Lipase-mediated deracemization of secondary 1-phenyl-substituted propargylic alcohols of different topology

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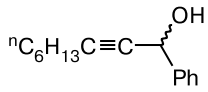
Acetylation of (±)-1-phenylnon-2-yn-1-ol, (±)-1-phenylhept-1-yn-3-ol, and (±)-1-phenylundec-4-yn-3-ol ((±)-**5**) in the presence of lipase from *Candida cylindracea* (CCL) proceeds slowly to give products with *ee* ≤20%. The acetates of these alcohols are hydrolyzed in the presence of porcine pancreatic lipase (PPL) equally unsatisfactorily. The (η^6-arene)tricarbonylchromium complex of alcohol (±)-**5** is acetylated in the presence of CCL up to ~22% conversion to give (*R*)-acetate whose oxidative decomplexation followed by saponification results in alcohol (*R*)-(−)-**5** with *ee* ≥95%. The configuration of alcohols (−)-**5** and (+)-**5** was determined by NMR spectroscopy of their esters with (*R*)- and (*S*)-Mosher´s acids.

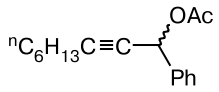
Key words: 1-phenyl-substituted secondary propargyl alcohols and acetates, topology; the efficiency of enzymatic deracemization; hapto-complexation of arenes, (η^6-arene)tricarbonylchromium complexes, increase in the enantioselectivity; lipases.

Secondary propargylic alcohols (SPA) with high enantiomeric purity are valuable chiral building blocks (CBB) for the synthesis of allenes,[1] lactones,[2] and heterocycles[3] often encountered among natural and biologically active compounds. These CBB are prepared by resolution of racemic SPA into antipodes *via* diastereomeric derivatives,[2a,b,3a] by reduction of α,β-acetylenic ketones with chiral metal hydrides[2c—h,4] or microbial oxidoreductases,[5] by various reactions of metallated acetylene derivatives in the presence of homochiral catalysts,[6] and by fragmentation of homochiral β-chloroepoxides.[7] At present, the resolution of racemic SPA is more and more often accomplished by enzymatic kinetic resolution (EKR) catalyzed by porcine pancreatic lipase (PPL),[2i,8] microbial lipases,[9—12] and the *Bacillus subtilis* culture.[13] Of these, PPL and lipase from the yeast *Candida cylindracea* (CCL) are most available.[9]

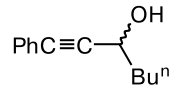
Deracemization of (±)-SPA by means of PPL and CCL sometimes gives products with high *ee* but the rate of this process is lower than that in the case of similar allylic alcohols or secondary alkanols.[9,10] In the present work, we studied the dependence of the rate and stereoselectivity of PPL- and CCL-catalyzed EKR of racemic SPA on their topology and describes an attempt to increase the enantioselectivity of EKR of phenyl-substituted SPA following their conversion into (η^6-arene)tricarbonylchromium complexes. This approach proved to be successful in the case of (±)-3-(4-methoxycarbonyl)phenyl-2-methylpropanol and its acetate,[14,15] but failed to provide deracemization of (±)-1-phenylethanol[16] and its acetate.[15] The dependence of the efficiency of EKR on the distance between the η^6-coordination site (Ph) and the reaction center (HCOH) was estimated by acetylating three different racemic SPA of the general formula as Ph—$(CH_2)_i$(C≡C)$_j$—CHOH—(C≡C)$_k$—Alk, where $i = j = 0$, $k = 1$ (**1**), or $i = k = 0$, $j = 1$ (**3**), or $i = 2$, $j = 0$, $k = 1$ (**5**), in the presence of lipases.



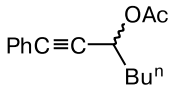
(±)-**1**



(±)-**2**



(±)-**3**



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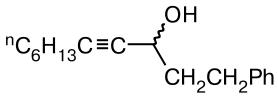
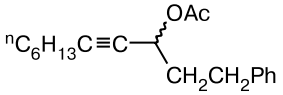


(±)-**5**



(±)-**6**

An alternative version of EKR, *viz.*, hydrolysis of the corresponding acetates, (±)-**2**, (±)-**4**, and (±)-**6** in the presence of PPL, was also studied.

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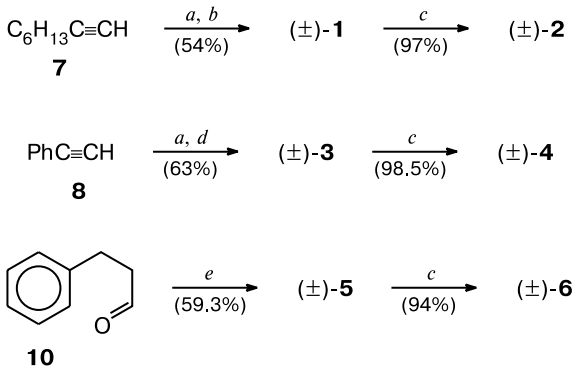
Alcohols (±)-**1** and (±)-**5** were prepared by the Jocić reaction from oct-1-yne (**7**) and benzaldehyde or hydrocinnamaldehyde (**10**), respectively. Similarly, alcohol (±)-**3** was prepared from phenylacetylene (**8**) and pentanal (**9**). The resulting alcohols were converted into acetates (±)-**2**, (±)-**4**, and (±)-**6** by a standard procedure (Scheme 1).

Scheme 1



Reagents and conditions: *a*. EtMgBr, Et_2O, 20→35 °C; *b*. PhCHO, 20→35 °C; *c*. Ac_2O—DMAP (cat.), Py, ~20 °C; *d*. $Me(CH_2)_3CHO$ (**9**), 20→35 °C; *e*. $C_6H_{13}C{\equiv}CMgBr$, Et_2O, 20→35 °C.

Results and Discussion

Enzymatic deracemization of propargylic alcohols. Acetylation of alcohols (±)-**1**, (±)-**3**, and (±)-**5** with vinyl acetate was carried out in Et_2O in the presence of PPL, CCL, and lipase from *Rhizopus* sp. (RSL). No reaction of alcohols (±)-**1** and (±)-**3** occurred in 2—5 days. Alcohol (±)-**5** did not react in the presence of RSL and exhibited low reactivity in the presence of PPL. Only in the case of CCL, did the transformation of (±)-**5** proceed rather rapidly and after 6 days the degree of conversion reached ~58% (Table 1). The fraction of the unreacted alcohol had $[\alpha]_D^{22}$ +5.3 ($CHCl_3$). This sample, (+)-**5A**, was converted according to Mosher—Lightner[17,18] into an ester of (*S*)-Mosher´s acid (α-methoxy-α-trifluoromethylphenylacetic acid) ((*S*)-MTPA-ester **I**). Judging by the diastereomer ratio (*dr*) in (*S*)-MTPA-ester **I**, the *ee* value for alcohol (+)-**5A** was ~20%.

Table 1. Efficiency of deracemization of propargylic substrates in the case of partial acetylation of alcohols[a]

Entry	Substrate	Lipase	τ/h	Degree of conversion	Yield of the acetate[b] (%)	Recovery of the alcohol[b]
1	(±)-**1**	PPL	60	~0	~0	98
2	(±)-**1**	CCL	48	~0	~0	97
3	(±)-**1**	RSL	120	0	0	100
4	(±)-**3**	CCL	84	~0	~0	100
5	(±)-**3**	RSL	120	0	0	100
6[c]	(±)-**5**	PPL	72	~5—6	5	93
7	(±)-**5**	CCL	144	58—60	58	41[d]
8	(±)-**5**	RSL	120	0	~0	~100

[a] In the vinyl acetate—Et_2O system at 20—22 °C; substrate : lipase = 1 : 1 (w/w).
[b] The yield of the chromatographically pure product.
[c] The alcohol (±)-**5** to PPL ratio is 1 : 2.
[d] $[\alpha]_D$ +5.3 ($CHCl_3$).

The PPL-mediated hydrolysis of acetates (±)-**2**, (±)-**4**, and (±)-**6** proceeds even more slowly (Table 2). A degree of conversion of acetates (±)-**4** and (±)-**6** satisfactory for preparative purposes was attained over 15 and 7 days, respectively.

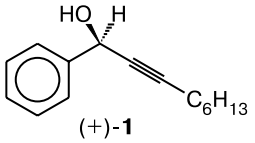
As appears from the amplitudes of $[\alpha]_D$, alcohols (+)-**1**, (−)-**3**, and sample (+)-**5B** with $[\alpha]_D$ +3.8 ($CHCl_3$) had low *ee*. In the (*S*)-MTPA-ester **I´** obtained from alcohol (+)-**5B**, the *dr* value corresponded to the *ee* of ~15%. For alcohol (+)-**1** isolated after hydrolysis of acetate

Table 2. Efficiency of deracemization of propargylic substrates in the enzymatic hydrolysis of acetates[a] by the PPL

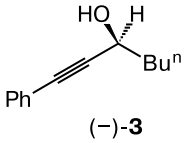
Entry	Substrate	τ/h	Degree of conversion (%)	Resulting alcohol		Recovery of the acetate[b] (%)
				Yield[b] (%)	$[\alpha]_D$ ($CHCl_3$)[c]	
1	(±)-**2**	168	16	(+)-**1**, 15	+6.8	84
2	(±)-**4**	360	35	(−)-**3**, 35	−0.77	64
3	(±)-**6**	72	11	(+)-**5**, 11[d]	+4.3	88
4	(±)-**6**	168	~46	(+)-**5B**, 45	+3.8	54

[a] In the phosphate buffer (pH 6.5, 20—22 °C), substrate : PPL = 1 : 2 (w/w).
[b] The yield of the chromatographically pure product.
[c] The polarimetric concentrations were 0.3—1.0.
[d] *ee* < 20%.

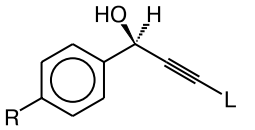
(±)-**2**, the sign of $[\alpha]_D$ coincides with the signs of $[\alpha]_D$ of enantiomers with known real configurations in the ArCH(OH)C≡CR chemotype.[6a,12] Taking into account the IUPAC seniority rules for substituents (MeC≡C > > Ph > HC≡C),[19] this attests to the (*S*)-configuration of alcohol (+)-**1**. Alcohol (−)-**3** isolated upon hydrolysis of acetate (±)-**4** is homologous to (*S*)-(−)-4-phenylbut-3-yn-2-ol[6a,11a] and (*S*)-(−)-1-pent-1-yn-3-ol.[6a] Apparently, it also has the *S*-configuration but the *ee* value for the sample in question is close to zero.



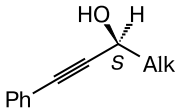
(+)-**1**



(−)-**3**



S (L = H) or *R* (L = Alk, Ar, SiR_3)



Lit. data:[6a] R = H, L = Ph, $[\alpha]_D$ +2.26, *ee* 43%; L = $SiMe_3$, $[\alpha]_D$ +10.3, *ee* 21%
Lit. data:[12] L = H, R = H, $[\alpha]_D$ +20, *ee* 72%; R = OMe, $[\alpha]_D$ +5.3, *ee* 10%; R = CN, $[\alpha]_D$ +21.1, *ee* 96%

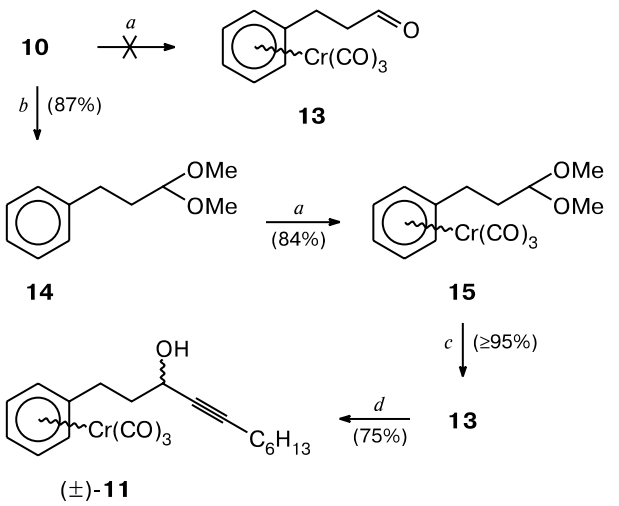
Lit. data:[6a,11a] Alk = Me, $[\alpha]_D$ −50.6, *ee* 95% or $[\alpha]_D$ −8.39, *ee* 40%
Alk = Et, $[\alpha]_D$ −13.7 (Et_2O), *ee* 70%

The low rates and low enantioselectivities of the EKR of alcohols (±)-**1**, (±)-**3**, and (±)-**5** and their acetates (±)-**2**, (±)-**4**, and (±)-**6** in the presence of PPL, CCL, and RSL makes this route to these propargyl CBB ineffective. It is notable that the vicinity of the reaction site, CHOR (R = H, Ac), and the conformationally rigid Ph or PhC≡C groups in substrates (±)-**1**, (±)-**3** and (±)-**2**, (±)-**4** has an adverse influence on the rates of their EKR. Meanwhile, substrates (±)-**5** and (±)-**6** in which one end of the C≡C—CH(OR) triad is linked to a conformationally flexible group react relatively fast.

(η⁶-Arene)tricarbonylchromium complexes of substrates (±)-5 and (±)-6 and their enzymatic kinetic resolution. Due to the low rate of PPL-mediated hydrolysis of acetates (±)-**2** and (±)-**4** (see Table 2) and the previously noted[14–16] decrease in the rate of enzymatic hydrolysis and acylation of other aliphatic-aromatic substrates upon transformation into (η⁶-arene)tricarbonylchromium complexes, we studied the effect of η⁶-complexation on the enantioselectivity of the EKR only for alcohol **5** and acetate **6**. Attempted transformation of compounds (±)-**5** and (±)-**6** into the corresponding η⁶-complexes (±)-**11** and (±)-**12** by heating the substrates with $Cr(CO)_6$ according to Pauson[20] failed. Viscous polymers were formed instead of η⁶-complexes.

An attempt to prepare [η⁶-(3-oxopropyl)benzene]tricarbonylchromium (**13**), an intermediate in the Jocić synthesis of alcohol (±)-**11**, by direct heating of aldehyde **10** with $Cr(CO)_6$ was also unsuccessful. Aldehyde **13** and alcohol (±)-**11** were synthesized in an alternative route (Scheme 2). Dimethyl acetal **14** prepared from aldehyde **10** smoothly reacted with $Cr(CO)_6$ to give crystalline η⁶-arene complex (**15**), whose mild hydrolysis afforded oxo complex **13**. The Jocić reaction of this product gave the target alcohol (±)-**11** in an overall yield of 52%.

Scheme 2



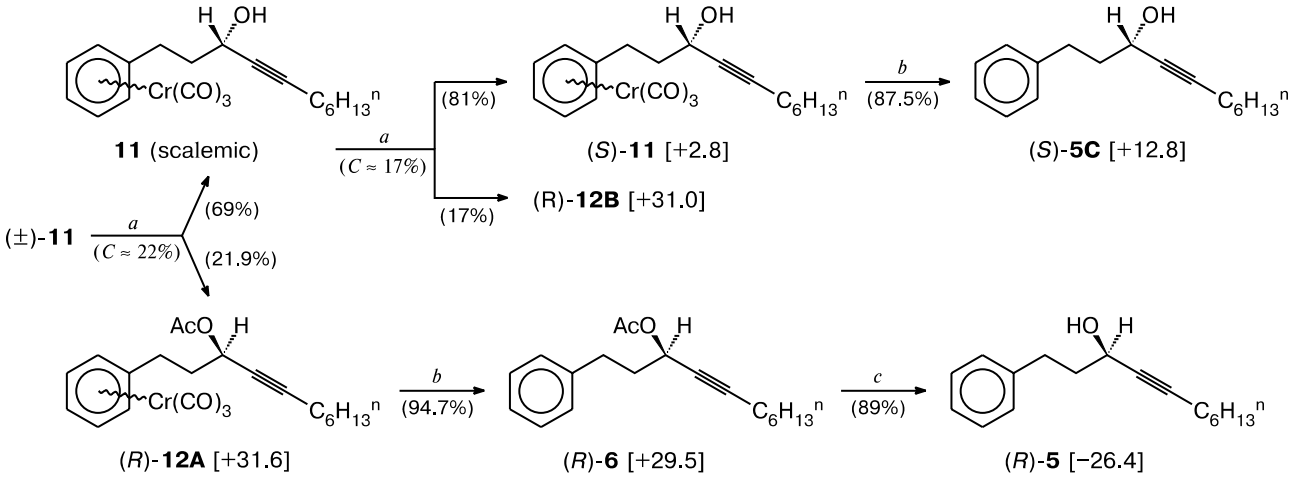
(±)-**11**

Regents and conditions: *a*. $Cr(CO)_6$, $(Bu^n)_2O$—THF (5 : 1), ~140 °C, Ar; *b*. MeOH—TsOH (cat.), 20—22 °C; *c*. Me_2CO—H_2O (4 : 1, v/v), $H_2C_2O_4$ (cat.), refluxing; *d*. *n*-$C_6H_{13}C{\equiv}CMgBr$, Et_2O, 20→35 °C.

The CCL-catalyzed asymmetrization of alcohol (±)-**11** by acylation with vinyl acetate in Et_2O (~20 °C, Ar) proceeded very slowly (the conversion $C \approx 22\%$ was attained in ~21 days) but it was much more enantioselective than the analogous EKR of alcohol (±)-**5**. The isolated acetate (+)-**12** (sample **A**) with $[\alpha]_D$ +31.6 ($CHCl_3$) was subjected to oxidative decomplexation by treatment with iodine to give acetate (+)-**6** with $[\alpha]_D$ +29.5 ($CHCl_3$), which was further saponified to alcohol (−)-**5** with $[\alpha]_D$ −26.4 ($CHCl_3$). In the (*R*)-MTPA-ester **II** obtained from this alcohol, the diastereomer ratio was 97.5 : 2.5 ($dr \geq 95$, ^1H and ^{19}F NMR data). Hence, in the sample of alcohol (−)-**5**, the *ee* value was ≥95% (Scheme 3).

The repeated acetylation of the "residual alcohol" **11** under the same conditions to a degree of conversion of 17% gave an additional amount of acetate (+)-**12** (sample **B**) with $[\alpha]_D$ +31.0 ($CHCl_3$). Alcohol **11** remaining after the second EKR (sample **11B**) had $[\alpha]_D$ +2.8 ($CHCl_3$). The oxidative decomplexation of alcohol **11B**

Scheme 3



Note. The values in parentheses are $[\alpha]_D$ for solutions in $CHCl_3$.

Reagents and conditions: *a*. H_2C=CHOAc—CCL, Et_2O, ~20 °C; *b*. I_2, THF, 20 °C; *c*. KOH—MeOH, 20 °C.

with iodine resulted in a sample of alcohol (+)-**5** with $[\alpha]_D$ +12.8 ($CHCl_3$). This alcohol (sample (+)-**5C**) was converted into (*S*)-MTPA and (*R*)-MTPA esters ((*S*)-MTPA **I″** and (*R*)-MTPA **III**, respectively) with nearly equal *dr* values (76:24 and 77:23), which implies that in the sample (+)-**5C**, *ee* ~52%.*

Acetylation of alcohols (±)-**5** and (±)-**11** in the presence of CCL (see Table 1 and Scheme 3) has shown that alcohol (−)-**5** and its η^6-complex (−)-**11** react more rapidly. Thus, the transformation of the starting SPA (±)-**5** into η^6-complex (±)-**11** does not change the sense of enantioselectivity of the EKR, whereas the coordination of $Cr(CO)_3$ to a primary aliphatic-aromatic alcohol[15] has resulted in its reversal.

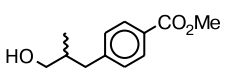
Acetate (±)-**12** was hydrolyzed in the presence of PPL in a phosphate buffer (pH 7) up to a ~75% conversion, which took 30 days. The isolated alcohol fraction had $[\alpha]_D$ −0.5 ($CHCl_3$). The residual acetate, *i.e.*, TLC-pure complex (−)-**12**, was subjected to oxidative decomplexation to give acetate (+)-**6** with $[\alpha]_D$ +4.3, which corresponds to *ee* ~16%. This *ee* value for *C* = 75% implies a very low enantioselectivity of the hydrolysis of η^6-complex (±)-**12** in the presence of PPL.

Absolute configuration of alcohols (+)-5 and (−)-5. The configuration of these alcohols was determined on the basis of regular features known for the ^{1}H [17,21,22] and ^{19}F NMR [21,23] spectra of their esters with (*S*)- or (*R*)-Mosher´s acid. The δ_H and δ_F values for the signals of each component in the spectra of MTPA esters, which depend on the configuration of Mosher´s acid, the *dr* values, and the corresponding *ee* values are summarized in Table 3.

In the ^{1}H NMR spectra of the (*S*)-MTPA esters of alcohol (+)-**5**, the signal for the H atom at C(1) in the major diastereomer occurs in a higher field, while the signals for the H atoms at C(6) are in a lower field with respect to the corresponding signals of the minor diastereomer; the MeO group is less shielded in the major diastereomer than in the minor component. In the ^{19}F NMR spectrum, the signal for the CF_3 group of the major diastereomer is located in the lower field than that for the minor diastereomer. These data altogether correspond to the arrangement of the $PhCH_2CH_2$ and n-$C_5H_{11}CH_2C{\equiv}C$ groups in the eclipsed conformation of the MTPA ester (Fig. 1) in which the C(1) unit is shielded by the Ph group of the acyl fragment, the C(6) unit lies outside the shielding area, the CF_3 group is coplanar with the neighboring C=O group, and the CH_3O group is not shielded by the Ph group at C(1). Since according to the IUPAC rules,[19] the n-$C_5H_{11}CH_2C{\equiv}C$ group is senior to the $PhCH_2CH_2$ group and, in addition, it has a greater calculated van der Waals volume,[24] the (*S*)-MTPA ester **I** was identified as having the 3*S*,2´*S*-configuration and alcohol (+)-**5**, as having the *S*-configuration.

The ^{1}H and ^{19}F NMR spectra of the (*R*)-MTPA ester **II** obtained from alcohol (−)-**5** contained virtually the

* It is notable that the η^6-arene complex (±)-**11** is acetylated in the presence of CCL with somewhat higher enantioselectivity than its precursor, secondary alcohol (±)-**5**, whereas similar acetylation of η^6-complex of the primary alcohol (±)-**16** in the presence of CCL proceeds with lower enantioselectivity than acetylation of its precursor, primary alcohol (±)-4-[$HOCH_2CH(Me)CH_2$]$C_6H_4CO_2Me$.[15]



(±)-**16**

Table 3. Diagnostic δ_H and δ_F signals in the spectra of binary esters formed by alcohol (+)-**5** and (*S*)-Mosher´s acid chloride ((*S*)-MTPA **I**, **I´**, **I″**) and binary esters formed by alcohols (−)-**5** and (+)-**5** and (*R*)-Mosher´s acid chloride ((*R*)-MTPA **II** and (*R*)-MTPA **III**)

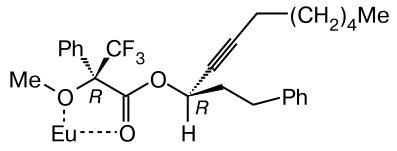
Starting alcohol	$[\alpha]_D^{20}$ [a]	MTPA ester (configuration)[b]	δ_H[c]			δ_F[d]	The *ee* value in the starting alcohol (%)[e]
			C(1)H_2	C(6)H_2	C(2´)OMe (s)		
(+)-**5A**	+5.3[f]	(*S*)-MTPA **I** (3*S*, 2´*S*)	2.66 (m) 2.70 (m)	2.10 (br.m) 2.07 (m)	3.62 ≥ 3.58	−71.20 −71.52 (60 : 40)	~20
(+)-**5B**	+3.8	(*S*)-MTPA **I´** (3*S*, 2´*S*)		Not determined		−71.19 −71.52 (57.5 : 42.5)	~15
(+)-**5C**	+12.8	(*S*)-MTPA **I´´** (3*S*, 2´*S*)	2.66 (m) 2.70 (m)	2.10 (br.m) 2.07 (m)	3.62 (~2.3 H) 3.58 (~0.7 H)	−71.20 −71.51 (76 : 24)	~52 (~54)
(+)-**5C**	+12.8	(*R*)-MTPA **III** (3*S*,2´*R*)	2.70 (br.m) 2.67 (m)	2.07 (br.m) 2.10 (m)	3.58 (~2.3 H) 3.63 (~0.7 H)	−71.48 −71.18 (76 : 24)	52 (~54)
(−)-**5**	−26.4	(*R*)-MTPA **II** (3*R*, 2´*R*)	2.67 (br.m) ~2.70 (m)[g]	2.10 (br.m) 2.08 (m)[g]	3.63 (~2.9 H) 3.59 (~0.1 H)	−71.16 −71.50 (97.5 : 2.5)	~95 (~94)

Note. $CDCl_3$ as the solvent; temperature for recording the spectra, 274 K.
[a] The specific rotations were determination for solutions in $CDCl_3$ (*c* 0.3—1.0).
[b] Configuration of the major diastereomer.
[c] The signals from the predominant component are underlined.
[d] The values in parentheses are the intensity ratios for the CF_3 peaks.
[e] The values in parentheses are the *ee* values calculated from the ratio of the integral intensities of the signals from the methoxy groups. The values in parentheses are the multiplicity and the integral intensity; the signals from the major component are underlined.
[f] $[\alpha]_D^{22}$.
[g] The signals from the minor MTPA ester barely differ from the base line noise in the spectrum.

same signals as those of the (*S*)-MTPA esters **I** and **I″** (see Table 3 and Fig. 1); the difference was only in *dr* values. This means that the (*R*)-MTPA ester **II** is the antipode to the major diastereomer in the (*S*)-MTPA esters **I** and **I″**. Hence, the (*R*)-MTPA ester **II** has the 3*R*,2´*R*-configuration and alcohol (−)-**5**, *R*-configuration.

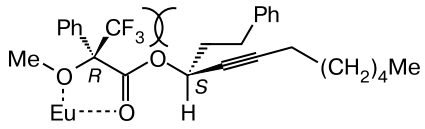
This is confirmed by the ^{19}F NMR spectra of MTPA esters. The signal of the CF_3 group of the major component in the spectrum of (*R*)-MTPA ester **III** occurs in the higher field than the signals of the CF_3 groups of the major components of (*S*)-MTPA ester **I** or (*R*)-MTPA ester **II**. This is typical of the ^{19}F NMR spectra of MTPA esters with different absolute configurations of the alcohol and the acyl moieties,[21,23] and in the case of (*R*)-MTPA ester **III**, it confirms the *S*-configuration of the alcoholic fragment.

The same conclusion can be drawn from determination of the configurations of alcohols (+)-**5** and (−)-**5** from the Eu(fod)$_3$-induced shifts of the signals for the MeO group in the ^1H NMR specrta.[21,25] In the ^1H NMR spectra of (*R*)-MTPA ester **II** recorded in the presence of 0.25—0.5 equiv. of Eu(fod)$_3$, the downfield shifts of the singlet for the MeO group in the major diastereomer ($\Delta\delta$) are greater than those of the corresponding signal in the minor diastereomer by 0.08 and 0.5 ppm, respectively. The chelate formed by the Eu ion with the predominant component of the (*R*)-MTPA ester **II** is sterically less hindered (more stable) than the chelate formed by the minor component, and, hence, the OMe group is deshielded more appreciably in the former case.



(*R*)-MTPA **II**

$\Delta\delta_H^{OMe} = 1.72$



(*R*)-MTPA **III**

$\Delta\delta_H^{OMe} = 1.22$

The lipases CCL, PPL, and RSL proved ineffective for the production of CBB from SPA of types (±)-**1** and

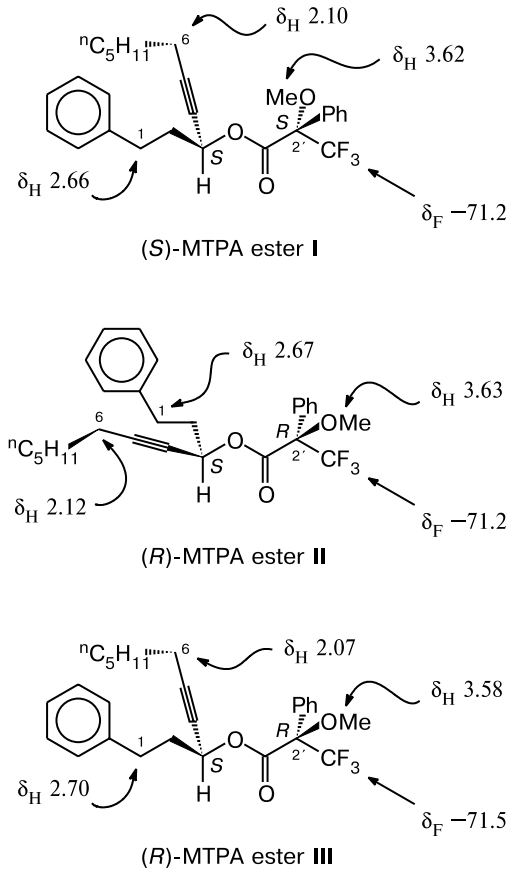


Fig. 1. Diagnostic signals δ_H and δ_F of the major isomers of MTPA esters. The "mirror" configurations of the major diastereomers in binary MTPA esters, (*S*)-MTPA **I** and (*R*)-MTPA **II**, are manifested in the coinciding δ_H and δ_F values for the diagnostic signals in their NMR spectra (see Table 3).

(±)-**3** in which the reaction center (CHOH, CHOAc) adjoins bulky, conformationally rigid Ph or PhC≡C groups. An increase in the distance between the Ph and CHOH groups in alcohol (±)-**5** and the higher conformational flexibility of its molecule enhance only slightly the efficiency of the EKR. A multiple increase in the enantioselectivity of the enzymatic deracemization of the secondary aliphatic-aromatic alcohol was attained for the first time by performing the reaction for the corresponding (η^6-arene)tricarbonylchromium complex;* moreover, no reversal of the process enantioselectivity, noted previously[14—16] for the primary alcohol, occurred in this case. Unfortunately, due to the difficulty of direct transformation of propargylic substrates like (±)-**5** into complexes (±)-**11** and low rates of the EKR of these complexes, this route is not attractive from the preparative standpoint.

* Before publication of the studies of our research group,[14,15] all examples of lipase-mediated deracemization of (η^6-arene)tricarbonylchromium complexes of aliphatic-aromatic alcohols referred to objects with a planar asymmetry, which arises upon hapto-complexation of *ortho*- or *meta*-disubstituted arenes with $Cr(CO)_3$.[26] Even in the case of η^6-arene complex formed by (±)-**1**-(2-methoxyphenyl)ethanol (a mixture of four diastereomers),[26c] the high selectivity of its EKR was due to the planar asymmetry rather than to the presence of the asymmetric center in the side chain.

Experimental

All boiling and melting points were not corrected. The ^1H and ^{13}C NMR spectra were recorded on a Bruker AM-300 instrument, and ^{19}F NMR spectra were run on a Bruker AC-200 spectrometer (with $FCCl_3$ as the standard) in $CDCl_3$ at 20±5 °C. IR spectra were measured for solutions in $CHCl_3$ (unless stated otherwise) on a Specord IR-80 instrument at 20—22 °C. The $[\alpha]_D$ values were determined on a JASCO-DIP 360 polarimeter for solutions in $CHCl_3$. The completeness of the reactions and the product purity were estimated by TLC on Silufol UV 254 plates, the spots being visualized by I_2 vapor and/or a solution of $KMnO_4$. Column chromatography was carried out on a neutral silica gel (Fluka, 0.04—0.06 mm). Powders of the PPL (Serva, 14 U mg^{-1}), CCL (Fluka, 2.3 U mg^{-1}), and RSL (Serva) were stored at −16±2 °C and, prior to use, they were maintained at a constant temperature in a vacuum block. (*S*)- and (*R*)-α-Methoxy-α-trifluoromethylphenylacetyl chlorides (MTPA-Cl) were prepared from (*R*)- and (*S*)-Mosher´s acid (Fluka) without special purification. Liquid reagents and solvents (including H_2O) were distilled prior to use and purified by the procedures recommended in the handbook.[27]

(±)-1-Phenylnon-2-yn-1-ol ((±)-1). A solution of EtBr (8 mL, 11.4 g, 0.105 mol) in 30 mL of anhydrous Et_2O was added with stirring under argon to magnesium chips (2.42 g, 0.101 mol). Then a solution of oct-1-yne (**7**) (10.4 mL, 7.72 g, 0.070 mol) in 30 mL of anhydrous Et_2O was added to the resulting EtMgBr, and the reaction mixture was stirred until the evolution of ethane ceased (2 h). A solution of PhCHO (7.1 mL, 7.42 g, 0.070 mol) in 20 mL of anhydrous Et_2O was added to the resulting Jocić reagent over a period of 45 min, and the mixture was refluxed for 30 min and left for 16 h. The yellowish suspension was diluted with Et_2O (20 mL) and mixed with a cold solution of NH_4Cl (10 g) in 100 mL of water. The colored upper layer and the ethereal extracts from the aqueous layer (3×25 mL) were combined, washed with saturated brine (3×25 mL), dried (Na_2SO_4), and concentrated *in vacuo* (40 °C (bath) (35 Torr)). The residue was fractionated *in vacuo* (0.5 Torr). After evaporation of volatile impurities (b.p. 77—78 °C), alcohol (±)-**1** was isolated as a yellowish oil with b.p. 130—132 °C (0.5 Torr) and R_f 0.65 (hexane—Et_2O, 3 : 1). The yield was 8.18 g (54%). ^1H NMR, δ: 0.91 (narrow m, 3 H, Me); 1.36—1.62 (m, 8 H); 2.03 (m, 2 H, $C(4)H_2$); 4.28 (narrow m, 1 H, $C(1)H_2$); 4.60 (br.s, 1 H, OH); 7.22—7.46 (m, 3 H and 2 H, Ph). IR, ν/cm^{-1}: 3340 m (OH), 355 and 3030 w (ArH), 2215 w (C≡C), 1610 m (C=C), 1040 s (C—O). The ^1H NMR and IR spectra of alcohol (±)-**1** were similar to those reported previously.[6a]

(±)-1-Phenylhept-1-yn-3-ol ((±)-3). A solution of phenylacetylene (**8**) (3.8 mL, 3.53 g, 0.035 mol) in 10 mL of Et_2O was added to a solution of EtMgBr prepared from Mg (0.92 g, 0.038 mol) and EtBr (3.2 mL, 4.6 g, 0.042 mol) in 25 mL of Et_2O, and the reaction mixture was brought to gentle boiling, which was maintained for 2 h. A solution of pentanal (**9**) (2.47 mL, 2.07 g, 0.024 mol) in 4.5 mL Et_2O was added over a

period of 45 min, and the mixture was refluxed for an additional 30 min, quenched with a cold solution of NH_4Cl (40 mL), and extracted with Et_2O (75 mL). The ethereal extract was washed with brine and dried ($MgSO_4$), and the ether was evaporated *in vacuo*. The residue (4.04 g) was fractionated *in vacuo*. The fraction with b.p. 30—50 °C (8 Torr) contained the excess **8**, while the major fraction (b.p. 119—121 °C (1 Torr)), a yellow oil with a "fat" smell (n_D^{20} 1.5290) that crystallized on storage as needles, represented pure alcohol (±)-**3** with R_f 0.49 (hexane—AcOEt, 5 : 1) (*cf.* Ref. 28a: b.p. 144 °C (1 Torr), n_D^{20} 1.5298). The yield was 2.75 g (63%). ^{1}H NMR, δ: 0.96 (t, Me, ^3J = 7.0 Hz); 1.35—1.56 (m, 4 H); 1.81—1.90 (m, 2 H, $C(4)H_2$); 4.61 (t, C(3)H, ^3J = 5.8 Hz); 5.10 (narrow m, 1 H, OH); 7.28—7.36 and 7.45—7.48 (both m, 3 H and 2 H, Ph). IR (film), ν/cm^{-1}: 3360 m (OH), 3370 and 3040 w (ArH); 2230 (C≡C), 1605 m (C=C), 1030 s (C—O). The ^{1}H NMR and IR spectra of alcohol (±)-**3** are similar to those described previously.[28b,c]

1-Phenylundec-4-yn-3-ol ((±)-5) was prepared similarly to alcohols (±)-**1** and (±)-**3**. A solution of 14 mL of oct-1-yne (**7**) (10.47 g, 0.095 mol) in 16 mL of Et_2O was added dropwise to a solution of EtMgBr prepared from Mg (2.51 g, 0.105 mol) and EtBr (8.8 mL, 12.55 g, 0.115 mol) in 20 mL of Et_2O, and the reaction mixture was gently refluxed for 2 h. When the mixture was cooled to ~25 °C, a fine precipitate was formed, whose dissolution required stirring under reflux for an additional 45 min. Then a solution of hydrocinnamaldehyde (**10**) (8.50 g, 0.063 mol) in 20 mL of Et_2O was added and the mixture was stirred for 30 min at 20—25 °C and for 30 min under reflux, and was kept for 16 h at 4—6 °C. Then ~50 mL of crushed ice and 100 mL of a saturated solution of NH_4Cl were added. The organic layer was separated, the aqueous layer was extracted with Et_2O (4×25 mL), and the combined organic phase was washed with a saturated solution of $NaHCO_3$ (2×25 mL) and brine (3×25 mL), dried (Na_2SO_4), and concentrated *in vacuo*. The residue (oil, 10.8 g) was fractionated on a column with SiO_2 in the hexane—Et_2O system (9 : 1, v/v). The fraction with R_f 0.49 (hexane—AcOEt, 5 : 1), a colorless oil, represented alcohol (±)-**5**. The yield was 9.19 g (59.3%). Found (%): C, 83.27; H, 10.06. $C_{17}H_{24}O$. Calculated (%): C, 83.55; H, 9.90. ^{1}H NMR, δ: 0.91 (narrow m, 3 H, Me); 1.23—1.41 (m, 6 H, 3 CH_2); 1.46—1.63 (m, 2 H $C(7')H_2$); 2.07 (m, 2 H, $C(6)H_2$); 2.20 (m, $C(2)H_2$); 2.68 (dt, 2 H, $C(1)H_2$, ^3J = 6.4 Hz, ^4J = 0.8 Hz); 4.25 (s, 1 H, OH); 4.40 (dt, 2 H, $C(3)H_2$, ^3J = 5.6 Hz, $^5J \approx$ 0.7 Hz); 7.22—7.39 (m, 5 H, PhH). ^{13}C NMR, δ: 14.15 (Me), 18.79, 22.65, 28,63, 28.73, 31.42, 31.58, 39.75 (7 CH_2), 62.15 (HCOH), 81.04 and 86.15 (C≡C), 125.94, 128.44, 128.52, and 141.56 (Ph). IR, ν/cm^{-1}: 3590 m (OH), 3070 and 3040 w (ArH), 2230 w (C≡C), 1605 (C=C), 1050 s (C—O).

Acetylation of alcohols (±)-1, (±)-3, and (±)-5 (general procedure). 4-Dimethylaminopyridine (0.4—1 mmol) was added to a solution of a substrate (4—10 mmol) in a mixture of anhydrous Ac_2O (8—20 mmol), anhydrous Py (4—10 mmol), and hexane (10—25 mL). The mixture was left for 48 h at 18—25 °C and stirred with cold 10% HCl (3×5 min). The upper layer was washed with a 10% solution of $NaHCO_3$ (3 times) and water (3 times), dried (Na_2SO_4), and concentrated *in vacuo*. According to TLC data and ^{1}H NMR and IR spectra, all products (pale yellow oils) were free from the starting compounds or side products; they were used in subsequent operations without additional purification.

(±)-1-Phenylnon-2-yn-1-ol acetate ((±)-2), yield 97%, R_f 0.74 (hexane—AcOEt, 85 : 15). ^{1}H NMR, δ: 0.89 (narrow m, 3 H, Me); 1.35—1.70 (m, 8 H); 2.04 (s, 3 H, COMe); 2.11 (m, 2 H, $C(4)H_2$); 5.12 (narrow m, 2 H, $C(1)H_2$); 7.22—7.46 (m, 3 H, 2 H, Ph). IR, ν/cm^{-1}: 3350 and 3030 w (ArH); 2235 w (C≡C), 1742 s (C=O); 1610 m (C=C).

(±)-1-Phenylhept-1-yn-3-ol acetate ((±)-4), yield 98.5%, yellowish oil, n_D^{20} 1.5125 (*cf.* Ref. 27a: n_D^{20} 1.5117), R_f 0.68 (hexane—AcOEt, 9 : 1). ^{1}H NMR, δ: 0.91 (t, Me, ^3J = 7.0 Hz); 1.35—1.67 (m, 4 H); 1.85—1.9 (m, 2 H, $C(4)H_2$); 2.10 (s, 3 H, COMe); 5.12 (t, C(3)H, ^3J = 5.8 Hz); 7.28—7.36 and 7.45—7.48 (both m, 3 H and 2 H, Ph). IR (film), ν/cm^{-1}: 3350 and 3040 w, 2230 (C≡C), 1742 s (C≡O); 1600 m, 1055 s.

1-Phenylundec-4-yn-3-ol acetate ((±)-6), yield 94%, R_f 0.68 (hexane—AcOEt, 85 : 15). ^{1}H NMR, δ: 0.93 (t, 3 H, Me, ^3J = 6.7 Hz); 1.25—1.40 (m, 6 H, $C(10)H_2$—$C(8)H_2$); 1.56—1.65 (dt, 2 H, $C(2)H_2$, ^3J = 6.2 and 6.8 Hz); 2.03 (s, 3 H, COMe); 2.10 (t, 2 H, $C(6)H_2$, ^3J = 7.0 Hz); 2.20 (dt, $C(2)H_2$, ^3J = 6.4 and 5.6 Hz); 2.75 (dt, 2 H, $C(1)H_2$, ^3J = 6.4 Hz, $^4J \approx$ 1.0 Hz); 5.35 (m, 1 H, C(3)H); 7.22—7.39 (m, 3 H and 2 H, PhH). ^{13}C NMR, δ: 14.15, 18.79, 22.65, 28,63, 28.73, 31.42, 31.58, 39.75, 62.15, 81.04, 86.15, 125.94, 128.44, 128.52, 141.56, 170.97. IR, ν/cm^{-1}: 3050 and 3040, 2230, 1740, 1620.

(3,3-Dimethoxypropyl)benzene (14). Neat $TsOH \cdot H_2O$ (0.10 g) was added to a solution of hydrocinnamaldehyde **10** (2.5 g, 18.7 mmol) in 40 mL of anhydrous MeOH under argon. The reaction mixture was stirred at 20 °C, the course of the reaction being monitored by TLC (hexane—AcOEt, 5 : 1, v/v); after 4 h, the starting aldehyde **10** was completely converted into acetal **14**. The catalyst was neutralized by adding KOH powder to pH 8. Methanol was evaporated *in vacuo* and the residue was washed with dry Et_2O (3×5 mL), the precipitate being separated by decantation. The combined ethereal extract was concentrated (40 °C (bath) (10 Torr)) and the residue was distilled at 96 °C (1 Torr) to give pure acetal **14** as a light oil with a sharp smell, n_D^{22} 1.4879 (*cf.* Ref. 29: n_D^{23} 1.4890). The yield was 2.92 g (87%). ^{1}H NMR, δ: 1.97 (m, 2 H, $C(2)H_2$); 2.72 (t, 2 H, $C(1)H_2$, ^3J = 6.7 Hz); 3.37 (s, 6 H, 2 MeO); 4.42 (t, 1 H, C(3)H, ^3J = 5.7 Hz); 7.20—7.38 (m, 5 H, Ph).

(±)-[η^6-(3,3-Dimethoxypropyl)benzene]tricarbonylchromium (15). Acetal **14** (0.74 g, 4.11 mmol), anhydrous di-*n*-butyl ether (10 mL), anhydrous THF (2 mL), and chromium hexacarbonyl (1.0 g, 4.5 mmol) were placed in an argon-filled flask. The mixture was refluxed under Ar (~140 °C) for 50 h, the sublimed $Cr(CO)_6$ being returned periodically into the flask. The content of the flask was cooled down to ~40 °C (bath) and concentrated *in vacuo*, the greenish-brown residue was triturated with Et_2O (3×10 mL), and the extract was decanted off and mixed with a small amount of SiO_2. The solvent was evaporated *in vacuo* and the residue was applied onto a column with SiO_2. Elution with hexane—Et_2O mixtures (5 : 1 and 4 : 1, v/v) yielded chromium complex **15** as a bright-yellow oil, which rapidly crystallized when stored under argon, m.p. 53—54 °C (hexane—Et_2O, 2 : 1). Yield 1.09 g (84%). ^{1}H NMR, δ: 2.45 (pseudoq, 2 H, $C(2)H_2$, ^3J = 6.7 Hz); 2.88 (m, 2 H, $C(1)H_2$); 3.35 (s, 6 H, 2 MeO); 4.42 (t, 1 H, C(3)H, ^3J = 5.7 Hz); 5.20 (m, 3 H, A_3B_2 system, η^6-arene fragment B); 5.38 (m, 2 H, A_3B_2 system, η^6-arene fragment A).

[η^6-(3-Oxopropyl)benzene]tricarbonylchromium (13). A solution of η^6-complex (±)-**15** (2.0 g, 6.33 mmol) in 40 mL of acetone was placed in an argon-filled flask. Water (10 mL) and oxalic acid ($H_2C_2O_4 \cdot 2H_2O$) (1.0 g, 7.9 mmol) were added. The

mixture was refluxed, the course of the reaction being monitored by TLC (hexane—AcOEt, 3 : 1, visualization by I_2 vapor). The reaction was complete in 2.5 h. The reaction mixture was cooled and neutralized with solid $NaHCO_3$ (1.68 g, 20 mmol) with stirring. The precipitated salts were filtered off and washed with acetone. The filtrate and the acetone washings were combined and concentrated *in vacuo*. The remaining aqueous emulsion was saturated with NaCl and extracted with AcOEt (3×25 mL). The extract was dried (Na_2SO_4) and concentrated to a constant weight at 45 °C (bath) (10 Torr) to give aldehyde **13** (TLC and ^{1}H NMR data) as a dark-yellow oil, which was used in the next synthetic step without further purification. The yield was 1.70 g (≥95%). ^{1}H NMR, δ: 2.72 (td, 2 H, C(2)H_2, J = 6.2 and 1.1 Hz*); 2.80 (dd, 2 H, C(1)H_2, J = 6.2 and ~0.8 Hz); 5.23 (m, 3 H, A_3B_2 system η^6-arene fragment B); 5.39 (m, 2 H, A_3B_2 system, η^6-arene fragment A with J = 6.5 Hz); 9.83 (br.s, 1 H, C(3)H, J = 1.1 Hz). IR (film), ν/cm^{-1}: 1975 and 1960 [m.-s, (η^6-ArH)·Cr(CO)$_3$], 1870, 1725 (s, CH=O). The ^{1}H NMR and IR spectral data almost coincided with those reported previously.[30]

(±)-[η^6-(3-Hydroxyundec-4-yn-1-yl)benzene]tricarbonylchromium ((±)-11). Magnesium (100 mg, 4.16 mmol), anhydrous Et_2O (10 mL), and a crystal of I_2 were placed in an argon-filled flask. The mixture was stirred until the color of iodine disappeared, EtBr (0.10 mL) was added, and, when the formation of EtMgBr started (the mixture became turbid), an additionaol portion of EtBr (0.24 mL) was added (total amount, 0.34 mL, 4.98 mmol). When magnesium completely dissolved, a solution of oct-1-yne (**7**) (0.56 mL, 416 mg, 3.78 mmol) in 3 mL of anhydrous Et_2O was added to the EtMgBr formed. The reaction mixture was stirred under reflux until the evolution of ethane ceased (2.5 h) and cooled to 20 °C, and a solution of aldehyde **13** (0.680 g, 2.52 mmol) in 5 mL of anhydrous Et_2O was added. The mixture was refluxed and stirred for an additional 0.5 h, cooled to ~20 °C, and left for 18 h. Crushed ice (5 mL) and a saturated aqueous solution of NH_4Cl (25 mL) were added with stirring at 0—5 °C. The aqueous layer was separated and extracted with Et_2O (3×10 mL). The organic layer and the ethereal extract were combined, washed with brine (4×15 mL), dried (Na_2SO_4), and concentrated *in vacuo*. The residue (oil, 0.9 g) was chromatographed on a column with SiO_2 (40 g) in a hexane—AcOEt gradient (95 : 5 → 75 : 25, v/v). Elution with a hexane—AcOEt mixture (4 : 1) gave pure alcohol (±)-**11** as a thick yellow oil with R_f 0.80 (hexane—AcOEt, 1 : 1) or 0.62 (hexane—AcOEt, 2 : 1). The yield was 0.721 g (75%). ^{1}H NMR*: 0.90 (t, 3 H, Me, ^3J = 6.8 Hz); 1.31—1.43 (m, 6 H, 3 CH_2); 1.54 (m, 2 H, C(7)H_2); 1.95 (m+s, 3 H, overlap of C(2)H_2 and OH); 2.22 (dt, 2 H, C(6)H_2, J = 6.7 Hz, J ≈ 0.8 Hz); 2.57 (dt, 2 H, C(1)H_2, J = 6.7 Hz, J ≈ 0.8 Hz); 4.12 (m, 1 H, C(3)H, J = 5.7 Hz); 5.17—5.23 (m, 3 H, A_3B_2 system, η^6-arene fragment B); 5.36—5.42 (m, 2 H, A_3B_2 system, η^6-arene fragment A). ^{13}C NMR, δ: 14.12, 18.74, 22.60, 28.63, 30,76, 31,36, 39.14, 61.66 (CHOH), 80.36 and 90.48 (C≡C), 92.65, 92.73, 93.82, and 112.97 (Ph), 177.02 (Cr...CO). IR, ν/cm^{-1}: 3565 m (OH), 2230 w (C≡C), 1980 and 1955 m.-s ((η^6-ArH)·Cr(CO)$_3$), 1600 (C=C), 1040 s (C—O).

(*R*)-(+)-[η^6-(3-Acetoxyundec-4-yn-1-yl)benzene]tricarbonylchromium ((*R*)-12). Freshly distilled vinyl acetate (0.146 mL, 137 mg, 1.90 mmol) and 200 mg of CCL were added under Ar to a solution of alcohol (±)-**11** (200 mg, 0.53 mmol) in 5 mL of dry Et_2O, and the mixture was stirred at 18—23 °C for 507 h (21 day), the course of the reaction being monitored by TLC. The lipase was separated from the liquid phase by filtering the reaction mixture through Florisil® (4 g). The filtrate was concentrated *in vacuo* (40 °C (bath) (10 Torr) and the reaction products were separated on a column with SiO_2 using a hexane—Et_2O mixture (2 : 1, v/v) as the eluent. Complex (*R*)-**12** (sample **A**) was formed as a yellow oil with R_f 0.75 (hexane—AcOEt, 2 : 1) and $[\alpha]_D^{25}$ +31.6 (*c* 1.0). The yield was 48.6 mg (21.9%). ^{1}H NMR*, δ: 0.91 (t, 3 H, Me, ^3J = 6.7 Hz); 1.20—1.41 (m, 6 H, 3 CH_2); 1.45—1.60 (m, 2 H, C(7)H_2); 1.99 (m, 2 H, C(2)H_2); 2.08 (s, 3 H, COMe); 2.23 (dt, 2 H, C(6)H_2, ^3J = 6.7 Hz, ^5J ≈ 0.9 Hz); 2.57 (dt, 2 H, C(1)H_2, ^3J = 6.7 Hz, ^4J = 0.7 Hz); 5.18—5.23 (m, 3 H, A_3B_2 system, η^6-arene fragment B); 5.32—5.48 (m, 1 H + 2 H, superposition of the signal from HCOAc onto the signal of two protons of the η^6-arene fragment A). IR, ν/cm^{-1}: 2230 w (C≡C), 1980 and 1955 m.-s ((η^6-ArH)·Cr(CO)$_3$), 1735 s (C=O), 1600, 1235 s (C—O). Further elution gave the fraction of recovered alcohol **11** (138 mg, 69%).

(*R*)-(+)-3-Acetoxy-1-phenylundec-4-yn (or 1-phenylundec-4-yn-3(*R*)-ol acetate) ((*R*)-6). Crystalline I_2 (38 mg, 0.149 mmol) was added under Ar to a solution of acetate (*R*)-**12A** (42.2 mg, 0.10 mmol) in 1.0 mL of anhydrous THF and the mixture was stirred for 30 min. During this period, the complex (*R*)-**12** completely disappeared (TLC data). The excess of I_2 was reduced by 1.5 mL of a saturated solution of $Na_2S_2O_3$ (the brown color changed to dark-green). The reaction mixture was extracted with Et_2O (3×3 mL), the extract was washed with a saturated solution of $Na_2S_2O_3$ and brine (2×2 mL), every aqueous layer obtained after extraction being washed once more with 1 mL of ether. The total ethereal extract was dried (Na_2SO_4), the solvent was evaporated *in vacuo* to give pure acetate (*R*)-**6** as a pale yellow oil with $[\alpha]_D^{25}$ +29.5 (*c* 0.63). The yield was 36 mg (94.8%). The R_f value and the ^{1}H NMR spectrum of acetate (*R*)-**6** were virtually identical to those of acetate (±)-**6** (see above).

(*R*)-(−)-1-Phenylundec-4-yn-3-ol ((*R*)-5). Powdered potassium hydroxide (10 mg, 0.178 mmol) was added to a solution of acetate (*R*)-**6** (50 mg, 0.175 mmol) in a mixture of anhydrous MeOH (3 mL) and anhydrous hexane (1 mL), and the mixture was stirred for 20 min (TLC monitoring, hexane—AcOEt, 10 : 1). The reaction mixture was neutralized to pH 7 with glacial AcOH. The solvents were evaporated (50 °C (bath) (5 Torr), water (1.5 mL) was added to the residue to dissolve the precipitated salts, and the aqueous emulsion was extracted with Et_2O (3×5 mL). The combined extracts were dried (Na_2SO_4) and concentrated *in vacuo* to a constant weight to give alcohol (*R*)-**5** (TLC data and ^{1}H NMR spectra) as a thick pale-yellow oil with $[\alpha]_D^{20}$ −26.4 (*c* 1.0). The yield was 40.1 mg (89%).

(*S*)-(+)-1-Phenylundec-4-yn-3-ol ((*S*)-5). *Method 1.* The fraction of scalemic alcohol **11** (138 mg) that has not entered into the CCL-mediated acetylation of alcohol (±)-**11** (see above) was subjected to the repeated EKR under identical conditions. Incubation under argon for 600 h followed by the conventioinal workup and separation of the products on a column with SiO_2 gave additional 26.2 mg (17%) of acetate (*R*)-**12B** with $[\alpha]_D^{22}$ +31.0 (*c* 1.0) and 93 mg (81.2%) alcohol (*S*)-**11** as a bright yellow oil, $[\alpha]_D^{22}$ +2.8 (*c* 0.82). Under argon, crystalline I_2 (76 mg, 0.3 mmol) was added to a solution of alcohol (*S*)-**11** (84 mg, 0.2 mmol) in 3 mL of anhydrous THF and the reaction mixture was stirred until (*S*)-**11** completely disappeared

* Apparent spin-spin coupling constants.

(TLC monitoring, 25 min). The excess of I_2 was reduced with a saturated solution of $Na_2S_2O_3$. The mixture was extracted with Et_2O and the extract was washed with a saturated solution of $NaHCO_3$ (2×2 mL) and brine (3×2 mL). The total ethereal extract was dried (Na_2SO_4) and concentrated *in vacuo* to give alcohol (*S*)-**5** as a pale yellow oil, $[\alpha]_D^{20}$ +12.8 (*c* 0.6). The yield was 54 mg (87.5%). The R_f value and ^{1}H NMR data for alcohol (*S*)-**5** were virtually identical to those of alcohols (±)-**5** and (*R*)-**5**. (see above)

Method 2. Vinyl acetate (10 mL, 95 mg, 1.11 mmol) and 90 mg of the CCL were added to a solution of alcohol (±)-**5** (90 mg, 0.37 mmol) in 3 mL of anhydrous Et_2O. The reaction mixture was vigorously stirred at 20—22 °C for 144 h. The lipase was filtered through a layer of Celite-539® (60—80 mesh), the filtrate was concentrated *in vacuo*, and the resulting product mixture was chromatographed on a column with SiO_2 in the hexane—Et_2O gradient (100 : 0 → 90 : 10). The isolated fractions were acetate **6** (60 mg, 57%) and unconsumed alcohol (*S*)-**5** with R_f 0.51 (hexane—AcOEt, 9 : 1) and $[\alpha]_D^{20}$ +5.3 (*c* 1.0). The yield was 37.1 mg (41%), which corresponds to a ~58% conversion of alcohol (±)-**5**.

Method 3. Acetate (±)-**6** (200 mg) and a PPL powder (400 mg) were added to 5 mL of 0.1 *M* aqueous phosphate buffer with pH 6.5. The mixture was vigorously stirred at 20—23 °C for 168 h. The lipase was filtered off through a layer of Celite-539®. The filtrate, a whitish emulsion, was extracted with ether (3×3 mL), the total extract was washed with brine, dried (Na_2SO_4), and concentrated *in vacuo*. The residue was chromatographed on a column with SiO_2. Elution with a hexane—Et_2O mixture (9 : 1) gave the fraction of recovered acetate **6** (110 mg, 55%) followed by the fraction of alcohol (*S*)-**5** (sample **B**) with $[\alpha]_D^{20}$ +3.8 (*c* 1.0), which corresponds to a degree of conversion of the substrate of about $35\% \le C \le 45\%$. The ^{1}H NMR spectra and R_f of the three samples of alcohol (*S*)-**5** were identical.

The efficiency of enzymatic kinetic resolution of alcohols into enantiomers (see Table 1) was determined with CCL, PPL, and RSL by analogy with the methods of preparation of acetates (*R*)-**6** and (*R*)-**12** from alcohols (±)-**5** and (±)-**11**, using alcohols (±)-**1**, (±)-**3**, and (±)-**5** (0.25—0.75 mmol).

The efficiency of enzymatic kinetic resolution of acetates into enantiomers (see Table 2) was determined with PPL by analogy with the methods of preparation of alcohol (±)-**5** from acetate (±)-**6**, using acetates (±)-**2**, (±)-**4**, and (±)-**6** (0.25—0.5 mmol).

Binary MTPA esters of alcohols (*S*)-5 and (*R*)-5. A solution of (*R*)-α-methoxy-α-(trifluoromethyl)phenylacetyl chloride ((*R*)-MTPA-Cl), prepared from (−)-Mosher´s acid ((*S*)-MTPA) (39 mg, 0.38 mmol) by a known procedure,[17] in 0.5 mL of anhydrous pyridine was added to a solution of alcohol (*S*)-**5** (48.5 mg, 0.2 mmol, sample (*S*)-**5C**) in 0.6 mL of CCl_4. The reaction mixture was kept at 20 °C for 24 h, treated with a solution of *N*,*N*-dimethylethylenediamine (20 mg, ~0.22 mmol) in a minimum volume of CCl_4 according to a known procedure,[18] and acidified with 1 *M* HCl (4 mL). The organic layer was separated and the aqueous phase was extracted with Et_2O (3×1 mL). The total organic phase was washed with 1 *M* HCl, a saturated solution of $NaHCO_3$, and brine, dried (Na_2SO_4), and concentrated *in vacuo*. The thick light yellow precipitate was dissolved in anhydrous benzene and the solution was passed through a column with SiO_2 (1.2 g) to give a binary mixture of the (3*S*,2´*S*)-MTPA ester (major component) and (3*R*,2´*S*)-MTPA ester (minor component), designated as (*S*)-MTPA ester **I″**. The yield was 85 mg (93%).

Similarly, acylation of alcohol (*R*)-**5** with *ee* ≥95% with (*R*)-Mosher´s acid chloride ((*S*)-MTPA-Cl) gave a binary mixture of ester (3*R*,2´*R*)-MTPA and ester (3*R*,2´*S*)-MTPA, designated as (*R*)-MTPA-ester **II**, while the reaction of alcohol (*S*)-**5** gave a binary mixture of ester (3*S*,2´*R*)-MTPA (major component) and (3*S*,2´*R*)-MTPA ester (minor component), designated as ester (*R*)-MTPA **III**. Both binary esters are light-yellow oils. The ^{1}H NMR spectra of ester (*S*)-MTPA **I**, ester (*R*)-MTPA **II**, and ester (*R*)-MTPA **III** are qualitatively similar to each other and to the spectra of acetates (*R*)-**6** and (*S*)-**6**. The δ_H and δ_F values essential for the determination of the absolute configuration of the alcohol residues in these MTPA esters are presented in Table 3.

Complexation with Eu(fod)$_3$. The absolute configurations of the major and minor components in esters (*R*)-MTPA **II** and (*R*)-MTPA **III** were determined according to known methods.[21,24]

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