Efficient Preparation of Highly Optically Active (*S*)-(−)-2,3-Allenols and (*R*)-(+)-2,3-Allenyl Acetates by a Clean Novozym-435-Catalyzed Enzymatic Separation of Racemic 2,3-Allenols**

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Abstract: Novozym-435 has been found to be an effective biocatalyst for the kinetic resolution of a series of racemic 2,3-allenols, affording highly optically active (*S*)-(−)-2,3-allenols and (*R*)-(+)-2,3-allenyl acetates in high yields and with excellent *ee* values. The reaction of 3-(*n*-butyl)-3,4-pentadien-2-ol (**1a**) was successfully performed on a 10 g scale to afford the corresponding (*S*)-(−)-2,3-allenol (**1a**) and (*R*)-(+)-2,3-allenyl acetate (**2a**) in synthetically useful amounts and with high *ee* values. The advantages of this reaction are the ready availability of the starting materials, high stereoselectivities for both (−)-2,3-allenols and (+)-2,3-allenyl acetates, the use of a relatively high substrate concentration, and a lower catalyst loading. The resulting (*S*)-(−)-2,3-allenol **1a** can be converted into the corresponding chiral 2,5-dihydrofuran and the vinylic epoxide.

Keywords: allenes · alcohols · enzymes · kinetic resolution

Introduction

It is well known that stereoisomers can show rather different bioactivities, and hence much attention has been focused on the formation or recognition of chemical bonds in a three-dimensional manner leading to the highly stereoselective preparation of enantiomers with one or more chiral center(s) (element(s)).[1, 2] Allenes are a class of compounds with interesting properties such as unique reactivity, chirality, etc.[3] The synthesis of the first allene was reported in 1887[4] and its structure was confirmed in 1954.[5] Allenes can also be found in many natural sources.[6] Due to the notion that these compounds would not be thermally stable, for a long time their chemistry and synthetic routes remained relatively unexplored. Thus, methodologies for the efficient synthesis of highly optically active allenes are quite limited. Recently, ourselves[7–9] and others[10–12] have developed some methodologies for the synthesis of 2,5-dihydrofurans, α-methylene lactones, vinylic epoxides, and α- or γ-amino alcohols starting from 2,3-allenols. Thus, it is highly desirable to develop efficient methodologies for the synthesis of highly optically active 2,3-allenols. We have investigated some protocols for the synthesis of optically active 2,3-allenols with high *ee*, but the efficiency proved to be low due to the lengthy procedure.[7, 9, 13] For chiral alcohols, enzymes or other biosystems are usually used to resolve the racemates, leading to both enantiomers with one isomer in the form of an alcohol and the corresponding opposite enantiomer in the form of an ester, which makes the separation very easy due to the huge difference in the physical properties of these two classes of products.[14] For these enzymatic processes, the common problems are: 1) the very limited scope of the substrates, 2) the enantiopurities of both the alcohols and esters, 3) the loading of the biocatalysts, 4) the concentration of the substrates, and 5) the reaction rate. Here, we wish to report an enzymatic protocol for the efficient synthesis of (*S*)-2,3-allenols and (*R*)-2,3-allenyl acetates of high *ee* values with a certain range of substrates by means of a kinetic resolution process employing a low catalyst loading and relatively high substrate concentrations.[15]

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Results and Discussion

Synthesis of starting racemic 2,3-allenols: Racemic 2,3-allenols can be synthesized very conveniently by a one-step reaction of a propargylic bromide and an aldehyde (for **1a**–**e** and **1g**–**l**)[16] or by the reduction of 1-benzylpropadienyl methyl ketone with $LiAlH_4$ for (**1f**) (Scheme 1).[17]

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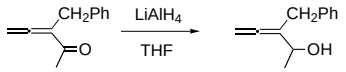
1a: $R^1 = CH_3$, $R^2 = n\text{-}C_4H_9$; **1b**: $R^1 = CH_3$, $R^2 = n\text{-}C_3H_7$
1c: $R^1 = CH_3$, $R^2 = n\text{-}C_5H_{11}$; **1d**: $R^1 = CH_3$, $R^2 = n\text{-}C_6H_{13}$
1e: $R^1 = CH_3$, $R^2 = n\text{-}C_7H_{15}$; **1g**: $R^1 = CH_3$, $R^2 = PhCH_2CH_2$
1h: $R^1 = CH_3$, $R^2 =$ 2-propenyl; **1i**: $R^1 = CH_2CH_3$, $R^2 = n\text{-}C_4H_9$
1j: $R^1 = CH_2CH_3$, $R^2 = n\text{-}C_3H_7$; **1k**: $R^1 = CH_2CH_3$, $R^2 = n\text{-}C_5H_{11}$
1l: $R^1 = CH_2CH_3$, $R^2 = n\text{-}C_7H_{15}$



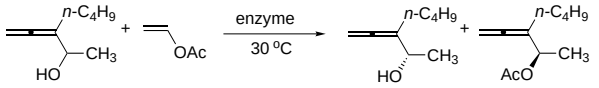
1f

Scheme 1. Synthesis of the racemic 2,3-allenols.

Kinetic resolution of racemic 2,3-allenols: The resolution of 3-(*n*-butyl)-3,4-pentadien-2-ol (**1a**) with vinyl acetate was studied using various enzymes. Some typical results are listed in Table 1. With Novozym 871 L and lipolase, no reaction was observed (entries 1 and 2, Table 1). With lipases AY, PS, and CCL, the results were rather disappointing (entries 3–5, Table 1). With lipase AK, which was used by Burgess to resolve 3-(trimethylsilyl)-3,4-pentadien-2-ol with good selectivity in favor of the corresponding ester (>95% *ee*) and 81% *ee* for the alcohol,[15] (−)-**1a** was obtained in 26% yield and 99% *ee* and (+)-**2a** in 39% yield and 79% *ee* (entry 6, Table 1). Fortunately, however, when we used an immobilized preparation of *Candida antartica* lipase B (Novozym-435) as the biocatalyst,[18] the yields of both the alcohols and esters were good and the *ee* values for both products were excellent!

These results stimulated our considerable interest in this enzymatic resolution reaction. Some typical results are presented in Table 2. From the results shown in Table 2, it can clearly be seen that the enzymatic resolution process is high-yielding and provides the (−)-2,3-allenols and (+)-2,3-allenyl acetates with excellent *ee*. This methodology can accommodate a wide range of different R^2 groups (entries 1–8, Table 2); with R^1 = Me, Et, the results are excellent. The absolute configurations of the products were determined by comparison of the sign of specific rotation of (−)-3-propyl-pentadien-2-ol (**1b**) with that of the known (*R*)-(+)-**1b**.[13c]

Table 1. Screening of various enzymes for the resolution of 3-(*n*-butyl)-3,4-pentadien-2-ol (**1a**) with vinyl acetate.[a]

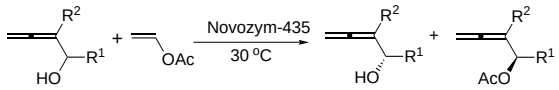


1a (*S*)-(-)-**1a** (*R*)-(+)-**2a**

Entry	Catalyst	*t* [d]	(*S*)-(−)-**1a**		(*R*)-(+)-**2a**	
			Yield [%][b]	*ee* [%][c]	Yield [%][b]	*ee* [%][c]
1	Novozym 871 L	4	NR	–	NR	–
2	Lipolase	4	NR	–	NR	–
3	CCL	4	40	9	17	22
4	Lipase AY	4	24	1	35	38
5	Lipase PS	4	34	39	20	96
6	Lipase AK	4	26	99	39	79
7	Novozym-435	4	39	[d]	31	99

[a] The reaction was carried out at 30 °C using **1a** (100 mg), vinyl acetate (5 mL), and enzyme (70 mg). [b] Isolated yield based on **1a**. [c] Enantiomeric excess determined by GC. [d] (+)-**1a** was not detected by GC.

Table 2. Novozym-435-catalyzed resolution of racemic 2,3-allenols.[a]

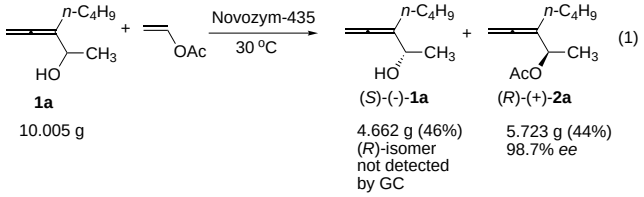


1 (racemate) (*S*)-(-)-**1** (*R*)-(+)-**2**

Entry	**1**		*t* [h]	(*S*)-(−)-**1**		(*R*)-(+)-**2**	
	R^1	R^2		Yield[b] [%]	*ee*[c] [%]	Yield[b] [%]	*ee*[c] [%]
1	Me	*n*Bu (**1a**)	96	39 (**1a**)	99.0	31	98.9 (**2a**)
2	Me	*n*Pr (**1b**)	72	36 (**1b**)	99.7	36	95.4 (**2b**)
3	Me	$n\text{-}C_5H_{11}$ (**1c**)	100	41 (**1c**)	99.5	39	99.0 (**2c**)
4	Me	$n\text{-}C_6H_{13}$ (**1d**)	82.5	40 (**1d**)	99.1	31	99.1 (**2d**)
5	Me	$n\text{-}C_7H_{15}$ (**1e**)	82.5	45 (**1e**)	99.0	49	99.2 (**2e**)
6	Me	$PhCH_2$ (**1f**)	72	42 (**1f**)	95.9	45	99.2 (**2f**)
7	Me	$Ph(CH_2)_2$ (**1g**)	82.5	50 (**1g**)	98.6	44	94.3 (**2g**)
8	Me	allyl (**1h**)	82.5	31 (**1h**)	99.7	38	98.8 (**2h**)
9	Et	$n\text{-}C_4H_9$ (**1i**)	102	49 (**1i**)	99.0[d]	43	99.5 (**2i**)
10	Et	$n\text{-}C_3H_7$ (**1j**)	74	45 (**1j**)	99.7[d]	37	96.4 (**2j**)
11	Et	$n\text{-}C_5H_{11}$ (**1k**)	84	39 (**1k**)	99.4[d]	38	99.7 (**2k**)
12	Et	$n\text{-}C_7H_{15}$ (**1l**)	102	49 (**1l**)	99.7[d]	47	99.4 (**2l**)

[a] The reaction was carried out at 30 °C using the alcohol (100 mg), vinyl acetate (5 mL), and Novozym-435 (70 mg). [b] Isolated yield based on alcohol. [c] Enantiomeric excess was determined by GC or HPLC. [d] Determined after conversion to the corresponding acetate.

This methodology can be efficiently applied to the synthesis of highly optically active (−)-2,3-allenols and (+)-2,3-allenyl acetates in large quantities. For example, after the treatment of **1a** (10.005 g, 71 mmol) with Novozym-435 (7.000 g) in vinyl acetate (500 mL) for 47 h at 30 °C, crude products were obtained following filtration, washing the solids with diethyl ether, and concentration of the combined filtrate and washings. The crude products could be easily separated by flash chromatography on silica gel (column length 12 cm, diameter 6.5 cm; petroleum ether/diethyl ether 20:1 (300 mL) → 10:1 (400 mL) → 5:1 (350 mL) → 3:1 (500 mL)) to afford 4.622 g of (*S*)-(−)-**1a** and 5.723 g of (*R*)-(+)-**2a**. It only took 55 min from packing of the column to complete the elution, illustrating the potential of this methodology [Eq. (1)].



(1)

1a 10.005 g

(*S*)-(-)-**1a** 4.662 g (46%) (*R*)-isomer not detected by GC

(*R*)-(+)-**2a** 5.723 g (44%) 98.7% *ee*

Abstract in Chinese:

Abstract in Chinese: Novozym-435 能有效地拆分一系列 2，3-联烯醇，以高产率、高 *ee* 值地得到光学活性的(*S*)-(-)-2，3-联烯醇和(*R*)-(+)-2，3-联烯基乙酸酯。当以 10g 3-正丁基-3，4-戊二烯-醇为底物时，反应能顺利进行并以合成意义上有用的产率和 *ee* 值得到光活的 2，3-联烯醇和 2，3-联烯基乙酸酯。该反应的优点是：原料易得、对 2，3-联烯醇和 2，3-联烯基乙酸酯都具有很高的立体选择性、底物浓度相对较高、催化剂用量较少。所得(*S*)-(-)-2，3-联烯醇 **1a** 能转化成相应的光学活性的 2，5-二氢呋喃化合物和烯基环氧化合物。

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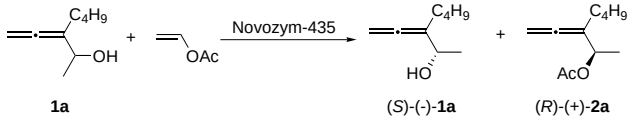
Typical drawbacks of biocatalyzed reactions are a low working concentration of the substrate, a high catalyst loading, and long reaction times. Further studies showed that this Novozym-435-catalyzed kinetic resolution could be performed at higher concentrations of the substrates and lower loadings of the catalyst (entries 1–3, Table 3). The immobilized enzyme showed much higher activity even at 60 °C, without any obvious loss of the enantioselectivity (entry 5, Table 3). At this temperature, the catalyst loading may be as low as 23 mg g^{-1} of substrate without obvious loss of stereoselectivity, and the reaction is complete within 24 h (entry 9, Table 3).

Table 3. Optimization of Novozym-435-promoted kinetic resolution of **1a**.



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

Entry	Solvent [mL]	Substrate [mg]	Enzyme [mg]	T [°C]	t [h]	(*S*)-(−)-**1a** Yield [%]	*ee* [%]	(*R*)-(+)-**2a** Yield [%]	*ee* [%]
1	2.5	100	35	30	96	37	[a]	32	97.2
2	1.25	100	18	30	95	32	[a]	35	99.6
3	5	100	70	40	48	40	[a]	45	99.1
4	5	100	70	50	40	40	[a]	43	97.8
5	5	100	70	60	24.5	36	[a]	39	[a]
6	1.25	100	18.5	60	23	33	[a]	36	96.2
7	3	500	46	60	24	40	[a]	41	96.0
8	1.5	500	23	60	24	35	[a]	39	95.6
9	1.5	1000	23	60	24	36	[a]	39	95.2

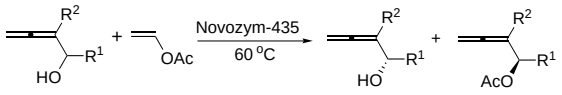
[a] The opposite enantiomer was not detected by GC.

Some typical results for this kinetic resolution, on a scale of 1.0 g at higher concentrations and lower catalyst loadings, are summarized in Table 4. From Table 4, it is interesting to note that: 1) at a lower catalyst loading, in some cases the stereoselectivity in favor of 2,3-allenyl acetate is of no practical value, while that for (−)-2,3-allenols is still reasonable (entries 2, 5, 11, 13, 14, 15, 17, 18, 20, and 21, Table 4); 2) for the same substrate, reaction at a lower concentration and a higher catalyst loading affords the products with higher *ee* values.

The prepared 2,3-allenols can be easily converted to optically active 2,5-dihydrofurans[8] and vinylic epoxide derivatives[7] (Scheme 2).

In conclusion, we have established a protocol for the preparation of (*S*)-(−)-2,3-allenols and (*R*)-(+)-2,3-allenyl acetates with *ee* values of practical value. The reaction can be carried out on a large scale to afford the pure products with high *ee* values following an efficient flash chromatographic separation. Due to the ready availability of racemic 2,3-allenols, high stereoselectivity for both products, a relatively high working concentration, a lower catalyst loading, and the synthetic potential of the products, this methodology should be useful in organic synthesis and provide information for studies of the interaction of 2,3-allenols with biosystems. Further studies on this reaction are being carried out in our laboratory.

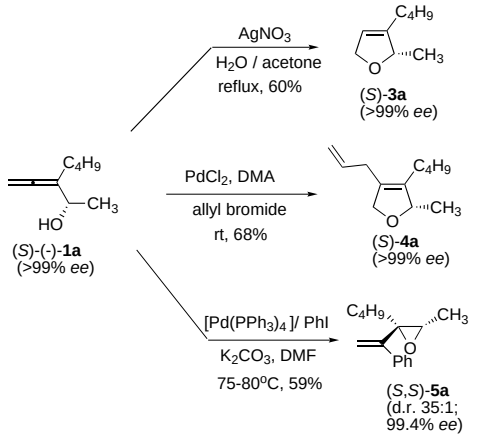
Table 4. Novozym-435-catalyzed resolution of racemic 2,3-allenols at different substrate concentrations and catalyst loadings.



1 (racemate) (*S*)-(-)-**1** (*R*)-(+)-**2**

Entry	**1**	Conc. [mL g^{-1}]	Cat. [mg g^{-1}]	t [h]	(*S*)-(−)-**1** Yield [%]	*ee* [%]	(*R*)-(+)-**2** Yield [%]	*ee* [%]
1	**1a**	1.5	23	24	36 (**1a**)	[a]	39 (**2a**)	95.2
2	**1b**	1.5	23	20	30 (**1b**)	82.2	38 (**2b**)	98.4
3	**1b**	6	92	21.5	31 (**1b**)	99.3	43 (**2b**)	95.8
4	**1b**	6	92	19	34 (**1b**)	96.3	41 (**2b**)	97.4
5	**1c**	1.5	23	24	41 (**1c**)	85.0	40 (**2c**)	98.2
6	**1c**	3	46	26	41 (**1c**)	[a]	48 (**2c**)	97.7
7	**1d**	1.5	23	28	43 (**1d**)	91.2	43 (**2d**)	96.8
8	**1d**	3	46	30	41 (**1d**)	99.4	43 (**2d**)	96.5
9	**1d**	3	46	28	45 (**1d**)	[a]	51 (**2d**)	99.0
10	**1e**	1.5	23	28	50 (**1e**)	98.7	50 (**2e**)	98.4
11	**1f**	1.5	23	24	48 (**1f**)	89.7	31 (**2f**)	99.3
12	**1f**	6	92	22	38 (**1f**)	[a]	41 (**2f**)	96.7
13	**1h**	3	46	21	35 (**1h**)	90.0	34 (**2h**)	98.3
14	**1i**	1.5	23	49	60 (**1i**)	28.5	24 (**2i**)	94.0
15	**1i**	3	46	44.5	52 (**1i**)	73.6	36 (**2i**)	97.9
16	**1i**	6	92	41	54 (**1i**)	96.4	41 (**2i**)	97.3
17	**1j**	1.5	23	26	58 (**1j**)	49.4	30 (**2j**)	98.0
18	**1j**	6	92	27	44 (**1j**)	74.7	38 (**2j**)	97.7
19	**1k**	1.5	23	43	39 (**1k**)	98.5	45 (**2k**)	99.1
20	**1l**	1.5	23	28	31 (**1l**)	70.7	40 (**2l**)	99.3
21	**1l**	6	92	43	48 (**1l**)	66.0	38 (**2l**)	97.0

[a] The opposite enantiomer was not detected by GC.



Scheme 2. Different reactions of (*S*)-(−)-**1a**.

Experimental Section

General procedures: All solvents were distilled prior to use. ^{1}H and ^{13}C NMR spectra were recorded from samples in $CDCl_3$ on a Varian 300 MHz spectrometer. IR spectra were obtained using a Perkin-Elmer 983 instrument. Mass spectra were obtained using a HP 5989 A instrument. High-resolution mass spectra (HRMS) were obtained using a Finnigan MAT 8430 instrument. GC analyses were performed on a Perkin-Elmer Autosystem XL gas chromatograph instrument. HPLC was carried out using a Perkin-Elmer 200 pump/785 A instrument.

Synthesis of racemic 2,3-allenols 1a–l: The racemic 2,3-allenols **1a–e** and **1g–l** were obtained by the reaction of propargylic bromide, the aldehyde,

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and $SnCl_2$[16]; **1f** was prepared by the reduction of the corresponding allenic ketone with $LiAlH_4$.[17]

Synthesis of (±)-3-(*n*-butyl)penta-3,4-dien-2-ol (1a): **Typical procedure**: A suspension of tin(II) chloride (4.70 g, 25.0 mmol), 1-bromo-hept-2-yne (3.90 g, 22.5 mmol), and sodium iodide (3.75 g, 25.0 mmol) in *N*,*N*-dimethylformamide (50 mL) was stirred at room temperature for 1 h. The reaction mixture was then cooled to 0 °C and acetaldehyde (2.20 g, 50 mmol) was added. The resulting mixture was stirred at this temperature for 12 h, quenched with water, and extracted with diethyl ether. The combined organic layers were washed with water, and dried over anhydrous magnesium sulfate. After evaporation of the solvent, the residue was purified by flash chromatography on silica gel (petroleum ether/diethyl ether 20:1) to afford **1a** (1.63 g, 50 %).

(±)-3-(*n*-Propyl)penta-3,4-dien-2-ol (1b): Reaction of 1-bromo-hex-2-yne (6.78 g, 42.4 mmol) with acetaldehyde (3.70 g, 84.8 mmol) afforded **1b** (2.41 g, 45 %).

(±)-3-(*n*-Pentyl)penta-3,4-dien-2-ol (1c): Reaction of 1-bromo-oct-2-yne (11.1 g, 59 mmol) with acetaldehyde (5.20 g, 118.0 mmol) afforded **1c** (7.20 g, 79 %).

(±)-3-(*n*-Hexyl)penta-3,4-dien-2-ol (1d): Reaction of 1-bromo-non-2-yne (4.06 g, 20.0 mmol) with acetaldehyde (1.76 g, 40.0 mmol) afforded **1d** (2.16 g, 64 %).

(±)-3-(*n*-Heptyl)penta-3,4-dien-2-ol (1e): Reaction of 1-bromo-dec-2-yne (6.48 g, 30.0 mmol) with acetaldehyde (2.64 g, 60.0 mmol) afforded **1e** (3.70 g, 67 %).

(±)-3-(2′-Phenylethyl)penta-3,4-dien-2-ol (1g): Reaction of 1-bromo-5-phenylpent-2-yne (4.01 g, 18.0 mmol) with acetaldehyde (3.70 g, 84.8 mmol) afforded **1g** (2.03 g, 60 %).

(±)-3-Allylpenta-3,4-dien-2-ol (1h): Reaction of 6-bromo-hex-1-en-4-yne (3.18 g, 20 mmol) with acetaldehyde (1.76 g, 40.0 mmol) afforded **1h** (1.10 g, 44 %).

(±)-4-(*n*-Butyl)hexa-4,5-dien-3-ol (1i): Reaction of 1-bromo-hept-2-yne (6.68 g, 38.4 mmol) with acetaldehyde (3.38 g, 76.8 mmol) afforded **1i** (3.68 g, 62 %).

(±)-4-(*n*-Propyl)hexa-4,5-dien-3-ol (1j): Reaction of 1-bromo-hex-2-yne (6.90 g, 43.2 mmol) with propionaldehyde (2.01 g, 34.6 mmol) afforded **1j** (4.10 g, 67 %).

(±)-4-(*n*-Pentyl)hexa-4,5-dien-3-ol (1k): Reaction of 1-bromo-dec-2-yne (7.10 g, 37.5 mmol) with propionaldehyde (1.74 g, 30.0 mmol) afforded **1k** (3.40 g, 68 %).

(±)-4-(*n*-Heptyl)hexa-4,5-dien-3-ol (1l): Reaction of 1-bromo-dec-2-yne (7.08 g, 37.5 mmol) with propionaldehyde (1.74 g, 30.0 mmol) afforded **1l** (3.40 g, 68 %).

Synthesis of (±)-3-benzylpenta-3,4-dien-2-ol (1f): A solution of 3-benzyl-penta-3,4-dien-2-one (1.60 g, 9.30 mmol) in THF (20 mL) was added dropwise to a suspension of $LiAlH_4$ (0.38 g, 10.0 mmol) in THF (20 mL) with cooling (ice bath). After the addition, the reaction mixture was stirred for a further 20 min at 0 °C. The excess $LiAlH_4$ was then decomposed by the dropwise addition of water until the gray slurry turned into white granules. The mixture was then filtered and the residual solid was washed with diethyl ether. The combined organic phases were washed with brine and dried over anhydrous sodium sulfate. After evaporation of the solvent, the residue was purified by flash chromatography on silica gel (petroleum ether (30–60 °C)/diethyl ether 8:1) to afford **1f** (1.17 g, 72 %).

Kinetic resolution of racemic 2,3-allenols 1a–l and allenyl acetates 2a–l

Synthesis of (*S*)-(−)-(3-*n*-butyl)penta-3,4-dien-2-ol and (*R*)-(+)-(3-*n*-butyl)penta-3,4-dien-2-yl acetate: **Typical procedure**: Novozym-435 (70 mg) was added to a racemic mixture of (3-*n*-butyl)penta-3,4-dien-2-ol (l00 mg) and vinyl acetate (5 mL). After stirring at 30 °C for 96 h, the reaction mixture was worked-up by filtration. After evaporation of the solvent, purification of the residue by flash chromatography on silica gel (petroleum ether/diethyl ether 40:1 → 10:1) afforded (*S*)-(−)-**1a** (39 mg, 39 %) and (*R*)-(+)-**2a** (40 mg, 31 %). (*S*)-(−)-**1a**: 99.0 % *ee* (GC conditions: column: RT-βDEXcst (30 m, ∅ 0.25 m, 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 (35 min)); liquid; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 4.82-4.78$ (m, 2H; CH_2), 4.20–4.02 (m, 1H; CH), 2.02–1.80 (m, 2H; CH_2), 1.60 (s, 1H, OH), 1.50–1.05 (m, 7H; 2CH_2 and CH_3), 0.82 (t, ^3J(H,H) = 6.7 Hz, 3H; CH_3); ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C): $\delta = 203.72$, 108.67, 78.50, 67.58, 29.69, 27.53, 22.37, 21.89, 13.84; IR (neat): $\tilde{\nu} = 3332$ cm^{-1} (OH), 1956 cm^{-1} (C=C=C); MS (70 eV): *m*/*z* (%): 140 (2) [M^+]. (*R*)-(+)-**2a**: 98.9 % *ee* (GC conditions: column: RT-βDEXcst (30 m, ∅ 0.25 m, 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 (35 min)); liquid; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 5.32-5.20$ (m, 1H; CH), 4.80–4.75 (m, 2H; CH_2), 1.97–1.78 (m, 5H; CH_2 and CH_3), 1.49–1.00 (m, 4H; 2CH_2), 1.22 (d, ^3J(H,H) = 6.6 Hz, 3H; CH_3), 0.81 (t, ^3J(H,H) = 6.7 Hz, 3H; CH_3); ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C): $\delta = 205.96$, 170.69, 105.03, 78.36, 70.47, 29.81, 28.25, 22.55, 21.44, 19.08, 14.10; IR (neat): $\tilde{\nu} = 1958$ cm^{-1} (C=C=C), 1739 cm^{-1} (C=O); APCI MS: *m*/*z*: 183 [M^++H]; HRMS: calcd for $C_9H_{15}O$ [$M^+ - COCH_3$]: 139.1123, found: 139.1130.

Synthesis of (*S*)-(−)-3-(*n*-propyl)penta-3,4-dien-2-ol and (*R*)-(+)-3-(*n*-propyl)penta-3,4-dien-2-yl acetate: Treatment of racemic 3-(*n*-propyl)penta-3,4-dien-2-ol (101 mg) with Novozym-435 (70 mg) afforded (*S*)-(−)-**1b** (36 mg, 36 %) and (*R*)-(+)-**2b** (48 mg, 36 %). (*S*)-(−)-**1b**: 99.7 % *ee* (GC conditions: column: RT-βDEXcst (30 m, ∅ 0.25 m, 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 (35 min)); liquid; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 4.93-4.80$ (m, 2H; CH_2), 4.29–4.13 (m, 1H; CH), 2.09–1.84 (m, 2H, CH_2), 1.68 (s, 1H, OH), 1.57–1.40 (m, 2H, CH_2), 1.30 (d, ^3J(H,H) = 6.7 Hz, 3H; CH_3), 0.93 (t, ^3J(H,H) = 7.3 Hz, 3H; CH_3); ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C): $\delta = 203.66$, 108.75, 78.90, 67.70, 30.17, 22.07, 20.88, 13.89; IR (neat): $\tilde{\nu} = 3350$ cm^{-1} (OH), 1955 cm^{-1} (C=C=C); MS (70 eV): *m*/*z* (%): 126 (1) [M^+].

(*R*)-(+)-**2b**: 95.4 % *ee* (GC conditions: column: RT-βDEXcst (30 m, ∅ 0.25 m, 0.25 μm DF); carrier: N_2, 10 psi; injector: 250 °C; detector (FID, H_2, 0.218 MPa): 250 °C; oven temperature: 85 °C (20 min), then 1.0 °C min^{-1} to 100 °C); liquid; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 5.38-5.22$ (m, 1H; CH), 4.93–4.80 (m, 2H; CH_2), 2.04 (s, 3H; CH_3), 2.00–1.80 (m, 2H; CH_2), 1.58–1.36 (m, 4H; 2CH_2), 1.32 (d, ^3J(H,H) = 5.7 Hz, 3H; CH_3), 0.91 (t, ^3J(H,H) = 7.3 Hz, 3H; CH_3); ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C): $\delta = 206.03$, 170.87, 104.89, 78.42, 70.55, 30.72, 21.53, 20.95, 19.14, 14.07; IR (neat): $\tilde{\nu} = 1958$ cm^{-1} (C=C=C), 1738 cm^{-1} (C=O); MS (70 eV): *m*/*z* (%): 126 (25) [$M^+ - COCH_2$]; HRMS: calcd for $C_8H_{13}O$ [$M^+ - COCH_3$]: 125.0966, found: 125.0946.

Synthesis of (*S*)-(−)-3-(*n*-pentyl)penta-3,4-dien-2-ol and (*R*)-(+)-3-(*n*-pentyl)penta-3,4-dien-2-yl acetate: Treatment of racemic 3-(*n*-pentyl)penta-3,4-dien-2-ol (l01 mg) with Novozym-435 (70 mg) afforded (*S*)-(−)-**1c** (41 mg, 41 %) and (*R*)-(+)-**2c** (50 mg, 39 %). (*S*)-(−)-**1c**: 99.5 % *ee* (GC conditions: column: RT-βDEXcst (30 m, ∅ 0.25 m, 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 (50 min), then 1.0 °C min^{-1} to 135 °C); liquid; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 4.93-4.80$ (m, 2H; CH_2), 4.27–4.07 (m, 1H; CH), 2.13–1.87 (m, 2H; CH_2), 1.68 (s, 1H; OH), 1.60–1.11 (m, 6H; 3CH_2), 1.25 (d, ^3J(H,H) = 6.6 Hz, 3H; CH_3), 0.88 (t, ^3J(H,H) = 6.7 Hz, 3H; CH_3); ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C): $\delta = 204.27$, 108.81, 78.36, 67.82, 31.78, 27.98, 27.48, 22.67, 22.07, 14.16; IR (neat): $\tilde{\nu} = 3346$ cm^{-1} (OH), 1956 cm^{-1} (C=C=C); APCI MS: *m*/*z*: 155 [M^++H]; HRMS: calcd for $C_{10}H_{19}O$ [M^++H]: 155.1436, found: 155.1436.

(*R*)-(+)-**2c**: 99.0 % *ee* (GC conditions: column: RT-βDEXcst (30 m, ∅ 0.25 m, 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 (30 min)); liquid; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 5.32-5.20$ (m, 1H; CH), 4.80–4.75 (m, 2H; CH_2), 1.98 (s, 3H; CH_3), 1.97–1.80 (m, 2H; CH_2), 1.49–1.00 (m, 9H; 3CH_2 and CH_3), 0.84 (t, ^3J(H,H) = 6.7 Hz, 3H; CH_3); ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C): $\delta = 205.99$, 170.72, 105.08, 78.38, 70.49, 31.70, 28.53, 27.34, 22.69, 21.44, 19.09, 14.25; IR (neat): $\tilde{\nu} = 1958$ cm^{-1} (C=C=C), 1740 cm^{-1} (C=O); APCI MS: *m*/*z*: 197 [M^++H]; HRMS: calcd for $C_{10}H_{17}O$ [$M^+ - COCH_3$]: 153.1279, found: 153.1269.

Synthesis of (*S*)-(−)-3-(*n*-hexyl)penta-3,4-dien-2-ol and (*R*)-(+)-3-(*n*-hexyl)penta-3,4-dien-2-yl acetate: Treatment of racemic 3-(*n*-hexyl)penta-3,4-dien-2-ol (l00 mg) with Novozym-435 (70 mg) afforded (*S*)-(−)-**1d** (40 mg, 40 %) and (*R*)-(+)-**2d** (39 mg, 31 %). (*S*)-(−)-**1d**: 99.1 % *ee* (GC conditions: column: RT-βDEXcst (30 m, ∅ 0.25 m, 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 (50 min), then 1.0 °C min^{-1} to 135 °C); liquid; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 4.96-4.80$ (m, 2H; CH_2), 4.33–4.09 (m, 1H; CH), 2.13–1.83 (m, 2H; CH_2), 1.65 (s, 1H; OH), 1.57–1.04 (m, 11H; 4CH_2

and CH_3), 0.87 (t, $^3J(H,H) = 6.7$ Hz, 3H; CH_3); ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C): $\delta = 203.64$, 108.83, 78.71, 67.62, 31.62, 28.98, 27.93, 27.52, 22.54, 21.96, 13.98; IR (neat): $\tilde{\nu} = 3339$ (OH), 1956 cm^{-1} (C=C=C); APCI MS: m/z: 169 [M^++H]; HRMS: calcd for $C_{11}H_{21}O$ [M^++H]: 169.1592, found: 169.1596.

(*R*)-(+)-**2d**: 99.1% *ee* (GC conditions: column: RT-βDEXcst (30 m, ∅ 0.25 m, 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 (50 min), then 1.0 °C min^{-1} to 135 °C); liquid; ^1H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta =$ 5.37–5.20 (m, 1H; CH), 4.89–4.71 (m, 2H; CH_2), 1.98 (s, 3H; CH_3), 1.97–1.80 (m, 2H; CH_2), 1.44–1.09 (m, 11H; 4 CH_2 and CH_3), 0.81 (t, $^3J(H,H) = 7.3$ Hz, 3H; CH_3); ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C): $\delta =$ 204.76, 169.59, 103.87, 77.20, 69.33, 30.65, 27.94, 27.37, 26.41, 21.60, 20.28, 17.89, 13.07; IR (neat): $\tilde{\nu} = 1958$ (C=C=C), 1740 cm^{-1} (C=O); APCI MS: m/z: 211 [M^++H]; HRMS: calcd for $C_{11}H_{19}O$ [$M^+ - COCH_3$]: 167.1436, found: 167.1441.

Synthesis of (*S*)-(−)-3-(*n*-heptyl)penta-3,4-dien-2-ol and (*R*)-(+)-3-(*n*-heptyl)penta-3,4-dien-2-yl acetate: Treatment of racemic 3-(*n*-heptyl)penta-3,4-dien-2-ol (l00 mg) with Novozym-435 (70 mg) afforded (*S*)-(−)-**1e** (45 mg, 45%) and (*R*)-(+)-**2e** (60 mg, 49%). (*S*)-(−)-**1e**: 99.0% *ee* (GC conditions: column: RT-βDEXcst (30 m, ∅ 0.25 m, 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 (50 min), then 1.0 °C min^{-1} to 135 °C); liquid; ^1H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 4.89-4.76$ (m, 2H; CH_2), 4.20–4.00 (m, 1H; CH), 2.09–1.78 (m, 2H; CH_2), 1.63 (s, 1H; OH), 1.53–1.00 (m, 13H; 5 CH_2 and CH_3), 0.78 (t, $^3J(H,H) = 6.1$ Hz, 3H; CH_3); ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C): $\delta = 204.18$, 108.94, 78.58, 67.87, 32.03, 29.56, 29.37, 28.11, 27.85, 22.82, 22.14, 14.21; IR (neat): $\tilde{\nu} = 3341$ (OH), 1956 cm^{-1} (C=C=C); APCI MS: m/z: 183 [M^++H]; HRMS: calcd for $C_{12}H_{23}O$ [M^++H]: 183.1749, found: 183.1749. (*R*)-(+)-**2e**: 99.2% *ee* (GC conditions: column: RT-βDEXcst (30 m, ∅ 0.25 m, 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 (50 min), then 1.0 °C min^{-1} to 135 °C); liquid; ^1H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 5.37-5.16$ (m, 1H; CH), 4.89–4.64 (m, 2H; CH_2), 1.98 (s, 3H; CH_3), 1.96–1.84 (m, 2H; CH_2), 1.53–1.04 (m, 13H; 5 CH_2 and CH_3), 0.81 (t, $^3J(H,H) = 6.1$ Hz, 3H; CH_3); ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C): $\delta =$ 204.76, 169.58, 103.87, 77.19, 69.32, 30.81, 28.25, 28.11, 27.37, 26.46, 21.63, 20.28, 17.89, 13.08; IR (neat): $\tilde{\nu} = 1958$ cm^{-1} (C=C=C), 1739 cm^{-1} (C=O); APCI MS: m/z: 225 [M^++H]; HRMS: calcd for $C_{12}H_{22}O$ [$M^+ - COCH_2$]: 182.1671, found: 182.1680.

Synthesis of (*S*)-(−)-3-benzylpenta-3,4-dien-2-ol and (*R*)-(+)-3-benzylpenta-3,4-dien-2-yl acetate: Treatment of racemic 3-benzylpenta-3,4-dien-2-ol (l00 mg) with Novozym-435 (70 mg) afforded (*S*)-(−)-**1f** (42 mg, 42%) and (*R*)-(+)-**2f** (55 mg, 45%). (*S*)-(−)-**1f**: 95.9% *ee* (HPLC conditions: Chiralpak AD column (∅ 0.46 cm × 25 cm); $\lambda = 254$ nm; rate: 0.7 mL min^{-1}; hexane/*i*PrOH 100:1.5); liquid; ^1H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 7.36-7.12$ (m, 5H; C_6H_5), 4.84–4.80 (m, 2H; CH_2), 4.24–4.16 (m, 1H; CH), 3.50–3.30 (m, 2H; CH_2), 1.60 (s, 1H; OH), 1.20 (d, $^3J(H,H) = 6.7$ Hz, 3H; CH_3); ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C): $\delta =$ 205.59, 139.76, 129.33, 128.58, 126.56, 108.33, 78.40, 67.19, 35.97, 22.40; IR (neat): $\tilde{\nu} = 3363$ (OH), 1956 cm^{-1} (C=C=C); MS (70 eV): m/z (%): 174 (0.1) [M^+].

(*R*)-(+)-**2f**: 99.2% *ee* (HPLC conditions: Chiralcel OJ column (∅0.46 cm × 25 cm); $\lambda = 254$ nm; rate: 0.7 mL min^{-1}; hexane/*i*PrOH 97:3); liquid; ^1H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 7.37-7.09$ (m, 5H; C_6H_5), 5.36–5.24 (m, 1H; CH), 4.89–4.80 (m, 2H; CH_2), 3.40–3.27 (m, 2H; CH_2), 1.99 (s, 3H; CH_3), 1.30 (d, $^3J(H,H) = 6.7$ Hz, 3H; CH_3); ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C): $\delta = 207.25$, 170.74, 139.23, 129.16, 128.49, 126.54, 104.52, 78.31, 69.93, 36.45, 21.37, 19.22; IR (neat): $\tilde{\nu} = 1958$ (C=C=C), 1737 cm^{-1} (C=O); APCI MS: m/z: 217 [M^++H]; elemental analysis calcd (%) for $C_{14}H_{16}O_2$: C 77.78, H 7.40; found C 77.75, H 7.30.

Synthesis of (*S*)-(−)-3-(2′-phenylethyl)penta-3,4-dien-2-ol and (*R*)-(+)-3-(2′-phenyl)ethylpenta-3,4-dien-2-yl acetate: Treatment of racemic 3-(2′-phenylethyl)penta-3,4-dien-2-ol (l00 mg) with Novozym-435 (70 mg) afforded (*S*)-(−)-**1g** (50 mg, 50%) and (*R*)-(+)-**2g** (54 mg, 44%). (*S*)-(−)-**1g**: 98.6% *ee* (HPLC conditions: Chiralcel AD column (∅0.46 cm × 25 cm); $\lambda = 254$ nm; rate: 0.7 mL min^{-1}; hexane/*i*PrOH 95:5); liquid; ^1H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 7.44-7.04$ (m, 5H; C_6H_5), 5.00–4.80 (m, 2H; CH_2), 4.33–4.09 (m, 1H; CH), 2.79 (t, $^3J(H,H) = 7.3$ Hz, 2H; CH_2), 2.40–2.22 (m, 2H; CH_2), 1.84 (s, 1H; OH), 1.32 (d, $^3J(H,H) = 3.7$ Hz, 3H; CH_3); ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C): $\delta = 203.95$, 141.91, 128.38, 128.25, 125.83, 108.24, 79.33, 67.83, 33.95, 29.63, 21.95; IR (neat): $\tilde{\nu} = 3368$ (OH), 1955 cm^{-1} (C=C=C); APCI MS: m/z: 189 [M^++H]; HRMS: calcd for $C_{13}H_{17}O$ [M^++H]: 189.1279, found: 189.1280.

(*R*)-(+)-**2g**: 94.3% *ee* (HPLC conditions: Chiralcel OJ column (∅ 0.46 cm × 25 cm); $\lambda = 254$ nm; rate: 0.7 mL min^{-1}; hexane/*i*PrOH 97:3); liquid; ^1H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 7.42-7.04$ (m, 5H; C_6H_5), 5.44–5.24 (m, 1H; CH), 4.96–4.84 (m, 2H; CH_2), 2.74 (t, $^3J(H,H) =$ 7.9 Hz, 2H; CH_2), 2.40–2.11 (m, 2H; CH_2), 2.03 (s, 3H; CH_3), 1.34 (d, $^3J(H,H) = 6.3$ Hz, 3H; CH_3); ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C): $\delta =$ 205.72, 170.28, 141.68, 128.26, 128.16, 125.75, 104.30, 78.72, 70.12, 33.71, 29.98, 21.07, 18.74; IR (neat): $\tilde{\nu} = 1958$ (C=C=C), 1737 cm^{-1} (C=O); APCI MS: m/z: 231 [M^++H]; HRMS: calcd for $C_{13}H_{15}O$ [$M^+ - COCH_3$]: 187.1123, found: 187.1118.

Synthesis of (*S*)-(−)-3-allylpenta-3,4-dien-2-ol and (*R*)-(+)-3-allylpenta-3,4-dien-2-yl acetate: Treatment of racemic 3-allylpenta-3,4-dien-2-ol (l00 mg) with Novozym-435 (70 mg) afforded (*S*)-(−)-**1h** (31 mg, 31%) and (*R*)-(+)-**2h** (51 mg, 38%). (*S*)-(−)-**1h**: 99.7% *ee* (GC conditions: column: RT-βDEXcst (30 m, ∅ 0.25 m, 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 (50 min), then 1.0 °C min^{-1} to 135 °C); liquid; ^1H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 5.84-5.64$ (m, 1H; CH), 5.09–4.96 (m, 2H; CH_2), 4.84–4.76 (m, 2H; CH_2), 4.29–4.04 (m, 1H; CH), 2.84–2.60 (m, 2H; CH_2), 1.57 (s, 1H; OH), 1.23 (d, $^3J(H,H) = 6.7$ Hz, 3H; CH_3); ^{13}C NMR (75.40 MHz, $CDCl_3$, 25 °C): $\delta = 204.70$, 135.90, 116.24, 107.01, 78.63, 67.61, 33.34, 22.10; IR (neat): $\tilde{\nu} = 3342$ (OH), 1957 cm^{-1} (C=C=C); MS (70 eV): m/z (%): 124 (0.7) [M^+]; HRMS: calcd for C_8H_{11} [M^+ − OH]: 107.0861, found 107.0856.

(*R*)-(+)-**2h**: 98.8% *ee* (GC conditions: column: RT-βDEXcst (30 m, ∅ 0.25 m, 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 (35 min)); liquid; ^1H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 5.89-5.67$ (m, 1H; CH), 5.40–5.23 (m, 1H; CH), 5.10–5.00 (m, 2H; CH_2), 4.91–4.78 (m, 2H; CH_2), 2.84–2.63 (m, 2H; CH_2), 2.05 (s, 3H; CH_3), 1.32 (d, $^3J(H,H) = 6.1$ Hz, 3H; CH_3); ^{13}C NMR (75.40 MHz, $CDCl_3$, 25 °C): $\delta = 206.06$, 170.55, 135.08, 116.17, 103.10, 78.31, 69.77, 33.53, 21.18, 18.74; IR (neat): $\tilde{\nu} = 1959$ (C=C=C), 1738 cm^{-1} (C=O); APCI MS: m/z: 167 [M^++H]; HRMS: calcd for $C_8H_{12}O$ [$M^+ - COCH_2$]: 124.0889, found: 124.0864.

Synthesis of (*S*)-(−)-4-(*n*-butyl)hexa-4,5-dien-3-ol and (*R*)-(+)-4-(*n*-butyl)hexa-4,5-dien-3-yl acetate: Treatment of racemic 4-(*n*-butyl)hexa-4,5-dien-3-ol (l01 mg) with Novozym-435 (70 mg) afforded (*S*)-(−)-**1i** (49 mg, 49%) and (*R*)-(+)-**2i** (55 mg, 43%). (*S*)-(−)-**1i**: 99.0% *ee* (GC conditions: column: RT-βDEXcst (30 m, ∅ 0.25 m, 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 (30 min), then 1.0 °C min^{-1} to 180 °C (20 min)); liquid; ^1H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 4.93-4.76$ (m, 2H; CH_2), 4.04–3.99 (m, 1H; CH), 2.09–1.80 (m, 2H; CH_2), 1.80–1.16 (m, 7H; 3 CH_2 and OH), 1.00–0.71 (m, 6H; 2 CH_3); ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C): $\delta = 204.64$, 107.52, 78.70, 73.38, 30.04, 28.54, 27.76, 22.72, 14.17, 9.92; IR (neat): $\tilde{\nu} = 3342$ (OH), 1956 cm^{-1} (C=C=C); APCI MS: m/z: 155 [M^++H]; HRMS: calcd for $C_{10}H_{19}O$ [M^++H]: 155.1436, found: 155.1431.

(*R*)-(+)-**2i**: 99.5% *ee* (determined after conversion to the corresponding acetate); liquid; ^1H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 5.20-5.04$ (m, 1H; CH), 4.93–4.68 (m, 2H; CH_2), 2.04 (s, 3H; CH_3), 2.00–1.80 (m, 2H; CH_2), 1.76–1.64 (m, 2H; CH_2), 1.49–1.20 (m, 4H; 2 CH_2), 1.00–0.71 (m, 6H; 2 CH_3); ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C): $\delta = 206.33$, 170.75, 103.50, 77.89, 75.56, 29.80, 28.00, 26.08, 22.55, 21.31, 14.08, 10.05; IR (neat): $\tilde{\nu} =$ 1958 (C=C=C), 1740 cm^{-1} (C=O); APCI MS: m/z: 197 [M^++H]; HRMS: calcd for $C_{10}H_{18}O$ [$M^+ - COCH_2$]: 154.1357, found: 154.1346.

Synthesis of (*S*)-(−)-4-(*n*-propyl)hexa-4,5-dien-3-ol (1j) and (*R*)-(+)-4-(*n*-propyl)hexa-4,5-dien-3-yl acetate: Treatment of racemic 4-(*n*-propyl)hexa-4,5-dien-3-ol (l01 mg) with Novozym-435 (70 mg) afforded (*S*)-(−)-**1j** (45 mg, 45%) and (*R*)-(+)-**2j** (48 mg, 37%). (*S*)-(−)-**1j**: 99.7% *ee* (GC conditions: column: RT-βDEXcst (30 m, ∅ 0.25 m, 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 (30 min), then 1.0 °C min^{-1} to 180 °C (20 min)); liquid; ^1H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 4.96-4.74$ (m, 2H; CH_2), 4.00–3.82 (m, 1H; CH), 2.02–1.80 (m, 2H; CH_2), 1.80–1.24 (m, 5H; 2 CH_2 and OH), 1.02–0.80 (m, 6H; 2 CH_3); ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C): $\delta = 204.64$, 107.30, 78.63, 73.36, 30.15, 28.52, 21.08, 14.14, 9.91; IR (neat): $\tilde{\nu} = 3361$ (OH), 1955 cm^{-1} (C=C=C), MS (70 eV): m/z (%): 140 (8) [M^+].

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(*R*)-(+)-**2j**: 96.4% *ee* (determined after conversion to the corresponding acetate); liquid; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 5.19-5.06$ (m, 1H; CH), 4.89–4.63 (m, 2H; CH_2), 2.02 (s, 3H; CH_3), 1.97–1.74 (m, 2H; CH_2), 1.74–1.52 (m, 2H; CH_2), 1.41 (q, ^3J(H,H) = 7.2 Hz, 2H, CH_2), 1.00–0.70 (m, 6H; $2CH_3$); ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C): $\delta = 206.02$, 170.49, 103.01, 77.61, 75.25, 30.11, 25.77, 21.06, 20.59, 13.73, 9.79; IR (neat): $\tilde{\nu} = 1958$ (C=C=C), 1740 cm^{-1} (C=O); MS (70 eV): *m*/*z* (%): 140 (3) [$M^+ - COCH_2$]; HRMS: calcd for $C_9H_{16}O$ [$M^+ - COCH_2$]: 140.1201, found: 140.1192.

Synthesis of (*S*)-(−)-4-(*n*-pentyl)hexa-4,5-dien-3-ol and (*R*)-(+)-4-(*n*-pentyl)hexa-4,5-dien-3-yl acetate: Treatment of racemic 4-(*n*-pentyl)hexa-4,5-dien-3-ol (l01 mg) with Novozym-435 (70 mg) afforded (*S*)-(−)-**1k** (39 mg, 39%) and (*R*)-(+)-**2k** (48 mg, 38%). (*S*)-(−)-**1k**: 99.4% *ee* (GC conditions: column: RT-βDEXcst (30 m, ∅ 0.25 m, 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), then 1.0 °C min^{-1} to 130 °C (20 min)); liquid; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 5.00-4.76$(m, 2H; CH_2), 4.04–3.80 (m, 1H; CH), 2.04–1.80 (m, 2H; CH_2), 1.80–1.08 (m, 9H; $4CH_2$ and OH), 1.08–0.80 (m, 6H; $2CH_3$); ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C): $\delta = 204.36$, 107.19, 78.28, 73.11, 31.56, 28.23, 27.65, 27.24, 22.46, 13.99, 9.64; IR (neat): $\tilde{\nu} = 3353$ (OH), 1955 cm^{-1} (C=C=C); MS (70 eV): *m*/*z* (%): 168 (2) [M^+].

(*R*)-(+)-**2k**: 99.7% *ee* (determined after conversion to the corresponding acetate); liquid; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 5.03-4.97$ (m, 1H; CH), 4.74–4.57 (m, 2H; CH_2), 1.93 (s, 3H; CH_3), 1.91–1.79 (m, 2H; CH_2), 1.75–1.50 (m, 2H; CH_2), 1.47–1.00 (m, 6H; $3CH_2$), 0.96–0.59 (m, 6H; $2CH_3$); ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C): $\delta = 206.03$, 170.48, 103.26, 77.67, 75.29, 31.43, 27.99, 27.05, 25.81, 22.42, 21.07, 13.98, 9.81; IR (neat): $\tilde{\nu} = 1958$ (C=C=C), 1740 cm^{-1} (C=O); MS (70 eV): *m*/*z* (%): 168 (2) [$M^+ - COCH_2$]; HRMS: calcd for $C_{11}H_{20}O$ [$M^+ - COCH_2$]: 168.1514, found: 168.1497.

Synthesis of (*S*)-(−)-4-(*n*-heptyl)hexa-4,5-dien-3-ol and (*R*)-(+)-4-(*n*-heptyl)hexa-4,5-dien-3-yl acetate: Treatment of racemic 4-(*n*-heptyl)hexa-4,5-dien-3-ol (l02 mg) with Novozym-435 (70 mg) afforded (*S*)-(−)-**1l** (49 mg, 49%) and (*R*)-(+)-**2l** (58 mg, 47%). (*S*)-(−)-**1l**: 99.7% *ee* (GC conditions: column: RT-βDEXcst (30 m, ∅ 0.25 m, 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), then 1.0 °C min^{-1} to 130 °C (20 min)); liquid; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 5.00-4.67$ (m, 2H; CH_2), 4.09–3.80 (m, 1H; CH), 2.13–1.80 (m, 2H; CH_2), 1.80–1.00 (m, 13H; $6CH_2$ and OH), 1.00–0.80 (m, 6H; $2CH_3$); ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C): $\delta = 204.32$, 107.34, 78.57, 73.10, 31.82, 29.36, 29.16, 28.30, 27.84, 27.63, 22.63, 14.09, 9.67; IR (neat): $\tilde{\nu} = 3344$ (OH), 1955 cm^{-1} (C=C=C); MS (70 eV): *m*/*z* (%): 196 (5) [M^+]; HRMS: calcd for $C_{13}H_{24}O$ [M^+]: 196.1827, found: 196.1781.

(*R*)-(+)-**2l**: 99.4% *ee* (determined after conversion to the corresponding acetate); liquid; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C); $\delta = 5.20-5.12$ (m, 1H; CH), 4.86–4.65 (m, 2H; CH_2), 2.05 (s, 3H; CH_3), 1.97–1.83 (m, 2H; CH_2), 1.80–1.57 (m, 2H; CH_2), 1.51–1.07 (m, 10H; $5CH_2$), 0.96–0.74 (m, 6H; $2CH_3$); ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C): $\delta = 206.05$, 170.56, 103.29, 77.71, 75.34, 31.80, 29.23, 29.11, 28.06, 27.41, 25.84, 22.62, 21.13, 14.05, 9.86; IR (neat): $\tilde{\nu} = 1958$ (C=C=C), 1740 cm^{-1} (C=O); MS (70 eV): *m*/*z* (%): 196 (14) [$M^+ - COCH_2$]; HRMS: calcd for $C_{13}H_{24}O$ [$M^+ - COCH_2$]: 196.1827, found: 196.1849.

$AgNO_3$-catalyzed cycloisomerization of 1a: **Synthesis of (*R*)-3-butyl-2-methyl-2,5-dihydrofuran ((*S*)-3a)**: $AgNO_3$ (170 mg, 1 mmol) was added to a solution of (*S*)-**1a** (*ee* > 99%) (140 mg, 1 mmol) in acetone/water (1:1) (2 mL) under nitrogen. After refluxing for 8 h, with TLC monitoring, the reaction was quenched with brine (10 mL), the mixture was extracted with diethyl ether (3 × 20 mL), and the combined extracts were washed twice with brine and dried over sodium sulfate. After evaporation of the solvent, the residue was purified by flash chromatography on silica gel (petroleum ether/diethyl ether 100:1) to afford (*S*)-3-butyl-2-methyl-2,5-dihydrofuran ((*S*)-**3a**) (84 mg, 60%) with > 99% *ee* (GC conditions: column: γ-cyclodextrin butyryl (20 m × 0.25 mm); carrier: N_2, 6 psi; injector: 250 °C; detector (FID, H_2, 0.218 MPa): 250 °C; oven temperature: 50 °C (40 min), then 1.0 °C min^{-1} to 120 °C); liquid; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 5.40-5.26$ (m, 1H; CH), 4.77–4.40 (m, 3H; OCH and OCH_2), 2.09–1.77 (m, 2H; CH_2), 1.54–1.20 (m, 4H; $2CH_2$), 1.14 (d, ^3J(H,H) = 5.4 Hz, 3H; CH_3), 0.83 (t, ^3J(H,H) = 6.6 Hz, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C): $\delta = 144.34$, 118.24, 82.94, 74.06, 29.48, 26.47, 22.53, 20.43, 13.91; IR (neat): $\tilde{\nu} = 1661$ cm^{-1} (C=C); MS (70 eV): *m*/*z* (%): 140 (8) [M^+] HRMS: calcd for $C_9H_{16}O$ [M^+]: 140.1201, found: 140.1219.

Pd^{II}-catalyzed coupling cyclization of 1a with allylic bromide: **Synthesis of (*S*)-4-allyl-3-butyl-2-methyl-2,5-dihydrofuran [(*S*)-4a]**: A mixture of (*S*)-**1a** (*ee* > 99%) (140 mg, 1 mmol), allylic bromide (5 mmol), and $PdCl_2$ (8.9 mg, 0.05 mmol) was stirred in *N*,*N*-dimethylacetamide (6 mL) at room temperature. When the reaction was complete, as monitored by TLC, diethyl ether 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/diethyl ether 100:1) to afford (*S*)-4-allyl-3-butyl-2-methyl-2,5-dihydrofuran (122 mg, 68%) with > 99% *ee* (GC conditions: column: γ-cyclodextrin butyryl (20 m × 0.25 mm); carrier: N_2, 6 psi; injector: 250 °C; detector (FID, H_2, 0.218 MPa): 250 °C; oven temperature: 80 °C (40 min), then 1.0 °C min^{-1} to 120 °C (20 min)); liquid; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 5.80-5.60$ (m, 1H; CH), 5.11–4.90 (m, 2H; CH_2), 4.90–4.71 (m, 1H; CH), 4.60–4.38 (m, 2H; CH_2), 2.81 (d, ^3J(H,H) = 6.3 Hz, 2H; CH_2), 2.26–2.03 (m, 1H; CH), 2.00–1.83 (m, 1H; CH), 1.54–1.03 (m, 4H; $2CH_2$), 1.22 (d, ^3J(H,H) = 6.4 Hz, 3H; CH_3), 0.89 (t, ^3J(H,H) = 6.3 Hz, 3H; CH_3); ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C): $\delta = 136.53$, 135.14, 128.97, 115.67, 83.87, 76.13, 30.17, 29.72, 24.51, 22.71, 20.59, 13.85; IR (neat): $\tilde{\nu} = 1639$ (C=C), 1071 cm^{-1} (C–O); MS (70 eV): *m*/*z* (%): 180 (3) [M^+].

Pd^0-catalyzed coupling cyclization of 1a with PhI: **Synthesis of (*S*,*S*)-2-butyl-3-methyl-2-(1′-phenylvinyl)oxirane ((*S*,*S*)-5a)**: $[Pd(PPh_3)_4]$ (58 mg, 0.05 mmol) was added to a mixture of (*S*)-**1a** (*ee* > 99%) (140 mg, 1 mmol), phenyl iodide (216 mg, 1.06 mmol), and potassium carbonate (552 mg, 4.01 mmol) in DMF (4 mL) under Ar, and the resulting mixture was heated at 75–80 °C for 18 h with monitoring by TLC. The reaction was then quenched with brine (10 mL), the mixture was extracted with diethyl ether (3 × 20 mL), and the combined extracts were washed twice with brine and dried over sodium sulfate. After evaporation of the solvent, the residue was purified by flash chromatography on silica gel (petroleum ether/diethyl ether 200:1) to afford (*S*,*S*)-2-butyl-3-methyl-2-(1′-phenylvinyl)oxirane ((*S*,*S*)-**5a**) (127 mg, 59%) with 99.4% *ee* (GC conditions: column: RT-βDEXcst (30 m, ∅ 0.25 m, 0.25 μm DF); carrier: N_2, 8 psi; injector: 250 °C; detector (FID, H_2, 0.218 MPa): 250 °C; oven temperature: 140 °C (20 min), then 1.0 °C min^{-1} to 180 °C); liquid; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): $\delta = 7.31-7.19$ (m, 5H; C_6H_5), 5.35 (d, ^3J(H,H) = 1.5 Hz, 1H; CH), 5.25 (d, ^3J(H,H) = 1.5 Hz, 1H; CH), 3.07 (q, ^3J(H,H) = 5.4 Hz, 1H; CH), 1.80–1.60 (m, 1H; CH), 1.30 (d, ^3J(H,H) = 3.9 Hz, 3H; CH_3), 1.31–1.02 (m, 4H; $2CH_2$), 0.80 (t, ^3J(H,H) = 2.6 Hz, 3H; CH_3); ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C): $\delta = 148.38$, 138.49, 128.28, 127.69, 126.46, 112.73, 64.83, 60.84, 28.72, 27.13, 22.58, 13.87, 13.77; IR (neat): $\tilde{\nu} = 1627$ cm^{-1} (C=C); MS (70 eV): *m*/*z* (%): 216 (14) [M^+]; HRMS: calcd for $C_{15}H_{20}O$ [M^+]: 216.1514, found: 216.1513.

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