.8 (d, J = 6.0 Hz, 2H), 7.2 (d, J = 6.0 Hz, 2H). EIMS (m/z): 252 (M^+).
R = *i*-butyl 2e: 0.95 (m, 6H), 1.5 (m, 2H), 1.8 (m, 2H), 3.45–3.8 (m, 4H), 3.9 (s, 3H), 4.45 (s, 2H), 6.8 (d, J = 6.0 Hz, 2H), 7.2 (d, J = 6.0 Hz, 2H). EIMS (m/z): 252 (M^+).
R = *t*-Bu 2f: 0.9 (m, 9H), 1.75 (m, 1H), 3.4–3.7 (m, 4H), 3.8 (s, 3H), 4.4 (ABq, J = 6.0 Hz, 2H), 6.8 (d, J = 6.0 Hz, 2H), 7.2 (d, J = 6.0 Hz, 2H). EIMS (m/z): 252 (M^+).
R = allyl 2g: 1.9 (m, 1H), 2.0 (m, 2H), 3.4–3.7 (m, 4H), 3.9 (s, 3H), 4.45 (s, 2H), 5.0 (m, 2H), 5.7 (m, 1H), 6.8 (d, J = 6.0 Hz, 2H), 7.2 (d, J = 6.0 Hz, 2H). EIMS (m/z): 236 (M^+).
R = Ph 2h: 2.4 (brs, 1H), 3.2 (m, 1H), 3.7–4.0 (m, 7H), 4.45 (s, 2H), 6.8 (d, J = 6.0 Hz, 2H), 7.2 (m, 7H). EIMS (m/z): 272 (M^+).
R = $PhCH_2$ 2i: 1.9 (m, 1H), 2.6 (d, J = 8.0 Hz, 2H), 3.4–3.7 (m, 4H), 3.8 (s, 3H), 4.4 (s, 2H), 6.8 (d, J = 6.0 Hz, 2H), 7.2 (m, 7H). EIMS (m/z): 286 (M^+).

4.3. (*R*)-3-(4-Methoxybenzyloxy)-2-substituted propyl acetate 3a–i

In a typical resolution experiment a solution of the monoprotected diol (1 g) in dry diisopropyl ether (50 mL) was stirred with vinyl acetate (3 mol equiv.), followed by addition of CRL (1 g). The reaction mixture was agitated in an orbit shaker at 250 rpm at rt for the time shown in the table. After 50% conversion (by GC analysis), the reaction mixture was filtered through Celite and evaporated to dryness. The (*R*)-alcohol and (*R*)-acetate were separated by column chromatography.

^{1}H NMR data:

R = Me 3a: 0.95 (d, J = 6.5 Hz, 3H), 1.7 (m, 1H), 2.0 (s, 3H), 3.4 (d, J = 6.0 Hz, 2H), 3.9 (s, 3H), 4.1 (d, J = 6.0 Hz, 2H), 4.45 (s, 2H), 6.8 (d, J = 6.0 Hz, 2H), 7.2 (d, J = 6.0 Hz, 2H).
R = Et 3b: 0.9 (t, J = 7.5 Hz, 3H), 1.4 (m, 2H), 1.75 (m, 1H), 2.0 (s, 3H), 3.3 (d, J = 6.0 Hz, 2H), 3.9 (s, 3H), 4.05 (d, J = 6.0 Hz, 2H), 4.45 (s, 2H), 6.8 (d, J = 6.0 Hz, 2H), 7.2 (d, J = 6.0 Hz, 2H).
R = *n*-Pr 3c: 0.9 (m, 3H), 1.3 (m, 4H), 1.9 (m, 1H), 2.0 (s, 3H), 3.35 (d, J = 7.0 Hz, 2H), 3.9 (s, 3H), 4.05 (d, J = 7.0 Hz, 2H), 4.4 (s, 2H), 6.8 (d, J = 6.0 Hz, 2H), 7.2 (d, J = 6.0 Hz, 2H).
R = *n*-Bu 3d: 0.9 (m, 3H), 1.2–1.4 (m, 6H), 1.8 (m, 1H), 2.0 (s, 3H), 3.4 (d, J = 6.8 Hz, 2H), 3.8 (s, 3H), 4.0 (d, J = 6.8 Hz, 2H), 4.4 (s, 2H), 6.8 (d, J = 6.0 Hz, 2H), 7.2 (d, J = 6.0 Hz, 2H).
R = *i*-Bu 3e: 0.95 (m, 6H), 1.5 (m, 2H), 1.8 (m, 2H), 2.0 (s, 3H), 3.45 (d, J = 6.8 Hz, 2H), 3.8 (s, 3H), 4.0 (d, J = 6.8 Hz, 2H), 4.4 (s, 2H), 6.8 (d, J = 6.0 Hz, 2H), 7.2 (d, J = 6.0 Hz, 2H).
R = *t*-Bu 3f: 0.9 (m, 9H), 1.85 (m, 1H), 2.0 (s, 3H), 3.45 (d, J = 6.8 Hz, 2H), 3.8 (s, 3H), 4.0 (d, J = 6.8 Hz, 2H), 4.4 (s, 2H), 6.8 (d, J = 6.0 Hz, 2H), 7.2 (d, J = 6.0 Hz, 2H).
R = allyl 3g: 1.9 (m, 1H), 2.0 (s, 3H), 2.1 (m, 2H), 3.4 (d, J = 6.8 Hz, 2H), 3.8 (s, 3H), 4.2 (d, J = 6.8 Hz, 2H), 4.4 (s, 2H), 5.0 (m, 2H), 5.6–5.8 (m, 1H), 6.8 (d, J = 6.0 Hz, 2H), 7.2 (d, J = 6.0 Hz, 2H).
R = Ph 3h: 1.9 (s, 3H), 3.2 (m, 1H), 3.6 (d, J = 6.8 Hz, 2H), 3.8 (s, 3H), 4.3 (m, 2H), 4.4 (s, 2H), 6.8 (d, J = 6.0 Hz, 2H), 7.2 (m, 7H).
R = $PhCH_2$ 3i: 2.0 (s, 3H), 2.2 (m, 1H), 2.65 (m, 2H), 3.3 (d, J = 6.8 Hz, 2H), 3.85 (s, 3H), 4.1 (d, J = 6.8 Hz, 2H), 4.4 (s, 2H), 6.8 (d, J = 6.0 Hz, 2H), 7.2 (m, 7H).

4.4. (*S*)-3-(4-Methoxybenzyloxy)-2-substituted-1-propanol 2a–i

To a solution of the (*R*)-acetate (1 mmol) in methanol was added K_2CO_3 (0.414 g, 3 mmol) and the mixture was stirred at rt for 1 h. The reaction mixture was then filtered through Celite. After evaporation of methanol, the remaining solid mass was taken up in water, extracted with DCM, washed with water, brine and dried (Na_2SO_4). Purification by column chromatography gave the alcohol in 80% yield.

R = Me: $[\alpha]_D^{25} = -15.2$ (c 1.2, $CHCl_3$);
R = Et: $[\alpha]_D^{25} = -12.8$ (c 1.0, $CHCl_3$);
R = *n*-Pr: $[\alpha]_D^{25} = -14.0$ (c 1.1, $CHCl_3$);
R = *n*-Bu: $[\alpha]_D^{25} = -10.2$ (c 1.5, $CHCl_3$);
R = *i*-Bu: $[\alpha]_D^{25} = -21.2$ (c 1.2, $CHCl_3$);
R = *t*-Bu: $[\alpha]_D^{25} = -5.2$ (c 1.1, $CHCl_3$);
R = allyl: $[\alpha]_D^{25} = -13.8$ (c 1.2, $CHCl_3$);
R = Ph: $[\alpha]_D^{25} = +40.3$ (c 0.8, $CHCl_3$);
R = benzyl: $[\alpha]_D^{25} = -28.9$ (c 1.0, $CHCl_3$).

4.5. (*R*)-3-(4-Methoxybenzyloxy)-2-substituted propanal 4a–i

A solution of the (*R*)-alcohol (1 mmol) in DCM (5 mL) was added to oxalyl chloride (1 mmol) and DMSO (2 mmol) in DCM at −78°C. The temperature was maintained at −78°C for a further 1 h. Triethylamine (5 mmol) was then added and after stirring for 5 min the mixture was allowed to warm to 25°C and stirred for a further 30 min at the same temperature. Water was added to the solution and the mixture was extracted with DCM. The organic extract was washed with water, brine and dried (Na_2SO_4). The organic extract was evaporated and purified by column chromatography to afford the aldehyde in 85% yield.

^{1}H NMR data:

R = Me 4a: 1.1 (d, J = 6.7 Hz, 3H), 2.6 (m, 1H), 3.6 (m, 2H), 3.9 (s, 3H), 4.4 (s, 2H), 6.8 (d, J = 6.0 Hz, 2H), 7.2 (d, J = 6.0 Hz, 2H), 9.6 (s, 1H).
R = Et 4b: 0.9 (t, J = 7.0 Hz, 3H), 1.4–1.8 (m, 2H), 2.4 (m, 1H), 3.6 (m, 2H), 3.8 (s, 3H), 4.4 (s, 2H), 6.8 (d, J = 6.0 Hz, 2H), 7.2 (d, J = 6.0 Hz, 2H), 9.6 (s, 1H).
R = *n*-Pr 4c: 0.9 (t, J = 7.0 Hz, 3H), 1.2–1.5 (m, 4H), 2.45 (m, 1H), 3.55 (m, 2H), 3.8 (s, 3H), 4.4 (s, 2H), 6.8 (d, J = 6.2 Hz, 2H), 7.2 (d, J = 6.2 Hz, 2H), 9.6 (s, 1H).
R = *n*-Bu 4d: 0.9 (t, J = 7.0 Hz, 3H), 1.2–1.6 (m, 6H), 2.5 (m, 1H), 3.6 (m, 2H), 3.8 (s, 3H), 4.4 (s, 2H), 6.8 (d, J = 6.2 Hz, 2H), 7.2 (d, J = 6.2 Hz, 2H), 9.6 (s, 1H).
R = *i*-Bu 4e: 0.9 (m, 6H), 1.3 (m, 1H), 1.5 (m, 1H), 1.8 (m, 1H), 2.5 (m, 1H), 3.6–3.7 (m, 2H), 3.8 (s, 3H), 4.4 (s, 2H), 6.8 (d, J = 6.2 Hz, 2H), 7.2 (d, J = 6.2 Hz, 2H), 9.7 (s, 1H).
R = *t*-Bu 4f: 1.0 (s, 9H), 2.4 (m, 1H), 3.6–4.0 (m, 2H), 3.9 (s, 3H), 4.4 (s, 2H), 6.8 (d, J = 6.0 Hz, 2H), 7.2 (d, J = 6.0 Hz, 2H), 9.55 (s, 1H).
R = allyl 4g: 2.2 (m, 1H), 2.4 (m, 1H), 2.6 (m, 1H), 3.8 (d, J = 6.0 Hz, 2H), 3.9 (s, 3H), 4.4 (s, 2H), 5.0 (m, 2H), 5.75 (m, 1H), 6.8 (d, J = 6.0 Hz, 2H), 7.2 (d, J = 6.0 Hz, 2H), 9.5 (s, 1H).
R = Ph 4h: 3.75 (m, 1H), 3.8 (m, 1H), 3.9 (s, 3H), 4.1 (m, 1H), 4.4 (s, 2H), 6.8 (d, J = 6.0 Hz, 2H), 7.2 (m, 7H), 9.6 (s, 1H).
R = $PhCH_2$ 4i: 2.5 (m, 1H), 2.6 (d, J = 8.0 Hz, 2H), 3.6 (m, 2H), 3.8 (s, 3H), 4.4 (s, 2H), 6.8 (d, J = 6.2 Hz, 2H), 7.2–7.4 (m, 7H), 9.7 (s, 1H).

4.6. 1-Methoxy-4-[2-substituted-(*Z*)-3-nonenyloxymethyl]benzene 5a–i

n-Hexyltriphenylphosphonium iodide (1 mmol) was taken up in THF:HMPA (6:1, 6 mL). *t*-BuOK (1.2 mmol) was added to the mixture at 0°C. The orange–red colored solution was stirred at the same temperature for 0.5 h. Aldehyde **4a–i** (0.3 mmol) in THF was added and the reaction mixture was stirred for a further 6 h at rt. This was then quenched with satd NH_4Cl, extracted with ether, washed with water, brine and dried (Na_2SO_4). The crude olefin was purified by column chromatography.

^{1}H NMR data:

R=Me 5a: 0.9 (t, $J=7.2$ Hz, 3H), 1.0 (d, $J=6.8$ Hz, 3H), 1.2–1.4 (m, 6H), 2.0 (m, 2H), 2.4 (m, 1H), 3.3 (m, 2H), 3.9 (s, 3H), 4.4 (s, 2H), 5.2 (m, 1H), 5.4 (m, 1H), 6.8 (d, $J=6.0$ Hz, 2H), 7.2 (d, $J=6.0$ Hz, 2H). EIMS (m/z): 276 (M^+).
R=Et 5b: 0.9 (m, 6H), 1.15–1.55 (m, 8H), 2.0 (m, 2H), 2.45 (m, 1H), 3.3 (m, 1H), 3.55 (m, 1H), 3.8 (s, 3H), 4.4 (s, 2H), 5.1 (m, 1H), 5.6 (m, 1H), 6.8 (d, $J=6.0$ Hz, 2H), 7.2 (d, $J=6.0$ Hz, 2H). EIMS (m/z): 290 (M^+).
R=*n*-Pr 5c: 0.95 (t, $J=7.2$ Hz, 6H), 1.2–1.6 (m, 10H), 2.0 (m, 2H), 2.35 (m, 1H), 3.2 (d, $J=7.0$ Hz, 2H), 3.85 (s, 3H), 4.35 (s, 2H), 5.0 (m, 1H), 5.4 (m, 1H), 6.8 (d, $J=6.0$ Hz, 2H), 7.2 (d, $J=6.0$ Hz, 2H). EIMS (m/z): 304 (M^+).
R=*n*-Bu 5d: 0.9 (m, 6H), 1.2–1.5 (m, 12H), 2.0 (m, 2H), 2.2 (m, 1H), 3.35 (m, 2H), 3.8 (s, 3H), 4.4 (s, 2H), 5.1–5.5 (m, 2H), 6.8 (d, $J=6.0$ Hz, 2H), 7.2 (d, $J=6.0$ Hz, 2H). EIMS (m/z): 318 (M^+).
R=*i*-Bu 5e: 0.9–1.0 (m, 9H), 1.4–1.6 (m, 8H), 1.8 (m, 1H), 2.0 (m, 2H), 2.45 (m, 1H), 3.4 (m, 2H), 3.8 (s, 3H), 4.4 (s, 2H), 5.2 (m, 1H), 5.5 (m, 1H), 6.8 (d, $J=6.0$ Hz, 2H), 7.2 (d, $J=6.0$ Hz, 2H). EIMS (m/z): 318 (M^+).
R=*t*-Bu 5f: 0.9–1.0 (m, 12H), 1.2–1.5 (m, 6H), 2.0 (m, 2H), 2.4 (m, 1H), 3.2 (m, 1H), 3.5 (m, 1H), 3.8 (s, 3H), 4.35 (s, 3H), 5.2–5.5 (m, 2H), 6.8 (d, $J=6.0$ Hz, 2H), 7.2 (d, $J=6.0$ Hz, 2H). EIMS (m/z): 318 (M^+).
R=allyl 5g: 0.9 (m, 3H), 1.2–1.5 (m, 6H), 2.0 (m, 2H), 2.2 (m, 2H), 2.75 (m, 1H), 3.3 (d, $J=7.0$ Hz, 2H), 3.85 (s, 3H), 4.5 (s, 2H), 4.9–5.2 (m, 3H), 5.4 (m, 1H), 5.65 (m, 1H), 6.8 (d, $J=6.0$ Hz, 2H), 7.2 (d, $J=6.0$ Hz, 2H). EIMS (m/z): 302 (M^+).
R=Ph 5h: 0.9 (t, $J=7.0$ Hz, 3H), 1.2–1.7 (m, 6H), 2.3 (m, 1H), 2.6 (t, $J=7.6$ Hz, 2H), 3.8 (d, $J=7.0$ Hz, 2H), 3.9 (s, 3H), 4.4 (s, 2H), 6.58 (d, $J=10.5$ Hz, 1H), 6.8–7.0 (m, 5H), 7.45 (m, 4H), 7.85 (dd, $J=14$ Hz, 10.5 Hz, 1H). EIMS (m/z): 338 (M^+).
R=$PhCH_2$ 5i: 0.9 (m, 3H), 1.2–1.6 (m, 6H), 1.9 (m, 2H), 2.35 (m, 1H), 2.8 (m, 2H), 3.4 (m, 1H), 3.55 (m, 1H), 3.8 (s, 3H), 4.4 (s, 2H), 5.2 (m, 1H), 5.55 (m, 1H), 6.8 (d, $J=6.0$ Hz, 2H), 7.2 (m, 7H). EIMS (m/z): 352 (M^+).

4.7. 2-Substituted (*Z*)-3-nonen-1-ol 6a–i

Olefinic compound **5a–i** (0.5 mmol) was dissolved in dichloromethane:water (19:1, 3 mL). DDQ (0.75 mmol) was added and the solution was stirred for 1 h at rt. The reaction mixture was filtered off, and the filtrate was washed with 5% $NaHCO_3$ solution, brine and dried (Na_2SO_4). Purification by chromatography gave the alkenol in 80% yield.

^{1}H NMR data:

R=Me 6a: 0.9 (t, $J=7.2$ Hz, 3H), 1.0 (d, $J=6.8$ Hz, 3H), 1.2–1.4 (m, 6H), 2.0 (m, 1H), 2.3 (m, 1H), 2.6 (m, 1H), 3.3 (m, 2H), 5.2 (m, 1H), 5.4 (m, 1H). EIMS (m/z): 157 (M^+).
R=Et 6b: 0.9 (m, 6H), 1.15–1.55 (m, 8H), 2.0 (m, 2H), 2.45 (m, 1H), 3.3 (m, 1H), 3.55 (m, 1H), 5.1 (m, 1H), 5.6 (m, 1H). EIMS (m/z): 171 (M^+).
R=*n*-Pr 6c: 0.95 (t, $J=7.2$ Hz, 6H), 1.2–1.6 (m, 10H), 2.0 (m, 2H), 2.6 (m, 1H), 3.2–3.5 (m, 2H), 5.0 (m, 1H), 5.4 (m, 1H). EIMS (m/z): 185 (M^+).
R=*n*-Bu 6d: 0.9 (m, 6H), 1.2–1.5 (m, 12H), 2.0 (m, 2H), 2.55 (m, 1H), 3.35 (t, $J=7.0$ Hz, 2H), 5.1–5.5 (m, 2H). EIMS (m/z): 199 (M^+).
R=*i*-Bu 6e: 0.9 (m, 9H), 1.2–1.5 (m, 9H), 2.0 (m, 2H), 2.4 (m, 1H), 3.2 (m, 1H), 3.55 (m, 1H), 5.0 (m, 1H), 5.5 (m, 1H).
R=*t*-Bu 6f: 0.9–1.0 (m, 12H), 1.2–1.5 (m, 6H), 2.0 (m, 2H), 2.3 (m, 1H), 3.2 (m, 1H), 3.5 (m, 1H), 5.2–5.5 (m, 2H).
R=allyl 6g: 0.85 (t, $J=6.8$ Hz, 3H), 1.2 (m, 6H), 1.8–2.0 (m, 4H), 2.5 (m, 1H), 3.2 (m, 1H), 3.4 (m, 1H), 4.8–5.0 (m, 3H), 5.4 (m, 1H), 5.6 (m, 1H). EIMS (m/z): 183 (M^+).
R=Ph 6h: 0.9 (t, $J=7.0$ Hz, 3H), 1.2–1.7 (m, 6H), 2.3 (m, 1H), 2.6 (t, $J=7.6$ Hz, 2H), 3.8 (d, $J=7.0$ Hz, 2H), 6.58 (d, $J=10.5$ Hz, 1H), 7.0–7.3 (m, 5H), 7.85 (dd, $J=14.0$ Hz, 10.5 Hz, 1H). EIMS (m/z): 220 (M^+).
R=$PhCH_2$ 6i: 0.9 (m, 3H), 1.2–1.6 (m, 6H), 1.9 (m, 2H), 2.35 (m, 1H), 2.8 (m, 2H), 3.4 (m, 1H), 3.55 (m, 1H), 5.2 (m, 1H), 5.55 (m, 1H), 7.1–7.3 (m, 5H). EIMS (m/z): 234 (M^+).

4.8. 2-Substituted (*Z*)-3-nonenal 7a–i

The reaction conditions are the same as described in Section 4.4.

^{1}H NMR data:

R=Me 7a: 0.9 (t, $J=7.0$ Hz, 3H), 1.15 (d, $J=6.8$ Hz, 3H), 1.2–1.5 (m, 6H), 2.2 (m, 2H), 3.35 (m, 1H), 5.2 (m, 1H), 5.6 (m, 1H), 9.5 (s, 1H).
R=Et 7b: 0.9 (m, 6H), 1.2–1.8 (m, 8H), 2.1 (m, 2H), 3.18 (m, 1H), 5.2 (m, 1H), 5.55 (m, 1H), 9.5 (s, 1H).
R=*n*-Pr 7c: 0.9 (m, 6H), 1.2–1.5 (m, 10H), 2.1 (m, 2H), 3.2 (m, 1H), 5.2 (m, 1H), 5.7 (m, 1H), 9.4 (s, 1H).

R=*n*-Bu 7d: 0.9 (m, 6H), 1.2–1.6 (m, 12H), 2.0 (m, 2H), 3.0 (m, 1H), 5.2 (m, 1H), 5.6 (m, 1H), 9.5 (s, 1H).
R=*i*-Bu 7e: 0.9 (m, 9H), 1.1–1.6 (m, 8H), 1.9 (m, 1H), 2.1 (m, 2H), 3.1 (m, 1H), 5.25 (m, 1H), 5.7 (m, 1H), 9.4 (s, 1H).
R=*t*-Bu 7f: 0.9–1.0 (m, 12H), 1.2–1.5 (m, 6H), 2.1 (m, 2H), 3.2 (m, 1H), 5.2 (m, 1H), 5.6 (m, 1H), 9.4 (s, 1H).
R=allyl 7g: 0.9 (m, 3H), 1.2–1.5 (m, 6H), 2.0–2.2 (m, 4H), 3.3 (m, 1H), 5.0–5.2 (m, 3H), 5.7 (m, 2H), 9.5 (s, 1H).
R=Ph 7h: 0.9 (t, $J=7.0$ Hz, 3H), 1.2–1.7 (m, 6H), 2.6 (t, $J=7.6$ Hz, 2H), 3.3 (m, 1H), 6.58 (d, $J=10.5$ Hz, 1H), 7.0–7.3 (m, 5H), 7.85 (dd, $J=14.0$ Hz, 10.5 Hz, 1H), 9.6 (s, 1H).
R=PhCH$_2$ 7i: 0.9 (t, $J=7.0$ Hz, 3H), 1.1–1.6 (m, 6H), 1.9 (m, 2H), 2.6 (m, 1H), 3.1 (m, 1H), 3.5 (m, 1H), 5.2 (m, 1H), 5.6 (m, 1H), 7.0–7.3 (m, 5H), 9.6 (s, 1H).

4.9. Methoxy-4-[5-substituted-(3*Z*,6*Z*)-3,6-dodecadienyloxymethyl]benzene 8a–i

The reaction conditions were the same as described in Section 4.5. Instead of *n*-hexyltriphenylphosphonium iodide, here we used 1-(3-triphenylphosphonium iodopropoxymethyl)-4-methoxybenzene.

^{1}H NMR data:

R=Me 8a: 0.9 (t, $J=7.0$ Hz, 3H), 1.0 (d, $J=7.0$ Hz, 3H), 1.2–1.4 (m, 6H), 2.0 (m, 2H), 2.4 (m, 2H), 2.9 (m, 1H), 3.4 (t, $J=7.0$ Hz, 2H), 3.8 (s, 3H), 4.4 (s, 2H), 5.2–5.4 (m, 4H), 6.8 (d, $J=6.0$ Hz, 2H), 7.2 (d, $J=6.0$ Hz, 2H). FABMS (m/z): 316 (M$^+$).
R=Et 8b: 0.9 (m, 6H), 1.2–1.4 (m, 8H), 2.0 (m, 2H), 2.3 (m, 2H), 3.15 (m, 1H), 3.35 (t, $J=7.2$ Hz, 2H), 3.8 (s, 3H), 4.4 (s, 2H), 5.0–5.4 (m, 4H), 6.8 (d, $J=6.0$ Hz, 2H), 7.2 (d, $J=6.0$ Hz, 2H). FABMS (m/z): 330 (M$^+$).
R=*n*-Pr 8c: 0.9 (m, 6H), 1.2–1.5 (m, 10H), 2.0 (m, 2H), 2.4 (m, 2H), 3.15 (m, 1H), 3.4 (m, 2H), 3.9 (s, 3H), 4.4 (s, 2H), 5.1–5.4 (m, 4H), 6.8 (d, $J=6.0$ Hz, 2H), 7.2 (d, $J=6.0$ Hz, 2H). FABMS (m/z): 344 (M$^+$).
R=*n*-Bu 8d: 0.9 (m, 6H), 1.2–1.5 (m, 12H), 2.0 (m, 2H), 2.4 (m, 2H), 3.4 (m, 3H), 3.8 (s, 3H), 4.4 (s, 2H), 5.1–5.4 (m, 4H), 6.8 (d, $J=6.0$ Hz, 2H), 7.2 (d, $J=6.0$ Hz, 2H). FABMS (m/z): 358 (M$^+$).
R=*i*-Bu 8e: 0.9–1.0 (m, 9H), 1.2–1.6 (m, 8H), 1.75 (m, 1H), 2.0 (m, 2H), 2.4 (m, 2H), 3.15 (m, 1H), 3.4 (m, 2H), 3.8 (s, 3H), 4.4 (s, 2H), 5.15–5.4 (m, 4H), 6.8 (d, $J=6.0$ Hz, 2H), 7.2 (d, $J=6.0$ Hz, 2H). FABMS (m/z): 358 (M$^+$).
R=*t*-Bu 8f: 0.9 (s, 12H), 1.3 (m, 6H), 2.2 (m, 2H), 2.4 (m, 2H), 3.15 (m, 1H), 3.4 (t, $J=7.0$ Hz, 2H), 3.9 (s, 3H), 4.4 (s, 2H), 5.15–5.4 (m, 4H), 6.8 (d, $J=6.0$ Hz, 2H), 7.2 (d, $J=6.0$ Hz, 2H). FABMS (m/z): 358 (M$^+$).
R=allyl 8g: 0.9 (t, $J=7.0$ Hz, 3H), 1.2–1.4 (m, 6H), 2.1 (m, 4H), 2.35 (m, 2H), 3.4 (m, 3H), 3.8 (s, 3H), 4.4 (s, 2H), 4.8–5.4 (m, 6H), 5.8 (m, 1H), 6.8 (d, $J=6.0$ Hz, 2H), 7.2 (d, $J=6.0$ Hz, 2H). FABMS (m/z): 342 (M$^+$).
R=Ph 8h: 0.9 (t, $J=7.0$ Hz, 3H), 1.2–1.7 (m, 6H), 2.2–2.5 (m, 4H), 3.48 (m, 3H), 3.8 (s, 3H), 4.4 (s, 2H), 5.6–5.8 (m, 2H), 6.58 (d, $J=10.5$ Hz, 1H), 6.8 (d, $J=6.2$ Hz, 2H), 7.0–7.3 (m, 5H), 7.2 (d, $J=6.2$ Hz, 2H), 7.85 (dd, $J=14.0$ Hz, 10.5 Hz, 1H). FABMS (m/z): 378 (M$^+$).
R=PhCH$_2$ 8i: 0.9 (m, 3H), 1.2–1.4 (m, 6H), 1.9 (m, 2H), 2.3 (m, 2H), 2.6 (d, $J=8.0$ Hz, 2H), 3.15–3.3 (m, 2H), 3.6 (m, 1H), 3.8 (s, 3H), 4.4 (s, 2H), 5.2–5.4 (m, 4H), 6.8 (d, $J=6.0$ Hz, 2H), 7.2 (m, 7H). FABMS (m/z): 392 (M$^+$).

4.10. 5-Substituted-(3*Z*,6*Z*)-3,6-dodecadien-1-ol 9a–i

Deprotection of the PMB ether group was done by DDQ as described in Section 4.6.

^{1}H NMR data:

R=Me 9a: 0.9 (t, $J=7.0$ Hz, 3H), 1.0 (d, $J=6.8$ Hz, 3H), 1.2–1.5 (m, 6H), 2.1 (m, 2H), 2.4 (m, 2H), 3.4 (m, 3H), 5.2–5.4 (m, 4H). EIMS (m/z): 197 (M$^+$).
R=Et 9b: 0.9 (m, 6H), 1.2–1.4 (m, 8H), 2.0 (m, 2H), 2.3 (q, $J=7.2$ Hz, 2H), 3.2 (m, 1H), 3.6 (t, $J=7.2$ Hz, 2H), 5.0–5.4 (m, 4H). EIMS (m/z): 211 (M$^+$).
R=*n*-Pr 9c: 0.9 (m, 6H), 1.2–1.5 (m, 10H), 2.0 (m, 2H), 2.4 (m, 2H), 3.2 (m, 1H), 3.4 (m, 2H), 5.1–5.4 (m, 4H). EIMS (m/z): 225 (M$^+$).
R=*n*-Bu 9d: 0.9 (m, 6H), 1.2–1.5 (m, 12H), 2.0 (m, 2H), 2.4 (m, 2H), 3.4 (m, 3H), 5.1–5.4 (m, 4H). EIMS (m/z): 239 (M$^+$).
R=*i*-Bu 9e: 0.9–1.0 (m, 9H), 1.2–1.6 (m, 8H), 1.75 (m, 1H), 2.0 (m, 2H), 2.4 (m, 2H), 3.15 (m, 1H), 3.4 (m, 2H), 5.15–5.4 (m, 4H).
R=*t*-Bu 9f: 0.9 (s, 12H), 1.3 (m, 6H), 2.0 (m, 2H), 2.4 (m, 2H), 3.15 (m, 1H), 3.4 (t, $J=7.0$ Hz, 2H), 5.15–5.4 (m, 4H).
R=allyl 9g: 0.9 (t, $J=6.8$ Hz, 3H), 1.4 (m, 6H), 2.1 (m, 4H), 2.4 (m, 2H), 3.4 (m, 1H), 3.6 (t, $J=7.0$ Hz, 2H), 5.0 (m, 2H), 5.2 (m, 1H), 5.4 (m, 3H), 5.7 (m, 1H). EIMS (m/z): 223 (M$^+$).
R=Ph 9h: 0.9 (t, $J=7.0$ Hz, 3H), 1.2–1.7 (m, 6H), 2.2–2.5 (m, 4H), 3.48 (m, 1H), 3.6 (t, $J=7.0$ Hz, 2H), 5.6–5.8 (m, 2H), 6.58 (d, $J=10.5$ Hz, 1H), 7.0–7.3 (m, 5H), 7.85 (dd, $J=14.0$ Hz, 10.5 Hz, 1H). EIMS (m/z): 260 (M$^+$).
R=PhCH$_2$ 9i: 0.9 (m, 3H), 1.2–1.4 (m, 6H), 1.9 (m, 2H), 2.3 (m, 2H), 2.6 (d, $J=8.0$ Hz, 2H), 3.15–3.3 (m, 2H), 3.6 (m, 1H), 5.2–5.4 (m, 4H), 7.1–7.3 (m, 5H). EIMS (m/z): 274 (M$^+$).

4.11. 5-Substituted-(3*Z*,6*Z*)-3,6-dodecadienyl-5-(4-methoxybenzyloxy)pentanoate 10a–i

5-(4-Methoxybenzyloxy)pentanoic acid (0.25 mmol) was dissolved in dichloromethane (2 mL). DCC (0.25 mmol) was added to the solution, followed by the addition of DMAP (10 mol%) at 0°C. The reaction mixture was stirred for 5 min and a solution of 5-substi-

tuted (3*Z*,6*Z*)-3,6-dodecadiene-1-ol (0.25 mmol) in dichloromethane was then added dropwise. The mixture was stirred for a further 3 h at rt. Dicyclohexylurea was filtered off, and the filtrate was washed with water, brine and dried (Na_2SO_4). After chromatographic separation the product was obtained in 60% yield.

^{1}H NMR data:

R=Me 10a: 0.9 (m, 3H), 1.0 (d, J=7.0 Hz, 3H), 1.2–1.4 (m, 6H), 1.6–1.8 (m, 4H), 2.0 (m, 2H), 2.2–2.4 (m, 4H), 3.4 (m, 3H), 3.8 (s, 3H), 4.0 (t, J=7.0 Hz, 2H), 4.4 (s, 2H), 5.2–5.4 (m, 4H), 6.8 (d, J=6.0 Hz, 2H), 7.2 (d, J=6.0 Hz, 2H). FABMS (m/z): 416 (M^+).
R=Et 10b: 0.9 (m, 6H), 1.2–1.4 (m, 8H), 1.6–1.8 (m, 4H), 2.0 (m, 2H), 2.3 (q, J=7.2 Hz, 2H), 2.4 (m, 2H), 3.15 (m, 1H), 3.4 (t, J=7.2 Hz, 2H), 3.8 (s, 3H), 4.1 (t, J=7.0 Hz, 2H), 4.4 (s, 2H), 5.0–5.4 (m, 4H). 6.8 (d, J=6.0 Hz, 2H), 7.2 (d, J=6.0 Hz, 2H). FABMS (m/z): 430 (M^+).
R=*n*-Pr 10c: 0.9 (m, 6H), 1.2–1.4 (m, 10H), 1.6 (m, 4H), 2.0 (m, 2H), 2.3 (m, 4H), 3.2 (m, 1H), 3.4 (t, J=7.0 Hz, 2H), 3.8 (s, 2H), 4.0 (t, J=7.0 Hz, 2H), 4.4 (s, 2H), 5.0–5.4 (m, 4H), 6.8 (d, J=6.0 Hz, 2H), 7.2 (d, J=6.0 Hz, 2H). FABMS (m/z): 444 (M^+).
R=*n*-Bu 10d: 0.9 (m, 6H), 1.2–1.4 (m, 12H), 1.6 (m, 4H), 2.0 (m, 2H), 2.4 (m, 4H), 3.2 (m, 1H), 3.4 (t, J=7.0 Hz, 2H), 3.8 (s, 3H), 4.0 (t, J=7.0 Hz, 2H), 4.4 (s, 2H), 5.0–5.4 (m, 4H), 6.8 (d, J=6.0 Hz, 2H), 7.2 (d, J=6.0 Hz, 2H). FABMS (m/z): 458 (M^+).
R=*i*-Bu 10e: 0.9 (m, 9H), 1.35 (m, 6H), 1.5–1.8 (m, 7H), 2.0 (m, 2H), 2.2–2.45 (m, 4H), 3.1 (m, 1H), 3.4 (t, J=7.0 Hz, 2H), 3.8 (s, 3H), 4.1 (t, J=7.0 Hz, 2H), 4.4 (s, 2H), 5.35 (m, 4H), 6.8 (d, J=6.0 Hz, 2H), 7.2 (d, J=6.0 Hz, 2H). FABMS (m/z): 458 (M^+).
R=*t*-Bu 10f: 0.9 (s, 12H), 1.35 (m, 6H), 1.6–1.9 (m, 4H), 2.0 (m, 2H), 2.3 (m, 4H), 3.1 (m, 1H), 3.4 (t, J=7.0 Hz, 2H), 3.9 (s, 3H), 4.0 (t, J=7.0 Hz, 2H), 4.4 (s, 2H), 5.2–5.4 (m, 4H), 6.8 (d, J=6.0 Hz, 2H), 7.2 (d, J=6.0 Hz, 2H). FABMS (m/z): 458 (M^+).
R=allyl 10g: 0.9 (t, J=7.0 Hz, 3H), 1.3 (m, 6H), 1.6 (m, 4H), 2.0 (m, 4H), 2.4 (m, 4H), 3.2 (m, 1H), 3.4 (t, J=7.2 Hz, 2H), 3.9 (s, 3H), 4.0 (t, J=7.2 Hz, 2H), 4.4 (s, 2H), 4.9–5.4 (m, 5H), 5.6–5.8 (m, 2H), 6.8 (d, J=6.0 Hz, 2H), 7.2 (d, J=6.0 Hz, 2H). FABMS (m/z): 442 (M^+).
R=Ph 10h: 0.9 (t, J=7.0 Hz, 3H), 1.2–1.8 (m, 10H), 2.2–2.5 (m, 6H), 3.48 (m, 1H), 3.6 (t, J=7.0 Hz, 2H), 3.8 (s, 3H), 4.1 (t, J=7.0 Hz, 2H), 4.4 (s, 2H), 5.6–5.8 (m, 2H), 6.58 (d, J=10.5 Hz, 1H), 6.8 (d, J=6.2 Hz, 2H), 7.0–7.3 (m, 5H), 7.2 (d, J=6.2 Hz, 2H), 7.85 (dd, J=14.0 Hz, 10.5 Hz, 1H). FABMS (m/z): 468 (M^+).
R=PhCH$_2$ 10i: 0.9 (m, 3H), 1.2 (m, 6H), 1.6 (m, 4H), 1.9 (m, 2H), 2.1–2.35 (m, 4H), 2.6 (d, J=8.0 Hz, 2H), 3.4 (t, J=7.0 Hz, 2H), 3.45 (m, 1H), 3.8 (s, 3H), 3.85 (m, 2H), 4.4 (s, 2H), 5.15–5.4 (m, 4H), 6.8 (d, J=6.0 Hz, 2H), 7.2 (m, 7H). FABMS (m/z): 482 (M^+).

4.12. 5-Substituted-(3*Z*,6*Z*)-3,6-dodecadienyl-5-hydroxypentanoate 1a–i

The deprotection of the PMB ether was completed as described in Section 4.6.

^{1}H NMR data:

R=Me 1a: 0.9 (m, 3H), 1.0 (d, J=7.0 Hz, 3H), 1.2–1.4 (m, 6H), 1.6–1.8 (m, 4H), 2.0 (m, 2H), 2.2–2.4 (m, 4H), 3.4 (m, 3H), 4.0 (t, J=7.0 Hz, 2H), 5.2–5.4 (m, 4H). FABMS (m/z): 296 (M^+). $[\alpha]_D^{25}$=+2.9 (*c* 1.0, $CHCl_3$). Anal. calcd for $C_{18}H_{32}O_3$: C, 72.93; H, 10.88. Found: C, 72.91; H, 10.94%.
R=Et 1b: 0.9 (m, 6H), 1.2–1.4 (m, 8H), 1.6–1.8 (m, 4H), 2.0 (m, 2H), 2.3 (q, J=7.2 Hz, 2H), 2.4 (m, 2H), 3.15 (m, 1H), 3.45 (t, J=7.2 Hz, 2H), 4.1 (t, J=7.0 Hz, 2H), 5.0–5.4 (m, 4H). FABMS (m/z): 310 (M^+). $[\alpha]_D^{25}$=+11.0 (*c* 1.2, $CHCl_3$). Anal. calcd for $C_{19}H_{34}O_3$: C, 73.50; H, 11.04. Found: C, 73.55; H, 11.02%.
R=*n*-Pr 1c: 0.9 (m, 6H), 1.2–1.4 (m, 10H), 1.6 (m, 4H), 2.0 (m, 2H), 2.4 (m, 4H), 3.2 (m, 1H), 3.4 (t, J=7.0 Hz, 2H), 4.0 (t, J=7.0 Hz, 2H), 5.0–5.4 (m, 4H). FABMS (m/z): 324 (M^+). $[\alpha]_D^{25}$=+5.2 (*c* 1.0, $CHCl_3$). Anal. calcd for $C_{20}H_{36}O_3$: C, 74.03; H, 11.18. Found: C, 74.08; H, 11.14%.
R=*n*-Bu 1d: 0.9 (m, 6H), 1.2–1.4 (m, 12H), 1.6 (m, 4H), 2.0 (m, 2H), 2.4 (m, 4H), 3.2 (m, 1H), 3.4 (t, J=7.0 Hz, 2H), 4.0 (t, J=7.0 Hz, 2H), 5.0–5.4 (m, 4H). FABMS (m/z): 338 (M^+). $[\alpha]_D^{25}$=+9.8 (*c* 1.0, $CHCl_3$). Anal. calcd for $C_{21}H_{38}O_3$: C, 74.51; H, 11.31. Found: C, 74.49; H, 11.26%.
R=*i*-Bu 1e: 0.9 (m, 9H), 1.35 (m, 6H), 1.5–1.8 (m, 7H), 2.0 (m, 2H), 2.2–2.45 (m, 4H), 3.19 (m, 1H), 3.4 (t, J=7.0 Hz, 2H), 4.1 (t, J=7.0 Hz, 2H), 5.35 (m, 4H). $[\alpha]_D^{25}$=+6.2 (*c* 1.1, $CHCl_3$). FABMS (m/z): 338 (M^+).
R=*t*-Bu 1f: 0.9 (s, 12H), 1.35 (m, 6H), 1.6–2.0 (m, 4H), 2.0 (m, 2H), 2.4 (m, 4H), 3.1 (m, 1H), 3.4 (t, J=7.0 Hz, 2H), 4.0 (t, J=7.0 Hz, 2H), 5.2–5.4 (m, 4H). $[\alpha]_D^{25}$=+1.9 (*c* 1.1, $CHCl_3$). FABMS (m/z): 338 (M^+).
R=allyl 1g: 0.9 (t, J=7.0 Hz, 3H), 1.3 (m, 6H), 1.7 (m, 4H), 2.0 (m, 4H), 2.2–2.4 (m, 4H), 3.2 (m, 1H), 3.4 (t, J=7.2 Hz, 2H), 4.0 (t, J=7.2 Hz, 2H), 4.9–5.4 (m, 5H), 5.6–5.8 (m, 2H). FABMS (m/z): 322 (M^+). $[\alpha]_D^{25}$=+10.1 (*c* 1.0, $CHCl_3$). Anal. calcd for $C_{20}H_{34}O_3$: C, 74.49; H, 10.63. Found: C, 74.53; H, 10.68%.
R=Ph 1h: 0.9 (t, J=7.0 Hz, 3H), 1.2–1.8 (m, 10H), 2.2–2.5 (m, 6H), 3.48 (m, 1H), 3.6 (t, J=7.0 Hz, 2H), 4.1 (t, J=7.0 Hz, 2H), 5.6–5.8 (m, 2H), 6.58 (d, J=10.5 Hz, 1H), 7.0–7.3 (m, 5H), 7.85 (dd, J=14.0 Hz, 10.5 Hz, 1H). FABMS (m/z): 358 (M^+). $[\alpha]_D^{25}$=−19.2 (*c* 1.0, $CHCl_3$). Anal. calcd for $C_{23}H_{34}O_3$: C, 77.05; H, 9.56. Found: C, 76.81; H, 9.87%.
R=PhCH$_2$ 1i: 0.9 (m, 3H), 1.2 (m, 6H), 1.6 (m, 4H), 1.9 (m, 2H), 2.1–2.35 (m, 4H), 2.6 (d, J=8.0 Hz, 2H), 3.4 (t, J=7.0 Hz, 2H), 3.45 (m, 1H), 3.85 (m, 2H),

5.15–5.4 (m, 4H), 2H), 7.2 (m, 5H). FABMS (m/z): 372 (M^+). $[\alpha]_D^{25}=+12.4$ (c 1.0, $CHCl_3$). Anal. calcd for $C_{24}H_{36}O_3$: C, 77.38; H, 9.74. Found: C, 77.21; H, 10.02%.

4.13. Preparation of FAC acid [2-(fluorophenoxy)-(2*S*)-propanoic acid]

A solution of DIAD (0.05 mol) in THF (35 mL) was added dropwise to a mixture of (*S*)-ethyl lactate (0.05 mol), 2-fluorophenol (0.05 mol) and TPP (0.05 mol) in THF (75 mL). The mixture was stirred overnight at rt. After evaporation of THF, a mixture of hexane:ether (1:1, 125 mL) was added to the viscous residue and stirring was continued until a crystalline precipitate had separated (1 h). The precipitate was filtered off, and the filtrate washed with 1N NaOH (2×50 mL), brine and water. After evaporation of the solvent, the crude product was directly hydrolyzed in methanol (200 mL) with 2N aq. NaOH (50 mL). Methanol was evaporated with minimum heat, and water (50 mL) was added. Extraction with ether (3×50 mL) eliminates most of the impurities. After cooling in an ice bath, the aq. layer was neutralized with conc. HCL (10 mL). The free acid was extracted with ether (3×50 mL). After drying (Na_2SO_4) it was recrystallized from hexane. ^{1}H NMR: 1.55 (d, $J=7.5$ Hz, 3H), 4.7 (q, $J=7.5$ Hz, 1H), 6.9–7.0 (m, 4H), 9.5 (brs, 1H). $[\alpha]_D^{25}=+31.6$ (c 1.15, $CHCl_3$). EIMS (m/z): 184 (M^+).

4.14. Coupling of FAC acid with alcohols

DCC (1 mmol), the chiral alcohol (1 mmol) and FAC acid (1 mmol) were dissolved in anhydrous THF. A few crystals of DMAP were added. The clear solution rapidly became cloudy on stirring. After stirring overnight the mixture was filtered. Solvent was evaporated without heating and the product was purified using column chromatography.

^{1}H NMR data:

R=Me: 0.9 (d, $J=7.0$ Hz, 3H), 1.64 (d, $J=7.2$ Hz, 3H), 1.8 (m, 1H), 3.2 (m, 2H), 3.8 (s, 3H), 4.2 (m, 2H), 4.4 (s, 2H), 4.89 (q, $J=7.2$ Hz, 1H), 6.8 (d, $J=6.2$ Hz, 2H), 6.9–7.1 (m, 4H), 7.2 (d, $J=6.2$ Hz, 2H).
R=Et: 0.9 (t, $J=7.0$ Hz, 3H), 1.2–1.4 (m, 2H), 1.6 (d, $J=7.0$ Hz, 3H), 1.8 (m, 1H), 3.2 (m, 2H), 3.8 (s, 3H), 4.15 (m, 2H), 4.35 (s, 2H), 4.7 (q, $J=7.0$ Hz, 1H), 6.8 (d, $J=6.2$ Hz, 2H), 6.9–7.1 (m, 4H), 7.2 (d, $J=6.2$ Hz, 2H).
R=*n*-Pr: 0.9 (t, $J=7.0$ Hz, 3H), 1.2–1.4 (m, 4H), 1.6 (d, $J=7.2$ Hz, 3H), 1.9 (m, 1H), 3.3 (m, 2H), 3.8 (s, 3H), 4.1–4.2 (m, 2H), 4.4 (s, 2H), 4.85 (q, $J=7.2$ Hz, 1H), 6.8 (d, $J=6.2$ Hz, 2H), 6.9–7.1 (m, 4H), 7.2 (d, $J=6.2$ Hz, 2H).
R=*n*-Bu: 0.9 (t, $J=7.0$ Hz, 3H), 1.2 (m, 6H), 1.6 (d, $J=7.2$ Hz, 3H), 1.8 (m, 1H), 3.3 (d, $J=6.8$ Hz, 2H), 3.9 (s, 3H), 4.2 (m, 2H), 4.45 (s, 2H), 4.75 (q, $J=7.2$ Hz, 1H), 6.8 (d, $J=6.0$ Hz, 2H), 6.9–7.2 (m, 6H).
R=*i*-Bu: 0.9 (m, 6H), 1.5 (m, 2H), 1.6 (d, $J=7.2$ Hz, 3H), 1.8 (m, 2H), 3.3–3.4 (m, 2H), 3.8 (s, 3H), 4.1–4.2 (m, 2H), 4.4 (s, 2H), 4.75 (q, $J=7.2$ Hz, 1H), 6.8 (d, $J=6.0$ Hz, 2H), 6.9–7.1 (m, 4H), 7.2 (d, $J=6.2$ Hz, 2H).
R=*t*-Bu: 0.9 (m, 9H), 1.6 (d, $J=7.2$ Hz, 3H), 1.75 (m, 1H), 3.4 (m, 2H), 3.8 (s, 3H), 4.1 (m, 2H), 4.4 (s, 2H), 4.75 (q, $J=7.2$ Hz, 1H), 6.8 (d, $J=6.0$ Hz, 2H), 7.0–7.2 (m, 6H).
R=allyl: 1.6 (d, $J=7.2$ Hz, 3H), 2.0 (m, 3H), 3.3 (m, 2H), 3.8 (s, 3H), 4.15 (m, 2H), 4.45 (s, 2H), 4.75 (q, $J=7.2$ Hz, 1H), 5.0 (m, 2H), 5.7 (m, 1H), 6.8 (d, $J=6.0$ Hz, 2H), 6.9–7.2 (m, 6H).
R=Ph: 1.55 (d, $J=7.2$ Hz, 3H), 3.2 (m, 1H), 3.6 (m, 2H), 3.8 (s, 3H), 4.4 (ABd, $J=6.0$ Hz, 2H), 4.5 (m, 2H), 4.7 (q, $J=7.2$ Hz, 1H), 6.8 (d, $J=6.0$ Hz, 2H), 6.9–7.3 (m, 11H).
R=PhCH$_2$: 1.6 (d, $J=7.2$ Hz, 3H), 1.9 (m, 1H), 2.6 (d, $J=8.0$ Hz, 2H), 3.4 (m, 2H), 3.8 (s, 3H), 4.15 (m, 2H), 4.4 (s, 2H), 4.72 (q, $J=7.2$ Hz, 1H), 6.8 (d, $J=6.0$ Hz, 2H), 6.9–7.2 (m, 11H).

4.15. 1-(4-*O*-*tert*-Butyldiphenylsilyl-1-butynyl)-(1*R*)-2-octynylalcohol 12

Deprotection of the acetate group was completed as described in Section 2.3. IR (TF): 3390, 3010 cm^{-1}. ^{1}H NMR: 0.85 (t, $J=7.0$ Hz, 3H), 1.0 (s, 9H), 1.2–1.5 (m, 6H), 2.25 (t, $J=7.0$ Hz, 2H), 2.5 (t, $J=7.0$ Hz, 2H), 3.7 (t, $J=7.0$ Hz, 2H), 5.0 (s, 1H), 7.35–7.7 (m, 10H). FABMS (m/z): 433 (M+1). $[\alpha]_D^{25}=+9.2$ (c 1.2, $CHCl_3$).

4.16. 1-Methoxy-4[1-(4-*O*-*tert*-butyldiphenylsilyl-1-butynyl-(1*R*)-2-octynyloxymethyl]benzene 13

A solution of the PMB alcohol (37.6 mmol) in ether (35 mL) was added to sodium hydride (60% suspension in oil, 5 mmol) in ether (40 mL) at rt. The resulting mixture was stirred at rt for 0.5 h and cooled to 0°C. Trichloroacetonitrile (37.6 mmol) was added, and the reaction mixture was allowed to warm slowly to rt over 4 h. The solution was concentrated to an orange syrup, which was dissolved in dry petroleum ether (50 mL) containing MeOH (0.2 mL). This suspension was shaken vigorously and filtered through Celite, and the filtrate was concentrated to a yellow syrup. The crude imidate (0.784 g, 2.7 mmol) was dissolved in cyclohexane (15 mL) and a solution of alcohol (1 g, 2.3 mmol) in DCM (8 mL) was added. The resulting solution was cooled to 0°C and treated with CSA (10 mol%). The reaction mixture was warmed to rt and stirred overnight; slowly, a white precipitate developed. The solution was filtered and then washed with DCM. The filtrate washed with satd $NaHCO_3$, brine and dried (Na_2SO_4). Purification by means of column chromatography afforded the title product (1.1 g, 86%). ^{1}H NMR: 0.9 (t, $J=6.9$ Hz, 3H), 1.1 (s, 9H), 1.2–1.4 (m, 6H), 2.2 (t, $J=6.9$ Hz, 2H), 2.5 (t, $J=6.9$ Hz, 2H), 3.8 (m, 5H), 4.5 (s, 2H), 4.8 (s, 1H), 6.8 (d, $J=6.2$ Hz, 2H), 7.2 (d, $J=6.2$ Hz, 2H), 7.3 (m, 5H), 7.6 (m, 5H). FABMS (m/z): 552 (M^+). $[\alpha]_D^{25}=+32.5$ (c 1.0, $CHCl_3$).

4.17. 5-(4-Methoxybenzyloxy)-(5*R*)-3,6-dodecadiyn-1-ol 11

The compound obtained in the previous step (1.1 g, 2 mmol) was taken up in dry THF (25 mL). At 0°C a solution of TBAF (1 M in THF, 3.8 mL, 4 mmol) was added. The resulting solution was stirred for 2 h at rt. After completion of the reaction, satd NH_4Cl was added and the mixture was extracted with EtOAc. The organic extract was washed with water, brine and dried (Na_2SO_4). The residue was purified by column chromatography to afford the product (600 mg, 95%). ^1H NMR: 0.9 (t, $J=7.0$ Hz, 3H), 1.2–1.4 (m, 6H), 2.2 (t, $J=7.0$ Hz, 2H), 2.5 (t, $J=7.0$ Hz, 2H), 3.6 (t, $J=7.0$ Hz, 2H), 3.8 (s, 3H), 4.5 (s, 2H), 4.9 (s, 1H), 6.8 (d, $J=6.0$ Hz, 2H), 7.2 (d, $J=6.0$ Hz, 2H). ^{13}C NMR: 159.41, 129.9, 129.4, 113.82, 86.35, 82.13, 78.12, 75.69, 68.73, 60.8, 57.94, 55.24, 31.04, 28.06, 23.16, 22.1, 18.69, 13.9. FABMS (m/z): 314 (M^+). $[\alpha]_D^{25}=+19.1$ (c 1.1, $CHCl_3$). Anal. calcd for $C_{20}H_{26}O_3$: C, 76.40; H, 8.33. Found: C, 76.48; H, 8.28%.

4.18. 5-(4-Methoxybenzyloxy)-(5*R*)-3,6-dodecadienyl-5-(4-methoxybenzyloxy)pentanoate 14

5-(4-Methoxybenzyloxy)pentanoic acid (460 mg, 2.0 mmol) was taken up in dichloromethane (8 mL). DCC (452 mg, 2.0 mmol) was added followed by the addition of DMAP (10 mg) at 0°C. The reaction mixture was stirred for 5 min, and a solution of 5-(4-methoxybenzyloxy)-(5*R*)-3,6-dodecadiyn-1-ol (600 mg, 1.9 mmol) in dichloromethane (5 mL) was added dropwise. The mixture was stirred for a further 3 h at rt. Dicyclohexylurea was filtered off and the filtrate was washed with water, brine and dried (Na_2SO_4). After chromatographic separation, the coupled ester was obtained (800 mg, 78%). ^1H NMR: 0.9 (t, $J=6.8$ Hz, 3H), 1.2–1.8 (m, 10H), 2.1–2.4 (m, 4H), 2.55 (t, $J=6.8$ Hz, 2H), 3.4 (t, $J=6.8$ Hz, 2H), 3.8 (s, 6H), 4.1 (t, $J=6.8$ Hz, 2H), 4.35 (s, 2H), 4.5 (s, 2H), 5.09 (s, 1H), 6.8 (d, $J=6$ Hz, 4H), 7.2 (d, $J=6$ Hz, 4H). FABMS (m/z): 534 (M^+). $[\alpha]_D^{25}=+4.8$ (c 0.9, $CHCl_3$). Anal. calcd for $C_{33}H_{42}O_6$: C, 74.13; H, 7.92. Found: C, 74.26; H, 7.99%.

4.19. 5-Hydroxy-(5*R*)-3,6-dodecadienyl-5-hydroxypentanoate 15

The compound obtained in the previous reaction (800 mg, 1.5 mmol) was taken up in dichloromethane:water (19:1, 15 mL). DDQ (1.1 g, 4.5 mmol) was added and the solution stirred for 1 h at rt. The reaction mixture was filtered off, and the filtrate was washed with 5% aq. $NaHCO_3$ solution, brine and dried (Na_2SO_4). Chromatographic purification gave the desired product (350 mg, 80%). ^1H NMR: 0.95 (t, $J=7.0$ Hz, 3H), 1.2–1.8 (m, 10H), 2.2 (t, $J=7.0$ Hz, 2H), 2.4 (t, $J=7.0$ Hz, 2H), 2.6 (t, $J=7.0$ Hz, 2H), 3.7 (t, $J=7.0$ Hz, 2H), 4.2 (t, $J=7.0$ Hz, 2H), 5.1 (s, 1H). ^{13}C NMR: 173.48, 80.14, 63.852, 62.168, 61.91, 60.72, 60.37, 52.17, 33.88, 31.0, 28.02, 22.1, 21.22, 21.12, 19.3, 18.62, 13.85. FABMS (m/z): 294 (M^+). $[\alpha]_D^{25}=+11.1$ (c 1.0, $CHCl_3$).

4.20. 5-Hydroxy-(3*Z*,5*R*,6*Z*)-3,6-dodecadienyl-5-hydroxypentanoate 1j

The diacetylenic alcohol (350 mg) in absolute ethanol (10 mL) was taken up in a small round-bottomed flask. Lindlar catalyst (35 mg, Pd on $CaCO_3$) and a few drops of quinoline were added. Hydrogen was supplied from balloons. The reaction was monitored by TLC (visualization was done by dipping the plates in Eckerts reagent and heating it at 120°C), where the olefinic product moves a little faster than the starting material. After completion of the reaction, it was filtered to remove the catalyst. Ethanol was removed on a rotary evaporator. Dichloromethane was added to the residue and it was then washed with 5% aq. HCl, brine and dried (Na_2SO_4). The product was purified by column chromatography to afford **1j** in 96% yield. ^1H NMR: 0.9 (t, $J=6.9$ Hz, 3H), 1.2–1.4 (m, 6H), 1.5–1.8 (m, 4H), 2.2 (m, 2H), 2.4 (t, $J=6.9$ Hz, 2H), 2.6 (m, 2H), 3.6 (t, $J=6.9$ Hz, 2H), 4.1 (m, 2H), 5.2 (t, $J=8$ Hz, 1H), 5.4–5.7 (m, 4H). ^{13}C NMR: 170.9, 132.12, 132.01, 128.58, 128.46, 81.0, 64.0, 62.11, 33.82, 31.42, 29.22, 27.72, 22.25, 22.48, 21.1, 19.8, 13.9. FABMS (m/z): 296 (M^+). $[\alpha]_D^{25}=+13.4$ (c 1.0, $CHCl_3$). Anal. calcd for $C_{17}H_{30}O_4$: C, 68.42; H, 10.13. Found: C, 68.36; H, 10.16%.

Acknowledgements

One of the authors (S.N.) is thankful to the Council of Scientific and Industrial Research (CSIR, New Delhi) for the award of a research fellowship.

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