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Novozym 435-catalyzed kinetic resolution of β-allenols. A facile route for the preparation of optically active β-allenols or allenyl acetates

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Abstract—A variety of optically active β-allenols and β-allenyl acetates were synthesized via the Novozym 435-mediated kinetic resolution of racemic β-allenols. A dramatic solvent effect was observed for the stereoselectivity. The scope of the substrates and the effect of the concentration and temperature on the reaction were also investigated.

1. Introduction

Allenes are a class of compounds with two cumulative carbon–carbon double bonds, which demonstrate interesting properties such as unique reactivity and chirality.[1] In the past decades, much attention has been paid to the synthesis and reaction of functionalized allenes.[2] Since the chirality of allenes can be transformed to the products with one or more chiral center, people are interested in the synthesis of optically active allenes.[3] Allenols are a very important class of functionalized allenes, which can be converted to many organic intermediates. For example, 2,3-allenols can be stereoselectively converted into oxiranes,[4] 2,5-dihydrofurans,[5] α-methylenelactones,[6] α or γ-amino alcohols[7] etc. Starting from β-allenols, 3-oxacyclohexanone,[8] 3,6-dihydro-2*H*-pyran,[9] 2,3-dihydrofuran[10] and furans[11] can also easily be obtained. Thus, the synthesis of optically active allenols is of current interest. For optically active 2,3-allenols, some synthetic methods were developed in recent years.[12] However, the methodologies for the synthesis of optically active β-allenols were very limited: the methodologies for the optically active β-allenols reported in the literature are mainly using optically active 3-en-5-yn-2-ols as the starting material, which are not easily available.[13] Biocatalytic methods are now well-established routes to enantiomerically pure or enriched alcohols with the advantages of easy availability of starting materials and the biocatalyst. The kinetic resolution of 2-methylpenta-3,4-dien-1-ol using Lipase AK and Novozym-435 (a form of *candida antarctica lipase B*) as the biocatalyst has been reported.[14] The kinetic resolution of those β-allenols with chiral centers connected with the hydroxyl group using an enzyme or a microorganism as the catalyst has not been reported. Previously, we have reported that Novozym-435 (a form of *candida antarctica lipase B*) is an efficient biocatalyst for the kinetic resolution of a series of racemic 2,3-allenols[15] and terminal aryl-substituted propargylic alcohols that can be converted to the corresponding 2,3-allenols.[16] Here we wish to report our recent results on Novozym-435-catalyzed kinetic resolution of β-allenols.

2. Results and discussion

2.1. Synthesis of starting racemic 2,3-allenols

The required racemic β-allenols can be synthesized according to the known procedure as shown in Scheme 1.[17]

2.2. Kinetic resolution

We started our research with the kinetic resolution of **1a** using the same reaction conditions reported in Ref. 15. Optically active **2a** was obtained in 35% yield with 96% ee

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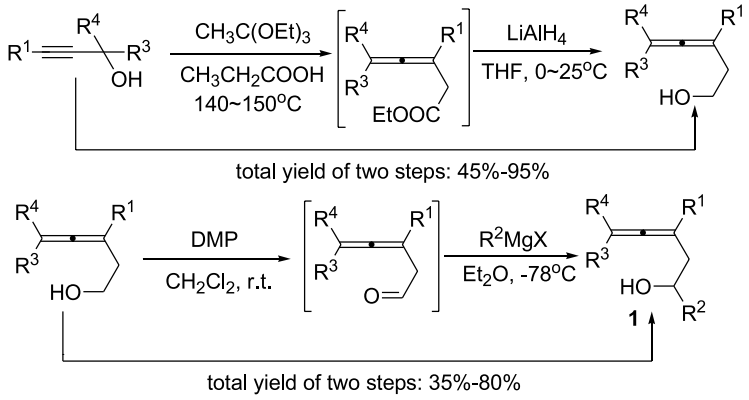


1a $R^1 = n\text{-}C_4H_9$, $R^2 = Et$, $R^3 = R^4 = H$ **1b** $R^1 = n\text{-}C_3H_7$, $R^2 = Et$, $R^3 = R^4 = H$

1c $R^1 = n\text{-}C_6H_{13}$, $R^2 = Et$, $R^3 = R^4 = H$ **1d** $R^1 = n\text{-}C_7H_{15}$, $R^2 = Et$, $R^3 = R^4 = H$

1e R^1 = allyl, $R^2 = Et$, $R^3 = R^4 = H$ **1f** $R^1 = PhCH_2$, $R^2 = Et$, $R^3 = R^4 = H$

1g $R^1 = H$, $R^2 = Et$, $R^3 = R^4 = CH_3$ **1h** $R^1 = n\text{-}C_4H_9$, $R^2 = Et$, $R^3 = R^4 = CH_3$

1i $R^1 = n\text{-}C_4H_9$, $R^2 = Et$, $R^3 = R^4 = (CH_2)_5$ **1j** $R^1 = n\text{-}C_4H_9$, $R^2 = Me$, $R^3 = R^4 = H$

1k $R^1 = n\text{-}C_4H_9$, $R^2 = Me$, $R^3 = R^4 = Me$ **1l** $R^1 = n\text{-}C_4H_9$, R^2 = ethenyl, $R^3 = R^4 = H$

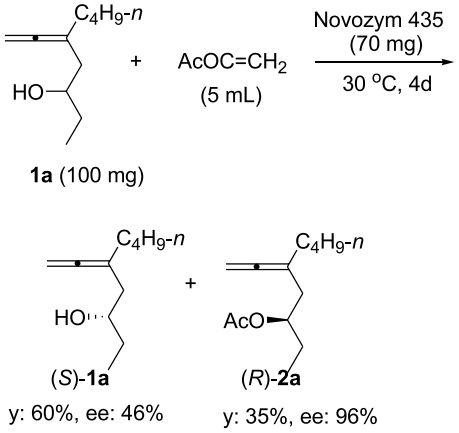
1m $R^1 = n\text{-}C_5H_{11}$, R^2 = ethenyl, $R^3 = R^4 = H$ **1n** $R^1 = n\text{-}C_4H_9$, R^2 = ethynyl, $R^3 = R^4 = H$

1o $R^1 = n\text{-}C_5H_{11}$, R^2 = ethynyl, $R^3 = R^4 = H$ **1p** $R^1 = n\text{-}C_4H_9$, $R^2 = n\text{-}Pr$, $R^3 = R^4 = H$

1q $R^1 = t\text{-}C_4H_9$, $R^2 = Et$, $R^3 = R^4 = H$ **1r** $R^1 = CH_3$, $R^2 = Me$, $R^3 = R^4 = H$

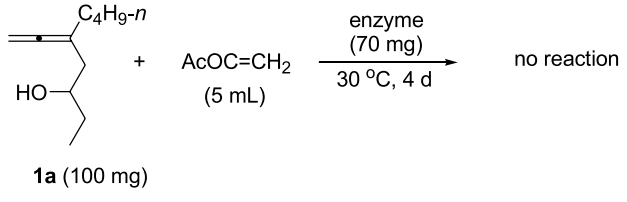
Scheme 1.

while the ee value of unreacted **1a** was not good (Eq. 1).



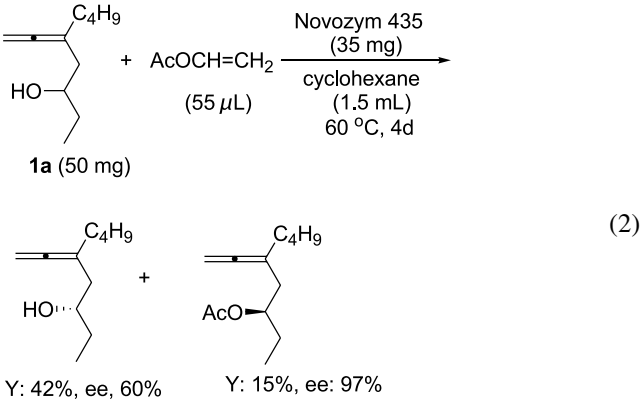
(1)

In order to identify the best enzyme for the present class of compounds, extensive screening experiments were carried out. Using PPL, CRL, Lipase AK, and Lipase Ps 30 as the catalyst, the reaction is extremely slow or does not even occur (Scheme 2).



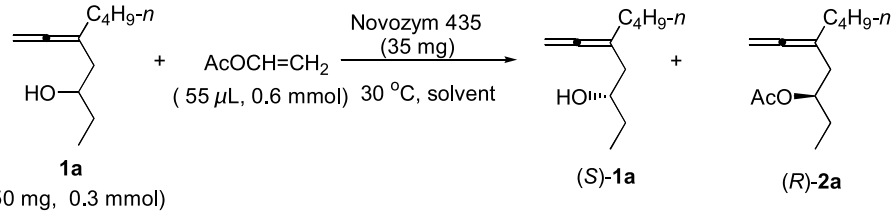
Scheme 2.

It was reported that the solvent may be critical to the enzyme-catalyzed reaction.[18] Some typical results using Novozym 435 as the biocatalyst in different solvent are listed in Table 1. As shown in Table 1, the solvent did affect the reaction dramatically: using 1,4-dioxane as the solvent, the reaction cannot occur (Table 1, entry 1); when the reaction was carried out in vinyl acetate, *E* value of the reaction is 62 (Table 1, entry 2); when using hexane, benzene, acetone, or acetonitrile, the results are better with the *E* values being 144, 148, 156, and 178, respectively (Table 1, entries 3, 4, 5, and 6); while using the cyclohexane as the solvent, optically active (*S*)-**1a** can be obtained in 44% yield and 74% ee and (*R*)-**2a** in 42% yield and 97% ee (Table 1, entry 7). Changing the concentration (Table 2) and reaction temperature (Eq. 2) did not greatly alter the selectivity of the reaction (Eq. 2).



(2)

Table 1. Novozym 435-catalyzed kinetic resolution of **1a** in different solvents[a]

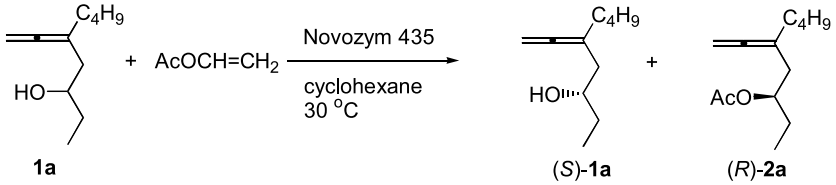


1a (50 mg, 0.3 mmol) (*S*)-**1a** (*R*)-**2a**

Entry	Time (d)	Solvent	Alcohol (**1a**)		Ester (**2a**)		E[b]
			Yield[c] (%)	ee (%)[d]	Yield[c] (%)	ee[e] (%)	
1	4	1,4-Dioxane			NR		
2	4	Vinyl acetate	56	43	29	95	62
3	3	Hexane	58	77	38	97	144
4	4	Benzene	64	67	34	97	148
5	3	Acetone	56	74	43	97	156
6	4	Acetonitrile	64	48	35	98	178
7	4	Cyclohexane	44	74	42	98	192

[a] The reaction was carried out at 30 °C using **1a** (50 mg), vinyl acetate (55 μL), solvent (1.5 mL) and enzyme (35 mg).
[b] $E=\ln[ee_P(1-ee_S)]/(ee_P+ee_S)/\ln[ee_P(1+ee_S)]/(ee_P+ee_S)$.
[c] Isolated yield based on **1a**.
[d] Determined after its conversion into the corresponding acetate.
[e] Enantiomeric excess determined via GC.

Table 2. Novozym 435-catalyzed kinetic resolution of **1a** at different concentrations[a]



1a (*S*)-**1a** (*R*)-**2a**

Entry	Solvent (mL)	(*S*)-**1a**		(*R*)-**2a**		E[b]
		Yield (%)[c]	ee (%)[d]	Yield (%)[c]	ee (%)[d]	
1	3.0	68	39	32	98	172
2	2.5	50	58	30	98	199
3	2	48	52	37	98	176
4	1	46	45	29	98	155

[a] The reaction was carried out at 30 °C using **1a** (50 mg), vinyl acetate (55 μL), solvent (1.5 mL) and enzyme (35 mg).
[b] $E=\ln[ee_P(1-ee_S)]/(ee_P+ee_S)/\ln[ee_P(1+ee_S)]/(ee_P+ee_S)$.
[c] Isolated yield based on **1a**.
[d] Enantiomeric excess determined by GC.

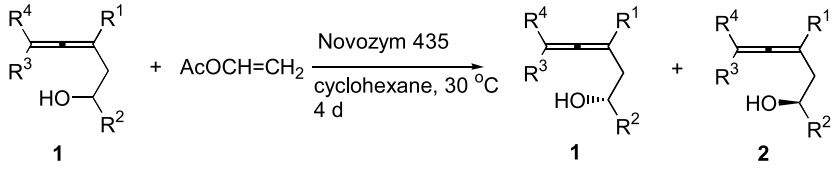
Subsequently, a series of β-allenols were resolved. Some typical results were listed in Table 3. From the results shown in Table 3, it can be clearly seen that this methodology can accommodate a wide range of substrates. In most cases, the reaction went well affording optically active β-allenols or allenyl acetates in good yields and good ees. The substituents have some effect on the stereoselectivity of the reaction. The result with R^2 being ethyl is better than those with R^2 being methyl, ethenyl, and ethynyl (Table 3, entries 1, 10, 12, and 14). When R^2 is beyond two carbon atoms, the reaction is extremely slow or even does not occur at all. Although R^3 and R^4 are far away from the chiral center, they also affect the stereoselectivity of the reaction. The results are different when R^3 and R^4 are H, methyl, and cyclohexylidene (Table 3, entries 1, 8, and 9). When R^1 is *t*-butyl, perhaps due to the stereic hindrance, the reaction did not occur. The absolute configuration of the obtained (+)-4-methylhexa-4,5-dien-2-ol (**1r**) was determined to be *S* by the comparison of the sign of the specific rotation with the known (*R*)-(−)-4-methylhexa-4,5-dien-2-ol (Scheme 3).[13] The absolute configuration of the compounds in Table 3 was tentatively assigned based on this result (Scheme 3).

(+)-**1r** (*R*)-(-)-**1r**

Scheme 3.

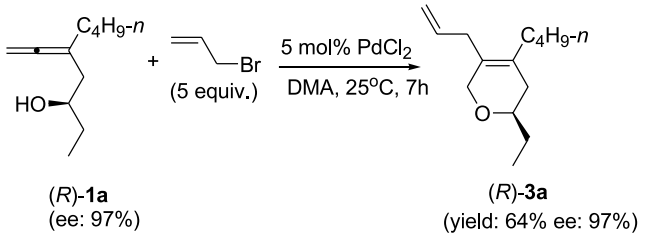
The resulting optically active allenol (**1a**) can easily be converted to the corresponding 3,6-dihydropyran without obvious racemization (Eq. 3).

Table 3. Novozym-435-catalyzed kinetic resolution of β-allenols[a]



Entry	1				1		2		E[b]
	R^1	R^2	R^3	R^4	Yield (%)[c]	ee (%)[d]	Yield (%)[c]	ee (%)[d]	
1	n-C_4H_9	Et	H	H (**1a**)	46	83 (*S*-**1a**)	42	97 (*R*-**2a**)	199
2	n-C_3H_7	Et	H	H (**1b**)	39	82 (*S*-**1b**)	36	96 (*R*-**2b**)	143
3	n-C_6H_{13}	Et	H	H (**1c**)	51	58 (*S*-**1c**)	28	98 (*R*-**2c**)	178
4	n-C_7H_{15}	Et	H	H (**1d**)	40	54 (*S*-**1d**)	25	98 (*R*-**2d**)	191
5[e]	Allyl	Et	H	H (**1e**)	48	50 (*S*-**1e**)	28	97 (*R*-**2e**)	111
6[e]	$PhCH_2$	Et	H	H (**1f**)	38	71 (*S*-**1f**)	44	72 (*R*-**2f**)	12
7[f]	H	Et	Me	Me (**1g**)	27	93 (*S*-**1g**)	59	22 (*R*-**2g**)	4
8	n-C_4H_9	Et	Me	Me (**1h**)	46	44 (*S*-**1h**)	26	95 (*R*-**2h**)	66
9	n-C_4H_9	Et	$(CH_2)_5$ (**1i**)		42	96 (*S*-**1i**)	51	82 (*R*-**2i**)	41
10[e]	n-C_4H_9	Me	H	H (**1j**)	37	88 (*S*-**1j**)	35	89 (*R*-**2j**)	52
11	n-C_4H_9	Me	Me	Me (**1k**)	38	91 (*S*-**1k**)	52	42 (*R*-**2k**)	31
12[e]	n-C_4H_9	Ethenyl	H	H (**1l**)	43	93 (*R*-**1l**)	56	75 (*S*-**2l**)	24
13	n-C_5H_{11}	Ethenyl	H	H (**1m**)	44	93 (*R*-**1m**)	40	85 (*S*-**2m**)	108
14	n-C_4H_9	Ethynyl	H	H (**1n**)	38	88 (*R*-**1n**)	56	44[f] (*S*-**2n**)	7
15	n-C_5H_{11}	Ethynyl	H	H (**1o**)	40	90 (*R*-**1o**)	40	60 (*S*-**2o**)	35

[a] The reaction was carried out at 30 °C using **1** (100 mg), vinyl acetate (2 equiv), Novozym 435 (100 mg), and cyclohexane (3.0 mL).
[b] $E=\ln[ee_P(1-ee_S)]/(ee_P+ee_S)/\ln[ee_P(1+ee_S)]/(ee_P+ee_S)$.
[c] Isolated yield based on **1**.
[d] Enantiomeric excess determined via GC or HPLC.
[e] Novozym 435 (70 mg).
[f] Reaction time: 1 day.



(3)

In conclusion, we have developed an efficient and facile method for the preparation of optically active β-allenols or β-allenyl acetates under mild conditions. Due to the easy availability of the catalyst and the synthetic potential of the products, this methodology should be useful in organic chemistry. Further studies on this reaction are being carried out in our laboratory.

3. Experimental

3.1. Synthesis of racemic β-allenols (1a–s)

The racemic β-allenols were synthesized according to the procedure reported in the literature.[17] A typical example was presented as follows:

3.1.1. Synthesis of (±)-5-(*n*-butyl)hepta-5,6-dien-3-ol (1a). To a dried three-neck flask were added hepta-2-yn-1-ol (6.12 g, 54.7 mmol), triethyl orthoacetate (34.8 mL, 189 mmol), and propionic acid (0.68 mL) under nitrogen. Additional 0.5 mL of propionic acid was added after 145 min. The mixture was stirred at 140–150 °C for 5 h as the resulting EtOH was removed by a Dean–Stark trap. After the starting material was completely consumed as monitored by TLC, the mixture was cooled to room temperature, evaporated, and purified by chromatography on silica gel to afford 3-(*n*-butyl)penta-3,4-dienoic acid ethyl ester, which was submitted to the next step without further characterization.

To a suspension of $LiAlH_4$ (2.13 g, 56.1 mmol) in dried THF (72 mL) was added a solution of the obtained 3-(*n*-butyl)penta-3,4-dienoic acid ethyl ester in dried THF (72 mL) dropwise at 0 °C. After stirring at rt for 1 h, the reaction was quenched by the careful addition of water at 0 °C. Filtration, drying over anhydrous Na_2SO_4, and concentration afforded the crude product, which was purified by chromatography on silica gel (eluent: petroleum ether/ethyl ether = 10/1) to afford pure 3-(*n*-butyl)penta-3,4-dien-1-ol (4.65 g, 61% (two steps)).

A solution of 3-(*n*-butyl)penta-3,4-diene-1-ol (1.57 g, 11.2 mmol) in CH_2Cl_2 (5 mL) was added to a suspension of Dess–Martin periodinane (DMP) (6.61 g, 17.6 mmol) in CH_2Cl_2 (15 mL). After 0.5 h, the reaction was diluted with ethyl ether (30 mL), and the resulting suspension was added to a solution of saturated $NaHCO_3$ (50 mL) with sodium thiosulfate (30.00 g, 121 mmol). After the mixture was stirred for 30 min, the ether layer was separated and the aqueous layer was extracted with ethyl ether (3×30 mL). The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated to afford the allenal, which was used without further purification.

To a solution of the obtained allenal in ethyl ether (20 mL) was added EtMgBr (1 M in THF, 20 mL) dropwise at −78 °C under nitrogen. Then, the resulting mixture was stirred for 10 h at −78 °C as monitored by TLC. The reaction was quenched with saturated NH_4Cl at −78 °C. After the temperature rose to rt, the organic layer was separated. The aqueous layer was extracted with ethyl ether (3×30 mL). The combined organic layer was dried over anhydrous Na_2SO_4, concentrated, and purified by chromatography on silica gel (eluent: petroleum ether/ethyl ether = 15/1) to afford racemic 5-(*n*-butyl)hepta-5,6-dien-3-ol (**1a**) (0.90 g, 48%); liquid; ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.80–4.70 (m, 2H), 3.75–3.64 (m, 1H), 2.20–1.90 (m, 5H), 1.58–1.28 (m, 6H), 0.96 (t, J=7.5 Hz, 3H), 0.90 (t, J=7.2 Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 205.7, 100.5, 75.9, 70.9, 39.9, 31.9, 29.5, 29.3, 22.2, 13.8, 9.8; IR (neat): 3388, 1956 cm^{-1}; MS (*m/z*) 168 (M^+, 2.47), 43 (100); HRMS Calcd for $C_{11}H_{20}O$ (M^+): 168.1514. Found 168.1488.

3.2. Kinetic resolution of racemic β-allenols (1a–1o)

3.2.1. Synthesis of (*S*)-5-(*n*-butyl)hepta-5,6-dien-3-ol ((*S*)-1a) and (*R*)-5-(*n*-butyl)hepta-5,6-dien-3-yl acetate ((*R*)-2a). *Typical procedure*. Novozym 435 (100 mg) was added into the mixture of racemic 5-(*n*-butyl)hepta-5,6-dien-3-ol (100 mg), cyclohexane (3 mL) and vinyl acetate (110 μL). After stirring at 30 °C for 96 h, the reaction was stopped by filtration. Evaporation and purification by flash chromatography on silica gel (petroleum ether/ether = 40/1→10/1) afforded (*S*)-**1a** (46 mg, 46%) and (*R*)-**2a** (52 mg, 42%). Compound (*S*)-**1a**: 83% ee (determined after its conversion to the corresponding acetate); $[\alpha]_D^{20}$ + 1.2 (*c* 1.10, $CHCl_3$); liquid; ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.80–4.70 (m, 2H), 3.75–3.64 (m, 1H), 2.20–1.90 (m, 5H), 1.58–1.28 (m, 6H), 0.96 (t, J=7.5 Hz, 3H), 0.90 (t, J=7.2 Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 205.7, 100.5, 75.9, 70.9, 39.9, 31.9, 29.5, 29.3, 22.2, 13.8, 9.8; IR (neat): 3388, 1956 cm^{-1}; MS (*m/z*) 168 (M^+, 2.47), 43 (100); HRMS Calcd for $C_{11}H_{20}O$ (M^+): 168.1514. Found 168.1488. Compound (*R*)-**2a**: 97% ee (GC condition: Column: RT-βDEXcst (30 m, 0.25 m ID, 0.25 μm DF); carrier: N_2, 10 psi; injector: 250 °C; Detector (FID, H_2, 0.218 MPa): 250 °C; Oven temperature: 120 °C (10 min), then 1.0 °C to 180 °C (20 min)); $[\alpha]_D^{20}$ + 5.8 (*c* 1.10, $CHCl_3$); liquid; ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.93–4.85 (m, 1H), 4.65–4.57 (m, 2H), 2.22–2.05 (m, 2H), 2.02 (s, 3H), 1.96–1.87 (m, 2H), 1.64–1.50 (m, 2H), 1.50–1.23 (m, 4H), 0.87 (t, J=7.5 Hz, 6H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 206.9, 170.5, 99.2, 75.2, 73.7, 36.6, 31.7, 29.5, 26.7, 22.2, 21.1, 13.8, 9.4; IR (neat): 1958, 1740 cm^{-1}; MS (*m/z*) 210 (M^+, 0.55), 43 (100); HRMS Calcd for $C_{13}H_{22}O_2$ (M^+): 210.1620. Found 210.1593.

3.2.2. Synthesis of (*S*)-5-(*n*-propyl)hepta-5,6-dien-3-ol ((*S*)-1b) and (*R*)-5-(*n*-propyl)hepta-5,6-dien-3-yl acetate ((*R*)-2b). The reaction of racemic 5-(*n*-propyl)hepta-5,6-dien-3-ol (100 mg) with Novozym-435 (100 mg) and vinyl acetate (117 μL) afforded (*S*)-**1b** (39 mg, 39%) and (*R*)-**2b** (46 mg, 36%). Compound (*S*)-**1b**: 81% ee (determined after its conversion to the corresponding acetate); $[\alpha]_D^{20}$ + 6.8 (*c* 0.75, $CHCl_3$); liquid; ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.80–4.72 (m, 2H), 3.76–3.62 (m, 1H), 2.20–2.00 (m, 2H), 2.00–1.88 (m, 3H), 1.60–1.40 (m, 4H), 0.96 (t, J=7.5 Hz, 3H), 0.91 (t, J=7.2 Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 205.8, 100.4, 76.0, 71.0, 40.0, 34.4, 29.6, 20.6, 13.7, 9.9; IR (neat): 3396, 1956 cm^{-1}; MS (*m/z*) 154 (M^+, 5.39), 43 (100); HRMS Calcd for $C_{10}H_{18}O$ (M^+): 154.1358. Found 154.1345. Compound (*R*)-**2b**: 96% ee (GC condition: Column: RT-βDEXcst (30 m, 0.25 m ID, 0.25 μm DF); carrier: N_2, 10 psi; injector: 250 °C; Detector (FID, H_2, 0.218 MPa): 250 °C; Oven temperature: 105 °C (40 min)); $[\alpha]_D^{20}$ + 19.5 (*c* 1.10, $CHCl_3$); liquid; ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.00–4.84 (m, 1H), 4.66–4.60 (m, 2H), 2.28–2.06 (m, 2H), 2.05 (s, 3H), 2.00–1.82 (m, 2H), 1.74–1.40 (m, 4H), 0.92 (t, J=7.2 Hz, 3H), 0.88 (t, J=7.2 Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 206.5, 170.7, 99.1, 75.2, 73.8, 36.7, 34.2, 26.8, 21.2, 20.6, 13.7, 9.5; IR (neat): 1958, 1740 cm^{-1}; MS (*m/z*) 196 (M^+, 1.64), 43 (100); HRMS Calcd for $C_{12}H_{20}O2$ (M^+): 196.1463. Found 196.1454.

3.2.3. Synthesis of (*S*)-5-(*n*-hexyl)hepta-5,6-dien-3-ol ((*S*)-1c) and (*R*)-5-(*n*-hexyl)hepta-5,6-dien-3-yl acetate ((*R*)-2c). The reaction of racemic 5-(*n*-hexyl)hepta-5,6-diene-3-ol (100 mg) with Novozym-435 (100 mg) and vinyl acetate (94 μL) afforded (*S*)-**1c** (51 mg, 51%) and (*R*)-**2c** (34 mg, 28%). Compound (*S*)-**1c**: 58% ee (determined after its conversion to the corresponding acetate); $[\alpha]_D^{20}$ + 1.4 (*c* 1.05, $CHCl_3$); liquid; ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.80–4.68 (m, 2H), 3.75–3.60 (m, 1H), 2.20–1.90 (m, 5H), 1.60–1.20 (m, 10H), 0.96 (t, J=7.5 Hz, 3H), 0.88 (t, J=6.6 Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 205.7, 100.7, 76.1, 71.0, 40.1, 32.4, 31.7, 29.6, 28.9, 27.4, 22.6, 14.1, 10.0; IR (neat): 3398, 1956 cm^{-1}; MS (*m/z*) 196 (M^+, 1.96), 43 (100); HRMS Calcd for $C_{13}H_{24}O$ (M^+): 196.1827. Found 196.1848. Compound (*R*)-**2c**: 98% ee (GC condition: Column: RT-βDEXcst (30 m, 0.25 m ID, 0.25 μm DF); carrier: N_2, 8.0 psi; injector: 250 °C; Detector (FID, H_2, 0.218 MPa): 250 °C; Oven temperature: 130 °C (80 min), then 1 °C/min to 150 °C (2 min)); $[\alpha]_D^{20}$ + 16.8 (*c* 1.10, $CHCl_3$); liquid; ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.98–4.85 (m, 1H), 4.66–4.60 (m, 2H), 2.25–2.06 (m, 2H), 2.03 (s, 3H), 1.98–1.87 (m, 2H), 1.70–1.45 (m, 2H), 1.43–1.23 (m, 8H), 0.92–0.80 (m, 6H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 206.4, 170.7, 99.3, 75.3, 73.8, 36.7, 32.1, 31.7, 28.9, 27.4, 26.8, 22.6, 21.2, 14.1, 9.5; IR (neat): 1958, 1740 cm^{-1}; MS (*m/z*) 238 (M^+, 4.76), 43 (100); HRMS Calcd for $C_{15}H_{26}O_2$ (M^+): 238.1933. Found 238.1916.

3.2.4. Synthesis of (*S*)-5-(*n*-heptyl)hepta-5,6-dien-3-ol ((*S*)-1d) and (*R*)-5-(*n*-heptyl)hepta-5,6-dien-3-yl acetate ((*R*)-2d). The reaction of racemic 5-(*n*-heptyl)hepta-5,6-dien-3-ol (100 mg) with Novozym-435 (100 mg) and vinyl acetate (88 μL) afforded (*S*)-**1d** (40 mg, 40%) and (*R*)-**2d** (30 mg, 25%). Compound (*S*)-**1d**: 54% ee (determined after its conversion to the corresponding acetate); $[\alpha]_D^{20}$ − 1.5 (*c* 1.00, $CHCl_3$); liquid; ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.80–4.70 (m, 2H), 3.74–3.62 (m, 1H), 2.20–1.92 (m, 5H), 1.70–1.38 (m, 4H), 1.38–1.20 (m, 8H), 0.96 (t, J=7.5 Hz, 3H), 0.87 (t, J=6.6 Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 205.7, 100.7, 76.1, 71.0, 40.1, 32.4, 31.8, 29.6, 29.2, 29.1, 27.4, 22.6, 14.1, 10.0; IR (neat): 3383, 1956 cm^{-1}; MS (*m/z*) 210 (M^+, 2.08), 43 (100); HRMS Calcd for $C_{14}H_{26}O$ (M^+): 210.1984. Found 210.1965. Compound (*R*)-**2d**: 98% ee (GC condition: Column: RT-βDEXcst (30 m, 0.25 m ID, 0.25 μm DF); carrier: N_2, 8.0 psi; injector: 250 °C; Detector (FID, H_2, 0.218 MPa): 250 °C; Oven temperature: 130 °C

(80 min), then 1 °C/min to 150 °C (2 min)); $[\alpha]_D^{20}+15.9$ (*c* 0.90, $CHCl_3$); liquid; ^1H NMR (300 MHz, $CDCl_3$): δ 4.94–4.87 (m, 1H), 4.66–4.59 (m, 2H), 2.23–2.04 (m, 2H), 2.02 (s, 3H), 1.95–1.87 (m, 2H), 1.70–1.45 (m, 2H), 1.43–1.19 (m, 10H), 0.91–0.83 (m, 6H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 206.4, 170.7, 99.3, 75.3, 73.8, 36.7, 32.1, 31.8, 29.2, 29.1, 27.4, 26.8, 22.6, 21.2, 14.1, 9.5; IR (neat): 1958, 1740 cm^{-1}; MS (*m/z*) 252 (M^+, 5.28), 43 (100); HRMS Calcd for $C_{16}H_{28}O_2$ (M^+): 252.2089. Found 252.2097.

3.2.5. Synthesis of (*S*)-5-allylhepta-5,6-dien-3-ol ((*S*)-1e) and (*R*)-5-allylhepta-5,6-dien-3-yl acetate ((*R*)-2e). The reaction of racemic 5-allylhepta-5,6-dien-3-ol (100 mg) with Novozym-435 (70 mg) and vinyl acetate (122 μL) afforded (*S*)-**1e** (48 mg, 48%) and (*R*)-**2e** (36 mg, 28%). Compound (*S*)-**1e**: 50% ee (determined after its conversion to the corresponding acetate); $[\alpha]_D^{20}+0.8$ (*c* 2.40, $CHCl_3$); liquid; ^1H NMR (300 MHz, $CDCl_3$): δ 5.86–5.76 (m, 1H), 5.12–5.04 (m, 2H), 4.80–4.70 (m, 2H), 3.73–3.67 (m, 1H), 2.76–2.74 (m, 2H), 2.20–2.03 (m, 2H), 1.92 (d, $J=3.0$ Hz, 1H), 1.60–1.47 (m, 2H), 0.97 (t, $J=7.5$ Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 206.1, 135.4, 116.3, 99.1, 76.2, 71.0, 39.5, 37.4, 29.6, 10.0; IR (neat): 3414, 1957, 1639 cm^{-1}; MS (*m/z*) 152 (M^+, 0.97), 79 (100); HRMS Calcd for $C_{10}H_{16}O$ (M^+): 152.1201. Found 152.1210. Compound (*R*)-**2e**: 97% ee (GC condition: Column: RT-βDEXcst (30 m, 0.25 m ID, 0.25 μm DF); carrier: N_2, 10 psi; injector: 250 °C; Detector (FID, H_2, 0.218 MPa): 250 °C; Oven temperature: 100 °C (60 min)); $[\alpha]_D^{20}+23.9$ (*c* 0.50, $CHCl_3$); liquid; ^1H NMR (300 MHz, $CDCl_3$): δ 5.84–5.73 (m, 1H), 5.11–5.03 (m, 2H), 4.96–4.91 (m, 1H), 4.69–4.65 (m, 2H), 2.75–2.72 (m, 2H), 2.22–2.15 (m, 2H), 2.30 (s, 3H), 1.68–1.54 (m, 2H), 0.89 (t, $J=7.5$ Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 206.8, 170.6, 135.4, 116.1, 97.7, 75.4, 73.6, 37.1, 36.0, 26.8, 21.2, 9.5; IR (neat): 1960, 1743, 1639 cm^{-1}; MS (*m/z*) 194 (M^+, 1.28), 43 (100); HRMS Calcd for $C_{12}H_{18}O_2$ (M^+): 194.1307. Found 194.1271.

3.2.6. Synthesis of (*S*)-5-benzylhepta-5,6-dien-3-ol ((*S*)-1f) and (*R*)-5-benzylhepta-5,6-dien-3-yl acetate ((*R*)-2f). The reaction of racemic 5-benzylhepta-5,6-dien-3-ol (100 mg) with Novozym-435 (70 mg) and vinyl acetate (92 μL) afforded (*S*)-**1f** (38 mg, 38%) and (*R*)-**2f** (53 mg, 44%). Compound (*S*)-**1f**: 71% ee (HPLC conditions: Chiralcel OD Column (0.46 cm$\phi\times$25 cm); λ 254 nm; rate: 0.7 mL/min; hexane: *i*-PrOH=100: 1.25); $[\alpha]_D^{20}-4.8$ (*c* 1.10, $CHCl_3$); liquid; ^1H NMR (300 MHz, $CDCl_3$): δ 7.40–7.20 (m, 5H), 4.82–4.70 (m, 2H), 3.80–3.60 (m, 1H), 3.35 (t, $J=2.4$ Hz, 2H), 2.20–1.98 (m, 3H), 1.60–1.40 (m, 2H), 0.94 (t, $J=7.2$ Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 206.7, 139.1, 128.9, 128.3, 126.4, 100.1, 75.9, 71.1, 39.8, 39.1, 29.6, 10.0; IR (neat): 3398, 1957 cm^{-1}; MS (*m/z*) 202 (M^+, 27.45), 91 (100); HRMS Calcd for $C_{14}H_{18}O$ (M^+): 202.1358. Found 202.1371. Compound (*R*)-**2f**: 72% ee (determined after its conversion to the corresponding alcohol); $[\alpha]_D^{20}+54.6$ (*c* 1.10, $CHCl_3$); liquid; ^1H NMR (300 MHz, $CDCl_3$): δ 7.33–7.12 (m, 5H), 5.00–4.80 (m, 1H), 4.67–4.63 (m, 2H), 3.32 (t, $J=2.4$ Hz, 2H), 2.23–2.09 (m, 2H), 2.03 (s, 3H), 1.70–1.52 (m, 2H), 0.94 (t, $J=7.5$ Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 207.4, 170.6, 139.1, 128.9, 128.2, 126.2, 98.8, 75.1, 73.6, 39.4, 35.6, 26.8, 21.2, 9.4; IR (neat): 1959, 1737 cm^{-1}; MS (*m/z*) 244 (M^+, 3.13), 43 (100); HRMS Calcd for $C_{16}H_{20}O_2$ (M^+): 244.1463. Found 244.1424.

3.2.7. Synthesis of (*S*)-7-methylocta-5,6-dien-3-ol ((*S*)-1g) and (*R*)-7-methylocta-5,6-dien-3-yl acetate ((*R*)-2g). The reaction of racemic 3-methylocta-5,6-dien-3-ol (100 mg) with Novozym-435 (100 mg) and vinyl acetate (132 μL) afforded (*S*)-**1g** (27 mg, 27%) and (*R*)-**2g** (77 mg, 59%). Compound (*S*)-**1g**: 93% ee (determined after its conversion to the corresponding acetate); $[\alpha]_D^{20}-2.1$ (*c* 0.50, $CHCl_3$); liquid; ^1H NMR (300 MHz, $CDCl_3$): δ 5.02–4.90 (m, 1H), 3.63–3.51 (m, 1H), 2.23–1.96 (m, 2H), 1.79 (d, $J=3.9$ Hz, 1H), 1.70 (s, 3H), 1.69 (s, 3H), 1.59–1.44 (m, 2H), 0.96 (t, $J=7.5$ Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 203.0, 95.3, 84.9, 72.4, 36.8, 29.3, 20.7, 20.6, 10.0; IR (neat): 3362, 1969 cm^{-1}; MS (*m/z*) 140 (M^+, 100), 125 (M^+-CH_3, 27.90); HRMS Calcd for $C_9H_{16}O$ (M^+): 140.1201. Found 140.1206. Compound (*R*)-**2g**: 22% ee (GC condition: Column: RT-βDEXcst (30 m, 0.25 m ID, 0.25 μm DF); carrier: N_2, 10 psi; injector: 250 °C; Detector (FID, H_2, 0.218 MPa): 250 °C; Oven temperature: 120 °C (20 min)); $[\alpha]_D^{20}+12.2$ (*c* 0.75, $CHCl_3$); liquid; ^1H NMR (300 MHz, $CDCl_3$): δ 4.81–4.74 (m, 2H), 2.20–2.06 (m, 2H), 1.99 (s, 3H), 1.60 (s, 3H), 1.59 (s, 3H), 1.59–1.42 (m, 2H), 0.82 (t, $J=7.5$ Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 202.9, 170.8, 95.0, 84.0, 74.9, 33.5, 26.3, 21.2, 20.52, 20.46, 9.5; IR (neat): 1970, 1740 cm^{-1}; MS (*m/z*) 182 (M^+, 8.40), 43 (100); HRMS Calcd for $C_{11}H_{18}O_2$ (M^+): 182.1307. Found 182.1292.

3.2.8. Synthesis of (*S*)-7-methyl-5-(*n*-butyl)octa-5,6-dien-3-ol ((*S*)-1h) and (*R*)-7-methyl-5-(*n*-butyl)octa-5,6-dien-3-yl acetate ((*R*)-2h). The reaction of racemic 7-methyl-5-(*n*-butyl)octa-5,6-diene-3-ol (100 mg) with Novozym-435 (100 mg) and vinyl acetate (94 μL) afforded (*S*)-**1h** (46 mg, 46%) and (*R*)-**2h** (31 mg, 26%). Compound (*S*)-**1h**: 44% ee (determined after its conversion to the corresponding acetate); $[\alpha]_D^{20}+0.7$ (*c* 1.45, $CHCl_3$); liquid; ^1H NMR (300 MHz, $CDCl_3$): δ 3.68–3.58 (m, 1H), 2.20–2.00 (m, 1H), 2.00–1.80 (m, 4H), 1.69 (s, 6H), 1.58–1.42 (m, 2H), 1.42–1.22 (m, 4H), 0.96 (t, $J=7.5$ Hz, 3H), 0.89 (t, $J=7.5$ Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 198.6, 99.2, 96.5, 71.1, 40.7, 33.0, 29.7, 29.5, 22.3, 21.1, 20.8, 14.0, 10.1; IR (neat): 3373, 1960 cm^{-1}; MS (*m/z*) 196 (M^+, 5.64), 96 (100); HRMS Calcd for $C_{13}H_{24}O$ (M^+): 196.1827. Found 196.1827. Compound (*R*)-**2h**: 95% ee (GC condition: Column: RT-βDEXcst (30 m, 0.25 m ID, 0.25 μm DF); carrier: N_2, 10 psi; injector: 250 °C; Detector (FID, H_2, 0.218 MPa): 250 °C; Oven temperature: 100 °C (60 min), then 2 °C/min to 150 °C (60 min)); $[\alpha]_D^{20}+10.7$ (*c* 1.40, $CHCl_3$); liquid; ^1H NMR (300 MHz, $CDCl_3$): δ 4.92–4.82 (m, 1H), 2.20–2.02 (m, 2H), 2.01 (s, 3H), 1.92–1.80 (m, 2H), 1.67 (s, 3H), 1.66 (s, 3H), 1.60–1.40 (m, 2H), 1.40–1.20 (m, 4H), 0.87 (t, $J=7.2$ Hz, 6H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 199.3, 170.7, 97.8, 95.6, 74.2, 37.1, 32.7, 29.7, 26.8, 22.2, 21.3, 20.74, 20.71, 14.0, 9.5; IR (neat): 1740 cm^{-1}; MS (*m/z*) 238 (M^+, 1.01), 195 (M^+-COCH_3, 3.11), 43 (100); HRMS Calcd for $C_{13}H_{23}O$ (M^+-COCH_3): 195.1749. Found 195.1765.

3.2.9. Synthesis of (*S*)-6-cyclohexylidene-5-(*n*-butyl)hexa-5-en-3-ol ((*S*)-1i) and (*R*)-6-cyclohexylidene-5-(*n*-butyl)-hex-5-en-3-yl acetate ((*R*)-2i). The reaction of racemic

6-cyclohexylidene-5-(*n*-butyl)hexa-5-en-3-ol (100 mg) with Novozym-435 (100 mg) and vinyl acetate (78 μL) afforded (*S*)-**1i** (42 mg, 42%) and (*R*)-**2i** (60 mg, 51%). Compound (*S*)-**1i**: 96% ee (determined after its conversion to the corresponding benzoate (HPLC conditions: Chiralcel OD Column (0.46 cm$\phi\times$25 cm); λ 254 nm; rate: 0.7 mL/min; hexane: *i*-PrOH=100: 0.1)); $[\alpha]_D^{20}+0.5$ (*c* 2.55, $CHCl_3$); liquid; ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.69–3.55 (m, 1H), 2.15–2.03 (m, 6H), 2.01–1.86 (m, 3H), 1.70–1.42 (m, 8H), 1.40–1.21 (m, 4H), 0.95 (t, J=7.2 Hz, 3H), 0.88 (t, J=7.2 Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 194.8, 104.3, 99.0, 71.2, 40.9, 33.0, 32.3, 32.0, 29.7, 29.4, 27.7, 26.2, 22.2, 15.3, 14.0, 10.1; IR (neat): 3375, 1959 cm^{-1}; MS (*m*/*z*) 236 (M^+, 8.77), 57 (100); HRMS Calcd for $C_{16}H_{28}O$ (M^+): 236.2140. Found 236.2170. Compound (*R*)-**2i**: 82% ee (determined after its conversion to the corresponding benzoate); $[\alpha]_D^{20}+5.3$ (*c* 1.75, $CHCl_3$); liquid; ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.92–4.87 (m, 1H), 2.21–2.08 (m, 2H), 2.08–2.00 (m, 7H), 1.92–1.82 (m, 2H), 1.78–1.40 (m, 8H), 1.40–1.20 (m, 4H), 0.88 (t, J=7.5 Hz, 6H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 195.7, 170.7, 103.3, 97.5, 74.2, 37.4, 32.7, 31.89, 31.86, 29.7, 27.7, 27.6, 26.6, 26.2, 22.2, 21.3, 14.0, 9.5; IR (neat): 1961, 1741 cm^{-1}; MS (*m*/*z*) 278 (M^+, 0.77), 147 (100); HRMS Calcd for $C_{18}H_{30}O_2$ (M^+): 278.2246. Found 278.2247.

3.2.10. Synthesis of (*S*)-4-(*n*-butyl)hexa-4,5-dien-2-ol ((*S*)-1j) and (*R*)-4-(*n*-butyl)hexa-4,5-dien-2-yl acetate ((*R*)-2j). The reaction of racemic 4-(*n*-butyl)hexa-4,5-dien-2-ol (100 mg) with Novozym-435 (70 mg) and vinyl acetate (120 μL) afforded (*S*)-**1j** (37 mg, 37%) and (*R*)-**2j** (45 mg, 35%). Compound (*S*)-**1j**: 88% ee (determined after its conversion to the corresponding acetate); $[\alpha]_D^{20}+7.7$ (*c* 1.85, $CHCl_3$); liquid; ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.69–4.74 (m, 2H), 4.00–3.80 (m, 1H), 2.10–2.00 (m, 3H), 2.00–1.88 (m, 2H), 1.43–1.26 (m, 4H), 1.20 (d, J=6.0 Hz, 3H), 0.88 (t, J=7.5 Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 205.7, 100.6, 76.1, 65.9, 42.2, 32.0, 29.5, 22.7, 22.3, 13.9; IR (neat): 3355, 1957 cm^{-1}; MS (*m*/*z*) 154 (M^+, 2.01), 43 (100); HRMS Calcd for $C_{10}H_{18}O$ (M^+): 154.1358. Found 154.1353. Compound (*R*)-**2j**: 89.3% ee (GC condition: Column: RT-βDEXcst (30 m, 0.25 m ID, 0.25 μm DF); carrier: N_2, 10 psi; injector: 250 °C; Detector (FID, H_2, 0.218 MPa): 250 °C; Oven temperature: 110 °C (5 min), then 1 °C/min to 120 °C (20 min)); liquid; $[\alpha]_D^{20}+2.3$ (*c* 1.95, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.08–4.94 (m, 1H), 4.64 (m, 2H), 2.32–2.18 (m, 1H), 2.10–2.02 (m, 1H), 2.01 (s, 3H), 2.00–1.92 (m, 2H), 1.50–1.26 (m, 4H), 1.23 (d, J=6.0 Hz, 3H), 0.89 (t, J=7.2 Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 206.3, 170.5, 99.3, 75.5, 69.5, 38.7, 31.9, 29.5, 22.3, 21.3, 19.9, 13.9; IR (neat): 1958, 1741 cm^{-1}; MS (*m*/*z*) 196 (M^+, 7.23), 43 (100); HRMS Calcd for $C_{12}H_{20}O_2$ (M^+): 196.1463. Found 196.1455.

3.2.11. Synthesis of (*S*)-6-methyl-4-(*n*-butyl)hepta-4,5-dien-2-ol ((*S*)-1k) and (*R*)-6-methyl-4-(*n*-butyl)hepta-4,5-dien-2-yl acetate ((*R*)-2k). The reaction of racemic 6-methyl-4-(*n*-butyl)hepta-4,5-diene-2-ol (100 mg) with Novozym-435 (100 mg) and vinyl acetate (102 μL) afforded (*S*)-**1k** (38 mg, 38%) and (*R*)-**2k** (64 mg, 52%). Compound (*S*)-**1k**: 91% ee (determined after its conversion to the corresponding acetate); $[\alpha]_D^{20}+6.0$ (*c* 1.45, $CHCl_3$); liquid; ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.93–3.85 (m, 1H), 2.11–1.88 (m, 5H), 1.70 (s, 3H), 1.69 (s, 3H), 1.40–1.25 (m, 4H), 1.20 (d, J=6.6 Hz, 3H), 0.89 (t, J=7.2 Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 198.6, 99.2, 96.4, 66.1, 42.8, 33.0, 29.7, 22.4, 22.2, 21.0, 20.8, 14.0; IR (neat): 3362, 1961 cm^{-1}; MS (*m*/*z*) 182 (M^+, 7.68), 45 (100); HRMS Calcd for $C_{12}H_{22}O$ (M^+): 182.1671. Found 182.1693. Compound (*R*)-**2k**: 42% ee (GC condition: Column: RT-βDEXcst (30 m, 0.25 m ID, 0.25 μm DF); carrier: N_2, 10 psi; injector: 250 °C; Detector (FID, H_2, 0.218 MPa): 250 °C; Oven temperature: 95 °C (120 min)); $[\alpha]_D^{20}-1.6$ (*c* 1.30, $CHCl_3$); liquid; ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.00–4.92 (m, 1H), 2.24–2.15 (m, 1H), 2.06–1.98 (m, 1H), 2.00 (s, 3H), 1.88 (t, J=6.9 Hz, 2H), 1.64 (s, 3H), 1.63 (s, 3H), 1.38–1.27 (m, 4H), 1.21 (d, J=6.6 Hz, 3H), 0.88 (t, J=7.2 Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 199.2, 170.6, 97.8, 95.8, 69.9, 39.3, 32.8, 29.7, 22.2, 21.4, 20.8, 20.7, 19.9, 14.0; IR (neat): 1961, 1740 cm^{-1}; MS (*m*/*z*) 182 (M^++1−$COCH_3$, 15.04), 181 (M^+−$COCH_3$, 33.90), 107 (100); HRMS Calcd for $C_{14}H_{24}O_2$ (M^+): 224.1776. Found 224.1778.

3.2.12. Synthesis of (*R*)-5-(*n*-butyl)hepta-1,5,6-trien-3-ol ((*R*)-1l) and (*S*)-5-(*n*-butyl)hepta-1,5,6-trien-3-yl acetate ((*S*)-2l). The reaction of racemic 5-(*n*-butyl)hepta-1,5,6-trien-3-ol (100 mg) with Novozym-435 (70 mg) and vinyl acetate (111 μL) afforded (*R*)-**1l** (43 mg, 43%) and (*S*)-**2l** (70 mg, 56%). Compound (*R*)-**1l**: 93% ee liquid; (determined after its conversion to the corresponding acetate); $[\alpha]_D^{20}-2.4$ (*c* 1.40, $CHCl_3$); liquid; ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.96–5.84 (m, 1H), 5.29 (dt, J=22.4, 1.5 Hz, 1H), 5.12 (dt, J=10.5, 1.5 Hz, 1H), 4.80–4.68 (m, 2H), 4.36–4.20 (m, 1H), 2.22–2.08 (m, 2H), 2.05–1.84 (m, 3H), 1.50–1.30 (m, 4H), 0.90 (t, J=7.2 Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 206.0, 140.2, 114.6, 99.9, 76.2, 70.7, 40.3, 31.9, 29.5, 22.3, 13.9; IR (neat): 3377, 1957, 1645 cm^{-1}; MS (*m*/*z*) 166 (M^+, 3.65), 107 (100); HRMS Calcd for $C_{11}H_{18}O$ (M^+): 166.1358. Found 166.1310. Compound (*S*)-**2l**: 75% ee (GC condition: Column: RT-βDEXcst (30 m, 0.25 m ID, 0.25 μm DF); carrier: N_2, 10 psi; injector: 250 °C; Detector (FID, H_2, 0.218 MPa): 250 °C; Oven temperature: 120 °C (40 min)); $[\alpha]_D^{20}+1.8$ (*c* 1.80, $CHCl_3$); liquid; ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.88–5.78 (m, 1H), 5.40–5.32 (m, 1H), 5.27 (dt, J=17.1, 1.5 Hz, 1H), 5.16 (dt, J=10.5, 1.5 Hz, 1H), 4.70–4.60 (m, 2H), 2.40–2.06 (m, 2H), 2.05 (s, 3H), 2.00–1.82 (m, 2H), 1.42–1.24 (m, 4H), 0.89 (t, J=7.2 Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 206.5, 170.2, 136.2, 116.6, 98.9, 75.8, 72.9, 37.2, 31.9, 29.5, 22.3, 21.2, 13.9; IR (neat): 1958, 1743, 1646 cm^{-1}; MS (*m*/*z*) 208 (M^+, 0.09), 166 (M^++1−$COCH_3$, 18.30), 165 (M^+−$COCH_3$, 4.74), 43 (100); HRMS Calcd for $C_{11}H_{17}O$ (M^+−$COCH_3$): 165.1280. Found 165.1318.

3.2.13. Synthesis of (*R*)-5-(*n*-pentyl)hepta-1,5,6-trien-3-ol ((*R*)-1m) and (*S*)-5-(*n*-pentyl)hepta-1,5,6-trien-3-yl acetate ((*S*)-2m). The reaction of racemic 5-(*n*-pentyl)hepta-1,5,6-trien-3-ol (100 mg) with Novozym-435 (100 mg) and vinyl acetate (103 μL) afforded (*R*)-**1m** (44 mg, 44%) and (*S*)-**2m** (49 mg, 40%). Compound (*R*)-**1m**: 93% ee (determined after its conversion to the corresponding acetate); $[\alpha]_D^{20}-1.3$ (*c*1.55, $CHCl_3$); liquid; ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.96–5.82 (m, 1H), 5.29 (dt, J=17.1, 1.5 Hz, 1H), 5.12 (dt, J=10.5, 1.5 Hz, 1H), 4.79–4.70 (m, 2H), 4.31–4.25 (m, 1H), 2.25–2.07 (m, 2H), 2.01–1.90 (m, 3H),

1.49–1.20 (m, 6H), 0.88 (t, $J=7.2$ Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 200.0, 140.2, 114.6, 100.0, 76.2, 70.7, 40.3, 32.2, 31.4, 27.0, 22.5, 14.0; IR (neat): 3384, 1957, 1644 cm^{-1}; MS (*m/z*) 180 (M^+, 0.40), 67 (100); HRMS Calcd for $C_{12}H_{20}O$ (M^+): 180.1514. Found 180.1481. Compound (*S*)-**2m**: 85% ee (GC condition: Column: RT-βDEXcst (30 m, 0.25 m ID, 0.25 μm DF); carrier: N_2, 10 psi; injector: 250 °C; Detector (FID, H_2, 0.218 MPa): 250 °C; Oven temperature: 120 °C (60 min)); $[\alpha]_D^{20}+1.1$ (*c* 1.10, $CHCl_3$); liquid; ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.87–5.74 (m, 1H), 5.39–5.10 (m, 3H), 4.69–4.60 (m, 2H), 2.35–2.10 (m, 2H), 2.03 (s, 3H), 1.96–1.86 (m, 2H), 1.44–1.20 (m, 6H), 0.86 (t, $J=6.9$ Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 206.5, 170.1, 136.2, 116.5, 98.9, 75.8, 72.9, 37.2, 32.1, 31.4, 27.0, 22.5, 21.2, 14.0; IR (neat): 1958, 1744, 1648 cm^{-1}; MS (*m/z*) 180 ($M^+ +1-COCH_3$, 1.07), 179 ($M^+ -COCH_3$, 1.21), 43 (100); HRMS Calcd for $C_{12}H_{19}O$ ($M^+ -COCH_3$): 179.1436. Found 179.1425.

3.2.14. Synthesis of (*R*)-5-(*n*-butyl)hepta-5,6-dien-1-yn-3-ol ((*R*)-1n) and (*S*)-5-(*n*-butyl)hepta-5,6-dien-1-yn-3-yl acetate ((*S*)-2n). The reaction of racemic 5-(*n*-butyl)hepta-5,6-dien-1-yn-3-ol (100 mg) with Novozym-435 (100 mg) and vinyl acetate (113 μL) afforded (*R*)-**1n** (38 mg, 38%) and (*S*)-**2n** (71 mg, 56%). Compound (*R*)-**1n**: 88% ee (determined after its conversion to the corresponding acetate); $[\alpha]_D^{20}+5.6$ (*c* 1.90, $CHCl_3$); liquid; ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.80–4.72 (m, 2H), 4.60–4.42 (m, 1H), 2.46 (d, $J=2.4$ Hz, 1H), 2.42–2.38 (m, 2H), 2.16 (bs, 1H), 2.08–1.96 (m, 2H), 1.50–1.22 (m, 4H), 0.90 (t, $J=7.2$ Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 205.9, 99.1, 84.5, 76.8, 72.7, 60.7, 40.4, 31.9, 29.4, 22.2, 13.9; IR (neat): 3310, 1957 cm^{-1}; MS (*m/z*) 164 (M^+, 0.50), 55 (100); HRMS Calcd for $C_{11}H_{16}O$ (M^+): 164.1201. Found 164.1179. Compound (*S*)-**2n**: 44% ee (GC condition: Column: RT-βDEXcst (30 m, 0.25 m ID, 0.25 μm DF); carrier: N_2, 8.0 psi; injector: 250 °C; Detector (FID, H_2, 0.218 MPa): 250 °C; Oven temperature: 120 °C (10 min), then 1 °C/min to 140 °C (30 min)); $[\alpha]_D^{20}-15.9$ (*c* 0.85, $CHCl_3$); liquid; ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.50–5.40 (m, 1H), 4.75–4.66 (m, 2H), 2.57–2.38 (m, 3H), 2.08 (s, 3H), 2.02–1.92 (m, 2H), 1.44–1.28 (m, 4H), 0.90 (t, $J=7.2$ Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 206.2, 169.8, 98.3, 81.2, 76.5, 73.4, 62.3, 37.4, 31.8, 29.5, 22.3, 20.9, 13.9; IR (neat): 2125, 1959, 1746 cm^{-1}; MS (*m/z*) 164 ($M^+ +1-COCH_3$, 7.73), 163 ($M^+ -COCH_3$, 6.92), 43 (100); HRMS Calcd for $C_{11}H_{15}O$ ($M^+ -COCH_3$): 163.1123. Found 163.1103.

3.2.15. Synthesis of (*R*)-5-(*n*-pentyl)hepta-5,6-dien-1-yn-3-ol ((*R*)-1o) and (*S*)-5-(*n*-pentyl)hepta-5,6-dien-1-yn-3-yl acetate ((*S*)-2o). The reaction of racemic 5-(*n*-pentyl)-hepta-5,6-dien-1-yn-3-ol (100 mg) with Novozym-435 (100 mg) and vinyl acetate (103 μL) afforded (*R*)-**1o** (40 mg, 40%) and (*S*)-**2o** (50 mg, 40%). Compound (*R*)-**1o**: 90% ee (determined after its conversion to the corresponding acetate); $[\alpha]_D^{20}+7.1$ (*c* 1.10, $CHCl_3$); liquid; ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.81–4.74 (m, 2H), 4.55–4.48 (m, 1H), 2.46 (d, $J=1.5$ Hz, 1H), 2.45–2.35 (m, 2H), 2.19–2.16 (m, 1H), 2.02–1.92 (m, 2H), 1.48–1.23 (m, 6H), 0.88 (t, $J=7.2$ Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 205.9, 99.2, 84.4, 76.8, 72.8, 60.7, 40.4, 32.2, 31.4, 27.0, 22.4, 14.0; IR (neat): 3385, 2249, 1957 cm^{-1}; MS (*m/z*) 178 (M^+, 0.31), 55 (100); HRMS Calcd for $C_{12}H_{18}O$ (M^+): 178.1358. Found: 178.1360. Compound (*S*)-**2o**: 60% ee (GC condition: Column: RT-βDEXcst (30 m, 0.25 m ID, 0.25 μm DF); carrier: N_2, 10 psi; injector: 250 °C; Detector (FID, H_2, 0.218 MPa): 250 °C; Oven temperature: 130 °C (50 min)); $[\alpha]_D^{20}-23.2$ (*c* 1.30, $CHCl_3$); liquid; ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.48–5.37 (m, 1H), 4.74–4.66 (m, 2H), 2.52–2.30 (m, 3H), 2.07 (s, 3H), 2.00–1.90 (m, 2H), 1.49–1.36 (m, 2H), 1.34–1.20 (m, 4H), 0.88 (t, $J=6.6$ Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 206.2, 169.8, 98.3, 81.2, 76.6, 73.4, 62.3, 37.4, 32.1, 31.4, 27.0, 22.5, 20.9, 14.0; IR (neat): 2257, 1959, 1746 cm^{-1}; MS (*m/z*) 220 (M^+, 0.31), 178 ($M^+ +1-COCH_3$, 4.43), 177 ($M^+ -COCH_3$, 2.83), 43 (100); HRMS Calcd for $C_{12}H_{17}O$ ($M^+ -COCH_3$): 177.1280. Found 177.1266.

3.2.16. Pd^{II}-catalyzed coupling cyclization of (*R*)-1a with allylic bromide: synthesis of (*R*)-(−)-6-ethyl-3-allyl-4-(*n*-butyl)-5,6-dihydro-2H-pyran ((*R*)-3a). A mixture of (*R*)-**1a** (52 mg, 0.3 mmol, 97% ee obtained from hydrolysis of (*R*)-**2a**), allylic bromide (0.13 mL, 1.5 mmol), and $PdCl_2$ (0.003 g, 5 mol%) was stirred in *N*,*N*-dimethylacetamide (1.8 mL) at room temperature. When the reaction was complete as monitored by TLC, diethyl ether (50 mL) was added. The resulting mixture was washed with brine (three times) and dried over anhydrous sodium sulfate. The product was purified by column chromatography on silica gel (petroleum ether/ethyl ether = 80/1) to afford (*R*)-(−)-6-ethyl-3-allyl-4-(*n*-butyl)-5,6-dihydro-2H-pyran ((*R*)-**3a**) (41 mg, 64%) with 97% ee; (GC condition: Column: RT-βDEXcst (30 m, 0.25 m ID, 0.25 μm DF); carrier: N_2, 10 psi; injector: 250 °C; Detector (FID, H_2, 0.218 MPa): 250 °C; Oven temperature: 135 °C (30 min)); $[\alpha]_D^{20}-118.7$ (*c* 1.05, $CHCl_3$); liquid; ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.86–5.59 (m, 1H), 5.10–4.85 (m, 2H), 4.02 (s, 2H), 3.39–3.32 (m, 1H), 2.78 (dd, $J=6.3$, 14.0 Hz, 1H), 2.60 (dd, $J=6.9$, 14.0 Hz, 1H), 2.10–1.89 (m, 4H), 1.65–1.40 (m, 2H), 1.39–1.21 (m, 4H), 0.95 (t, $J=7.8$ Hz, 3H), 0.88 (t, $J=7.5$ Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 135.9, 129.7, 126.3, 115.2, 75.6, 68.3, 34.0, 33.0, 32.1, 30.2, 28.7, 22.8, 14.0, 9.9; IR (neat): 1637, 1465, 1150 cm^{-1}; MS (*m/z*) 208 (M^+, 5.85), 167 (100); HRMS Calcd for $C_{14}H_{24}O$ (M^+): 208.1827. Found 208.1859.

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