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Kinetic resolution of propargylic and allylic alcohols by *Candida antarctica* lipase (Novozyme 435)

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Abstract—A number of chiral propargylic and allylic alcohols were resolved by lipase-catalyzed kinetic resolution (Novozyme 435). In some cases the enantiomeric excess was high (up to >99%).

1. Introduction

Chiral allylic and propargylic alcohols are versatile building blocks for the synthesis of natural products and biologically active compounds.[1] Among the various methods available for the synthesis of such systems, we can mention the addition of organometallics to aldehydes in the presence of a chiral ligand,[2] asymmetric organozinc additions to aldehydes[3] and the elimination of chiral vinyl sulfoxides.[4] As well as these methods to access chiral unsaturated alcohols, biocatalytic procedures have emerged as advantageous alternatives to meet this goal. In this way, chiral propargylic alcohols have been obtained by enzymatic esterifications[5] and hydrolysis[6] using lipases, asymmetric reduction of acetylenic ketones by alcohol dehydrogenases[7] and microbial hydrolysis.[8] Recently, it has been reported that Novozyme 435 (*Candida antarctica* lipase B) efficiently resolves allenols[9] and aryl propargylic alcohols[10] with high enantiomeric excess. Over the course of a study on the hydrotelluration of propargylic alcohols we needed these compounds enantiomerically pure. For this end we decided to use CAL-B (Novozyme 435) as the lipase for the kinetic resolution of a number of propargylic alcohols **1a**–**e** with different steric demand around the chiral carbinolic carbon (Tables 1 and 2). The same enzyme was used to resolve allylic enynes **2a** and **b** (Table 3).

2. Results and discussion

2.1. Kinetic resolution of propargylic and allylic alcohols by Novozyme 435

In Tables 1–3 are shown the allylic and propargylic alcohols used in this study as well as the reactions performed. Initially, we investigated the influence of the solvent in the kinetic resolution. Racemic alcohol **1a** was used in this exploratory study in view of the results reported in the literature on the kinetic resolution of this substrate using other enzymes and reaction conditions.[10] In this way, the efficiency of the reported studies and the present work could be compared. In Table 1 are shown the results obtained by us.

As can be observed from the data in Table 1, tetrahydrofuran and diethyl ether were not efficient solvents for the kinetic resolution of **1a**. The conversion was very low and did not increase over time. Using hexane and benzene as solvents, the kinetic resolution was very efficient, with both the (*S*)-(+)-**1a** alcohol and the (*R*)-(+)-**3a** acetate were obtained in up to 99% ee. In order to check if the reaction in hexane was also efficient on a preparative scale, it was repeated using 560 mg of (*RS*)-**1a** (see Section 4.3). After 40 min at 32 °C, (*S*)-(+)-**1a** was obtained in 39% isolated yield with 99% ee while (*R*)-(+)-**3a** was obtained in 46% isolated yield with 98% ee. The enantiomeric rate (*E*) for the kinetic resolution of compound (*RS*)-**1a** was $E > 200$.[11] A recent study reported the resolution of 1-phenyl-2-propynol **1a** using the enzyme Novozyme 435 and vinyl acetate both as the acetate donor and the reaction solvent.[10] Under these

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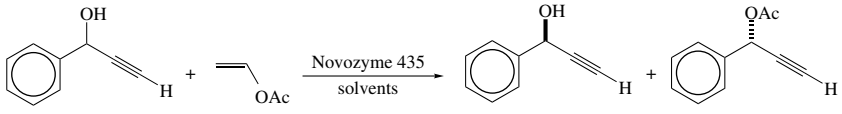
Table 1. Kinetic resolution of (*RS*)-phenyl propargylic alcohol **1a** catalyzed by Novozyme 435[a]

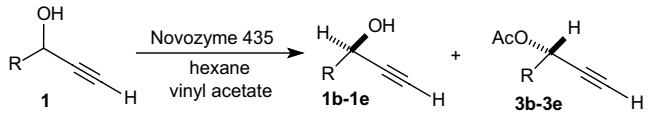


1a (racemic) (*S*)-**1a** (*R*)-**3a**

t	THF or Et_2O				Benzene				Hexane			
	c	Ee **1a**	Ee **3a**	*E*	*c*	Ee **1a**	Ee **3a**	*E*	*c*	Ee **1a**	Ee **3a**	*E*
20	2	2 (*S*)	99 (*R*)	Nc	45	80 (*S*)	>99 (*R*)	491	49	96 (*S*)	>99 (*R*)	789
40	2	2 (*S*)	99 (*R*)	Nc	49	94 (*S*)	>99 (*R*)	712	50	>99 (*S*)	>99 (*R*)	1057
70	2	2 (*S*)	99 (*R*)	Nc	50	99 (*S*)	>99 (*R*)	1057	50	>99 (*S*)	>99 (*R*)	1057
100	2	2 (*S*)	99 (*R*)	Nc	50	99 (*S*)	>99 (*R*)	1057	50	>99 (*S*)	>99 (*R*)	1057
160	2	2 (*S*)	99 (*R*)	Nc	50	99 (*S*)	>99 (*R*)	1057	50	>99 (*S*)	99 (*R*)	1057
220	2	2 (*S*)	99 (*R*)	Nc	50	99 (*S*)	>99 (*R*)	1057	50	>99 (*S*)	99 (*R*)	1057
280	2	2 (*S*)	99 (*R*)	Nc	50	99 (*S*)	>99 (*R*)	1057	50	>99 (*S*)	98 (*R*)	525
340	2	2 (*S*)	99 (*R*)	Nc	50	99 (*S*)	>99 (*R*)	1057	50	>99 (*S*)	98 (*R*)	525
400	2	2 (*S*)	99 (*R*)	Nc	50	99 (*S*)	>99 (*R*)	1057	50	>99 (*S*)	98 (*R*)	525
460	2	2 (*S*)	99 (*R*)	Nc	50	99 (*S*)	>99 (*R*)	1057	50	>99 (*S*)	98 (*R*)	525
520	2	2 (*S*)	99 (*R*)	Nc	50	99 (*S*)	>99 (*R*)	1057	50	>99 (*S*)	97 (*R*)	347

[a] The reaction was carried out at 32 °C using alcohol **1a** (50 μL), vinyl acetate (100 μL), solvents (10 mL) and Novozyme 435 (100 mg); *t*: time (minutes); *c* (%): calculated from the ee's of the substrate (ee_s) and the product (ee_p): *c*: $ee_s/(ee_p + ee_s)$; ee (%) enantiomeric excess; *E*: enantiomeric ratio; Nc: Not calculated.

Table 2. Kinetic resolution of (*RS*)-propargylic alcohols **1b–d** catalyzed by Novozyme 435[a]



R = *n*-C_6H_{13} (**1b**, **3b**); *i*-C_3H_7 (**1c**, **3c**); Et (**1d**, **3d**); Me (**1e**, **3e**)

t	*c*	Ee **1b**	Ee **3b**	*E*	*c*	Ee **1c**	Ee **3c**	*E*	*c*	Ee **1d**	Ee **3d**	*E*
20	21	27 (*R*)	99 (*S*)	259	8	8 (*R*)	93 (*S*)	29	50	26 (*R*)	26 (*S*)	2.2
40	33	49 (*R*)	99 (*S*)	324	14	15 (*R*)	93 (*S*)	31	73	51 (*R*)	19 (*S*)	2.3
70	41	67 (*R*)	98 (*S*)	199	21	24 (*R*)	93 (*S*)	21	87	75 (*R*)	11 (*S*)	2.3
100	46	81 (*R*)	97 (*S*)	164	26	33 (*R*)	92 (*S*)	33	95	99 (*R*)	5 (*S*)	2.3
160	51	98 (*R*)	95 (*S*)	179	39	58 (*R*)	90 (*S*)	34	98	99 (*R*)	2 (*S*)	2.6
220	52	99 (*R*)	93 (*S*)	144	44	70 (*R*)	88 (*S*)	32	>99	—	0	2.6
280	52	98 (*R*)	92 (*S*)	110	46	75 (*R*)	87 (*S*)	32	—	—	—	–
340	51	94 (*R*)	90 (*S*)	67	49	82 (*R*)	86 (*S*)	33	—	—	—	–
400	51	91 (*R*)	89 (*S*)	54	53	93 (*R*)	84 (*S*)	38	—	—	—	–
460	50	85 (*R*)	86 (*S*)	35	53	93 (*R*)	82 (*S*)	33	—	—	—	–
520	50	84 (*R*)	85 (*S*)	32	55	97 (*R*)	79 (*S*)	35	—	—	—	–

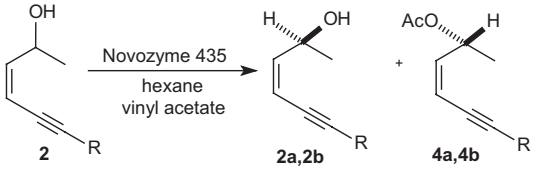
[a] The reaction was carried out at 32 °C using alcohols **1b**,**c** and **1d** (50 μL), vinyl acetate (100 μL), hexane (10 mL) and Novozyme 435 (100 mg); *t*: time (min); *c* (%): calculated from the ee's of the substrate (ee_s) and the product (ee_p): *c*: $ee_s/(ee_p + ee_s)$; ee (%) enantiomeric excess; *E*: enantiomeric ratio.

conditions, (*S*)-**1a** and (*R*)-**3a** were obtained in 36% yield (95% ee) and 35% yield (96% ee), respectively, after 24 h at 60 °C.[10] Resolution of **1b** under these conditions gave (*R*)-**1b** in 40% yield and 97% ee and (*S*)-**3b** in 45% yield and 67% ee after 14 h at 60 °C.[10]

By using our reaction conditions (Table 2), the same compounds (*R*)-**1b** and (*S*)-**3b** were obtained in 41% and 45% yield, respectively, both with 96% ee. Comparison of our results with the above mentioned study showed that the use of hexane as the solvent gave a better resolution in a shorter reaction time.

After determining the ideal reaction conditions, we decided to apply them to different alcohols. The results summarized in Table 2 indicate that compounds **1c** and **d** show moderate kinetic resolution under the standard conditions employed by us. This is expected in view of the size of the substituents, which are not large enough to ensure a good resolution.[5a,12] Methyl alcohol **1e** was not acetylated by the lipase CAL-B (results not shown). Allylic alcohols **2a** and **2b** were obtained by deprotection of the corresponding dimethyl *tert*-butylsilyl ether prepared by a method recently developed in our laboratory, which consists of the coupling of vinylic

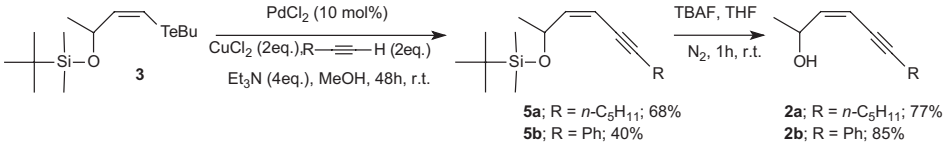
Table 3. Kinetic resolution of (*RS*)-allylic alcohols **2a** and **b** catalyzed by Novozyme 435[a]



R = *n*-C_5H_{11} (**2a**, **4a**); Ph (**2b**, **4b**)

t	*c*	Ee **2a**	Ee **4a**	*E*	*c*	Ee **2b**	Ee **4b**	*E*
20	37	57 (*S*)	99 (*R*)	354	32	46 (*S*)	96 (*R*)	77
40	37	57 (*S*)	99 (*R*)	354	43	85 (*S*)	63 (*R*)	11
70	42	73 (*S*)	95 (*R*)	85	45	83 (*S*)	68 (*R*)	13
100	42	73 (*S*)	95 (*R*)	85	52	86 (*S*)	79 (*R*)	23
160	50	99 (*S*)	95 (*R*)	205	46	94 (*S*)	79 (*R*)	29
220	51	99 (*S*)	94 (*R*)	170	56	95 (*S*)	77 (*R*)	27
280	51	99 (*S*)	92 (*R*)	125	—	—	—	
340	52	99 (*S*)	91 (*R*)	111	—	—	—	
400	52	99 (*S*)	92 (*R*)	125	—	—	—	
460	52	99 (*S*)	91 (*R*)	111	—	—	—	
520	53	99 (*S*)	87 (*R*)	74	—	—	—	

[a] The reaction was carried out at 32 °C using alcohols **2a** and **2b** (50 μL), vinyl acetate (100 μL), hexane (10 mL) and Novozyme 435 (100 mg); *t*: time (min); *c* (%): calculated from the ee's of the substrate (ee_s) and the product (ee_p): *c*: $ee_s/(ee_p + ee_s)$; ee (%) enantiomeric excess; *E*: enantiomeric ratio.



Scheme 1. Synthesis of allylic alcohols.

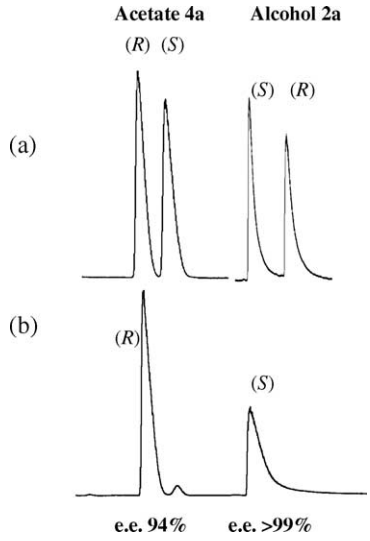


Figure 1. (a) Chromatograms of (±)-**2a** and (±)-**4a**. (b) Chromatogram of the kinetic resolution of alcohol (±)-**2a** by Novozyme 435 (220 min).

tellurides with alkynes under $PdCl_2$ catalysis (Scheme 1).[13] These compounds were submitted to a kinetic resolution with Novozyme 435 in hexane at 32 °C. The results are shown in Table 3. Compound **2a** was efficiently resolved by Novozyme 435 as illustrated in Figure 1.

3. Conclusion

In conclusion, propargylic alcohols and allylic enynes are efficiently resolved by Novozyme 435 in hexane following the Kazlauskas predictions concerning stereochemical demands in the enzymatic resolution of secondary alcohols.

4. Experimental

4.1. General

Chemical syntheses were monitored by TLC analyses on precoated silica gel foils (Aluminum foil, 60 F_{254} Merck). Spots were visualized by *p*-anisaldehyde/sulfuric acid or vanillin followed by heating at about 120 °C. The purification of the compounds was carried out by column chromatography using silica gel (230–400 or 230–80 mesh). Conversions and enantiomeric excesses of the enzyme-catalyzed reactions were determined using a Shimadzu GC-17A gas chromatograph equipped with a chiral capillary column Chirasil-Dex CB β-cyclodextrin (25 m × 0.25 mm). The carrier gas was hydrogen with a pressure of 100 kPa. GCMS analyses were performed in equipment Shimadzu (QP 5050A) equipped with capillary column DB-5 (JW Scientific 30 m × 0.25 mm × 0.25 μm) and the carrier gas was

helium. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DPX300 (^{1}H: 300 MHz; ^{13}C: 75 MHz) or AC-200 (^{1}H: 200 MHz; ^{13}C: 50 MHz) spectrometers using $CDCl_3$ as solvent. Near IR spectra were obtained on a Bomen MB-100 spectrometer. Optical rotation values were measured in a Jasco DIP-378 polarimeter and the reported data refer to the Na-line value using a 1 dm cuvette. Novozyme 435: Immobilized lipase from *Candida antartica* was obtained as a gift from Novo Nordisk (Paraná-Brazil). Vinyl acetate, 4-pentyn-3-ol **1d** and 3-butyn-2-ol **1e** were purchased from Aldrich Company.

4.2. Synthesis of the substrates

4.2.1. Propargylic alcohols. 1-Phenyl-prop-2-yn-1-ol **1a**, non-1-yn-3-ol **1b** and 4-methyl-pent-1-yn-3-ol **1c** were synthesized by literature procedures[14] and purified by horizontal distillation under reduced pressure.

4.2.2. Allylic alcohols 2a and b. To a 25 mL two-necked round-bottomed flask under nitrogen atmosphere was added the appropriate allylic dimethyl *tert*-butylsilyl ether (**5a** or **5b**, 3 mmol)[13] and tetrabutylammonium fluoride (1.0 mol L^{-1} solution in THF) (6 mL, 6 mmol). The reaction mixture was stirred for 1 h at room temperature. After that, the reaction was quenched by the addition of brine (50 mL) and extracted with ethyl acetate (3 × 50 mL). The combined organic phases were dried over magnesium sulfate and then filtered. The organic solvent was evaporated under reduced pressure and the residue purified by silica gel column chromatography using hexane/ethyl acetate (8:2) as eluent.

4.2.2.1. (*Z*)-Undec-3-en-5-yn-2-ol 2a. Yield 0.384 g (77%) after horizontal distillation under reduced pressure; 200 MHz ^{1}H NMR ($CDCl_3$) (ppm) 5.85 (dd, J = 11.0 Hz, 7.9 Hz, 1H), 5.48 (dtd, J = 10.8 Hz, 2.2 Hz, 0.9 Hz, 1H), 4.82 (dqd, J = 7.9 Hz, 6.6 Hz, 0.9 Hz, 1H), 2.33 (td, J = 7.0 Hz, 2.2 Hz, 2H), 2.11 (s_{broad}, 1H), 1.55 (quint, J = 7.0 Hz, 2H); 1.38–1.33 (m, 4H), 1.29 (d, J = 6.6 Hz, 3H), 0.91 (t, J = 7.0 Hz, 3H); 50 MHz ^{13}C NMR ($CDCl_3$) (ppm) 144.93, 109.66, 96.50, 76.25, 66.25, 31.02, 28.32, 22.45, 22.11, 19.42, 13.88. Near IR (film) (cm^{-1}) 3348, 3025, 2960, 2932, 2861, 2217, 1619, 1461, 1367, 1288, 1110, 1056, 755; LRMS *m*/*z* (relative intensity) 166 (M$^+$, 0.3%), 165 (1.0%), 151 (2.2%), 137 (2.2%), 123 (7.2%), 109 (67.3%), 95 (27.7%), 81 (44.4%), 67 (26.1%), 55 (17.8%), 43 (100.0%).

4.2.2.2. (*Z*)-6-Phenyl-hex-3-en-5-yn-2-ol 2b. Yield 0.440 g (85%); 200 MHz ^{1}H NMR ($CDCl_3$) (ppm) 7.46–7.39 (m, 2H), 7.35–7.30 (m, 3H), 5.99 (dd, J = 10.7 Hz, 8.1 Hz, 1H), 5.72 (dd, J = 11.0 Hz, 0.9 Hz, 1H), 4.94 (dqd, J = 8.1 Hz, 6.1 Hz, 0.9 Hz, 1H), 1.86 (s_{broad}, 1H), 1.35 (d, J = 6.1 Hz, 3H); 50 MHz ^{13}C NMR ($CDCl_3$) (ppm) 146.28, 131.43, 128.41, 128.35, 123.04, 109.17, 95.03, 85.00, 66.46, 22.57. Near IR (film) (cm^{-1}) 3357, 3059, 3026, 2972, 2927, 2198, 1680, 1599, 1490, 1061, 756, 691; LRMS *m*/*z* (relative intensity) 172 (M$^+$, 22.3%), 171 (36.6%), 157 (100.0%), 152 (12.4%), 128 (97.8%), 115 (33.4%), 102 (24.7%), 95 (13.6%), 77 (33.0%), 64 (23.8%), 51 (30.8%), 43 (86.7%).

4.2.3. Racemic propargylic and allylic acetates. (*RS*)-1-Phenyl-prop-2-yn-1-acetyloxy **3a**, (*RS*)-non-1-yn-3-acetyloxy **3b**, (*RS*)-4-methyl-pent-1-yn-3-acetyloxy **3c**, (*RS*)-4-pentyn-3-acetyloxy **3d**, (*RS*)-3-butyn-2-acetyloxy **3e**, (*RS*)-undec-3-en-5-yn-2-acetyloxy **4a** and (*RS*)-6-phenyl-hex-3-en-5-yn-2-acetyloxy **4b** were prepared by literature procedure,[15] by treating the appropriate alcohol with excess acetic anhydride in pyridine.

4.2.3.1. (*RS*)-Undec-3-en-5-yn-2-acetyloxy 4a. Yield 90 mg (72%); 300 MHz ^{1}H NMR ($CDCl_3$) (ppm) 5.84–5.70 (m, 2H), 5.53 (dt, J = 10.1 Hz, 2.2 Hz, 1H), 2.33 (td, J = 7.0 Hz, 2.2 Hz, 2H), 2.04 (s, 3H), 1.55 (quint, J = 7.0 Hz, 2H), 1.45–1.28 (m, 4H), 1.34 (d, J = 6.1 Hz, 3H), 0.91 (t, J = 7.0 Hz, 3H); 75 MHz ^{13}C NMR ($CDCl_3$) (ppm) 140.42, 111.27, 97.44, 75.98, 69.47, 31.10, 29.72, 28.36, 22.19, 21.28, 20.03, 19.56, 13.97; near IR (film) (cm^{-1}) 2960, 2930, 2863, 2215, 1743, 1460, 1372, 1240; LRMS *m*/*z* (relative intensity) 208 (M$^+$, 2.3%), 193 (1.4%), 179 (0.4%), 165 (13.9%), 151 (8.7%), 137 (4.3%), 123 (6.4%), 109 (14.6%), 95 (30.0%), 91 (21.5%), 81 (10.9%), 67 (9.0%), 43 (100.0%).

4.2.3.2. (*R*,*S*)-6-Phenyl-hex-3-en-5-yn-2-acetyloxy 4b. Yield 92 mg (74%); 300 MHz ^{1}H NMR ($CDCl_3$) (ppm) 7.79–7.42 (m, 2H), 7.38–7.30 (m, 3H), 5.99–5.82 (m, 2H) 5.78 (d, J = 10.1 Hz, 1H), 2.05 (s, 3H), 1.40 (d, J = 6.6 Hz, 3H); 75 MHz ^{13}C NMR ($CDCl_3$) (ppm) 170.11, 141.70, 131.55, 128.42, 128.29, 123.03, 110.77, 95.82, 84.72, 69.21, 21.18, 20,00; near IR (film) (cm^{-1}) 3059, 3030, 2959, 2929, 2855, 2199, 1739, 1446, 1371, 1240, 757, 692; LRMS *m*/*z* (relative intensity) 214 (M$^+$, 5.6%), 199 (5.8%), 185 (0.3%), 171 (34.0%), 157 (90.4%), 153 (18.1%), 128 (13.3%), 115 (6.8%), 102 (4.1%), 89 (1.8%), 77 (14.0%), 63 (5.4%), 43 (100.0%).

4.3. Preparative-scale enzymatic reaction

To a 50 mL Erlenmeyer flask containing 10 mL of hexane (HPLC grade), 1 mL of vinyl acetate and 300 mg Novozyme was added the appropriate alcohol [**1a**–**c** (500 μL), **2a**, **b** (100 μL)]. The reaction mixture was stirred on a rotary shaker (32 °C, 170 rpm) until appropriate consumption of the starting material. After that, the mixture was filtered and the solvent evaporated. The residue was purified by silica gel column chromatography using hexane/ethyl acetate (9:1) as eluent.

4.4. Small scale enzymatic reactions[16]

To a 50 mL Erlenmeyer flask containing 10 mL of hexane (HPLC grade), 50–100 μL of vinyl acetate and 100 mg of Novozyme were added 50 μL of the appropriate alcohol (**1a**–**e** and **2a**,**b**). The reaction mixture was stirred on a rotary shaker (32 °C, 170 rpm) until appropriate consumption of the starting material. Alternatively, the reactions were performed using 50 μL of

propargylic alcohol **1**, 20 mL of hexane, 50 μL of vinyl acetate and 32 mg (1000 PLU) of Novozyme.

4.5. Control of the enzymatic resolution of propargylic and allylic alcohols by Novozyme 435

The reaction progress was monitored (Tables 1–3) by collecting 0.1 mL samples from time to time. These samples were analyzed by GC/FID (1 μL) in a chiral capillary column. The products of the biocatalyzed reactions were compared with the racemic mixtures previously analyzed. General GC conditions: injector 200 °C; detector 220 °C.

4.5.1. (*RS*)-1-Phenyl-prop-2-yn-1-ol 1a and (*RS*)-1-phenyl-prop-2-yn-1-acetyloxy 3a. Oven 100 °C; rate 0 °C (30 min); retention time for **1a** (R = 23.5 min; S = 24.1 min); **3a** (S = 12.1 min; R = 15.8 min).

4.5.2. (*RS*)-Non-1-yn-3-ol (1b) and (*RS*)-non-1-yn-3-acetyloxy 3b. Oven 100 °C; rate 0 °C (15 min); retention time for **1b** (S = 11.1 min; R = 11.9 min); **3b** (R = 8.1 min; S = 9.7 min).

4.5.3. (*RS*)-4-Methyl-pent-1-yn-3-ol 1c and (*RS*)-4-methyl-pent-1-yn-3-acetyloxy 3c. Oven 70 °C; rate 0 °C (10 min); retention time for **1c** (S = 7.4 min; R = 8.0 min); **3c** (R = 5.2 min; S = 6.9 min).

4.5.4. (*RS*)-Undec-3-en-5-yn-2-ol 2a and (*RS*)-undec-3-en-5-yn-2-acetyloxy 4a. Oven 90 °C; rate 0 °C (70 min); retention time for **2a** (R = 51.4 min; S = 59.9 min); **4a** (S = 44.6 min; R = 46.1 min).

4.5.5. (*RS*)-6-Phenyl-hex-3-en-5-yn-2-ol 2b and (*RS*)-6-phenyl-hex-3-en-5-yn-2-acetyloxy 4b. Oven 100 °C; rate 1 °C/70 min; retention time for **2b** (R = 33.8 min; S = 36.4 min); **4b** (S = 29.5 min; R = 30.1 min).

4.6. Assignment of the absolute configuration

The absolute configurations were determinated by comparison of the sign of the measured optical rotation with those of the literature.

4.6.1. (*S*)-(+)-1-Phenyl-prop-2-yn-1-ol 1a. $[\alpha]_D^{25} = +16.3$ (c 4.34, $CHCl_3$), ee 99%; {Lit. $[\alpha]_D^{25} = +20.0$ (c 1.13, $CHCl_3$), ee 72%}.[6b]

4.6.2. (*R*)-(+)-1-Phenyl-prop-2-yn-1-acetyloxy 3a. $[\alpha]_D^{25} = +4.4$ (c 4.33, $CHCl_3$), ee 98%; {Lit. $[\alpha]_D^{25} = +3.4$ (c 1.07, $CHCl_3$), ee 85%}.[6b]

4.6.3. (*R*)-(+)-Non-1-yn-3-ol 1b. $[\alpha]_D^{25} = +9.15$ (c 4.59, $CHCl_3$), ee 96%.

4.6.4. (*S*)-(−)-Non-1-yn-3-acetyloxy 3b. $[\alpha]_D^{25} = -48.6$ (c 4.01, $CHCl_3$), ee 96%.

4.6.5. (*R*)-(+)-4-Methyl-pent-1-yn-3-ol 1c. $[\alpha]_D^{25} = +17.2$ (c 46.4, $CHCl_3$); {Lit. $[\alpha]_D^{25} = +13.8$ (c 2.00, dioxane), ee 86%}.[7c]

4.6.6. (*S*)-(−)-4-Methyl-pent-1-yn-3-acetyloxy 3c. $[\alpha]_D^{25} = -80.8$ (c 6.88, $CHCl_3$).

The absolute configuration of (*S*)-**2a** was attributed after its hydrogenation using Pd/C to give (*S*)-(+)-undecan-2-ol.[7e] The last compound was prepared by kinetic resolution of (±)-undecan-2-ol using Novozyme 435.

4.6.7. (*S*)-(−)-Undec-3-en-5-yn-2-ol 2a. $[\alpha]_D^{25} = -35.2$ (c 0.54, $CHCl_3$), ee 99%.

4.6.8. (*R*)-(+)-Undec-3-en-5-yn-2-acetyloxy 4a. $[\alpha]_D^{25} = -55.7$ (c 1.31, $CHCl_3$), ee 94%.

4.6.9. (*S*)-(+)-Undecan-2-ol. $[\alpha]_D^{25} = +5.5$ (c 2.01, EtOH); {Lit. $[\alpha]_D^{25} = +7.44$ (c 1.27, EtOH)}.[12]

4.6.10. (*S*)-(+)-6-Phenyl-hex-3-en-5-yn-2-ol 2b. $[\alpha]_D^{25} = +46.9$ (c 3.37, $CHCl_3$), ee 80%.

4.6.11. (*R*)-(−)-6-Phenyl-hex-3-en-5-yn-2-acetyloxy 4b. $[\alpha]_D^{25} = -116.6$ (c 3.32, $CHCl_3$), ee 70%.

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