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Diastereoselective Preparation of (*R*)- and (*S*)-2-Methoxy-2-phenylpent-3-ynoic Acids and Their Use as Reliable Chiral Derivatizing Agents

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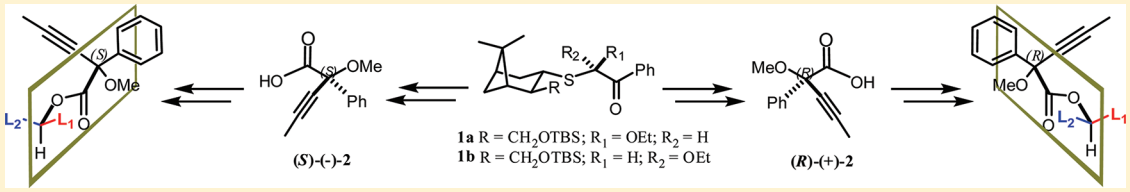
Supporting Information



ABSTRACT: Benzoyl-S,O-acetals **1a** and **1b** were used as chiral auxiliaries to achieve the diastereoselective preparation of both enantiomers of 2-methoxy-2-phenylpent-3-ynoic acids (MPPAs). The latter were condensed with several chiral secondary alcohols and some primary amines to evaluate their potential as chiral derivatizing agents (CDAs). The ^{1}H NMR spectra of the corresponding esters and amides showed strong consistency with the absolute configuration of the carbinol and amine moieties, whose observed $\Delta\delta L_1$ and $\Delta\delta L_2$ values were in the ranges of 0.1−0.4 and 0.02−0.12 ppm, respectively.

INTRODUCTION

The use of chiral derivatizing agents (CDAs) is one of the most reliable and effective methods to determine the absolute configuration of chiral alcohols and amines by ^{1}H NMR. Since the pioneer work of Mosher[1] describing the use of α-methoxy-α-trifluoromethylphenylacetic acid (MTPA) as the first prototype of a CDA, a diversity of Mosher analogues have been developed and used in the assignment of the absolute configuration of a wide variety of chiral alcohol and amine derivatives, among other compounds.[2] During the course of our work focused on the development of new chiral auxiliaries derived from (1*R*)-(−)-myrtenal, we described the synthesis of benzoyl-*S*,*O*-acetals **1a** and **1b** as well as their use to obtain either enantiomer of chiral α-hydroxyacids through a highly diastereoselective process.[3a] Taking advantage of this highly stereocontrolled process, we envisioned the diastereoselective synthesis of the new enantiomeric pair of 2-methoxy-2-phenylpent-3-ynoic acids (α,α,α-methoxyphenylpropynylacetic acids, MPPAs) (*R*)-(+)-**2** and (*S*)-(−)-**2** as strong candidates for use as CDAs to determine the absolute configuration of chiral alcohols and amines. The main structural feature of these CDAs is the simultaneous presence of propynyl and phenyl groups at C-2, which in principle would exert opposite anisotropic effects on substituents L_1 and L_2 present at the carbinol and amine fragments, thus inducing optimal discrimination of such groups by means of their relative chemical shifts (Figure 1). Herein we describe an easy and practical protocol for the synthesis of new CDAs (*R*)-(+)-**2** and (*S*)-(−)-**2** and a representative number of examples supporting its use as a very reliable alternative for determining the absolute configuration of chiral secondary carbinols and chiral primary amines.

RESULTS AND DISCUSSION

The preparation of thioacetals **1a** and **1b** was efficiently achieved according to the synthetic protocol developed by our research group.[3a−c] These compounds were treated with MeC≡CMgBr to give the corresponding carbinols **3a** and **3b** in quantitative yield and >99:1 dr (Scheme 1), with a stereochemistry in agreement with the Cram chelated model, which states that the Grignard reagent is preferably coordinated with oxygen instead of sulfur, thus giving, for instance the nucleophilic addition mainly through the *re* face of the carbonyl group of thioacetal **1a**.[4] After successive treatment of **3a** and **3b** with NaH and CH_3I, diastereomeric methylethers **3c** and **3d** were obtained in yields higher than 95% without the need of any particular purification protocol for the last two steps. Hydrolysis of thioacetals **3c** and **3d** was readily accomplished with NCS and $AgNO_3$ in CH_3CN/H_2O, affording the corresponding aldehydes. The crude products were oxidized to the MPPAs (*R*)-(+)-**2** and (*S*)-(−)-**2** with Jones reagent

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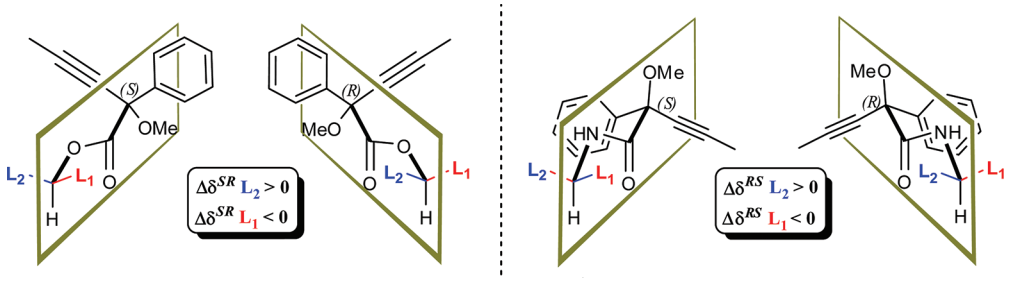
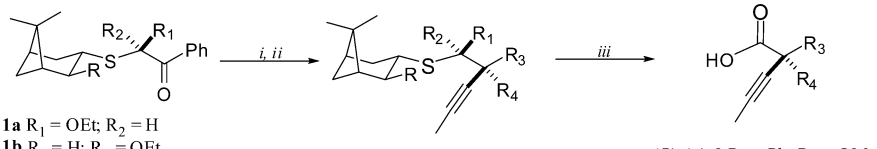


Figure 1. *Syn* and *anti* periplanar perspective views of the diastereomeric pair of esters and amides formed by condensation of CDAs (*R*)-(+)-**2a** and (*S*)-(−)-**2b** with chiral secondary carbinols and primary amines, respectively, and their expected $\Delta\delta^{SR}$ and $\Delta\delta^{RS}$ values for ligands L_1 and L_2.

Scheme 1. Reaction Sequence Yielding MPPAs (*R*)-(+)-2 and (*S*)-(−)-2[a]



1a R_1 = OEt; R_2 = H
1b R_1 = H; R_2 = OEt
R = CH_2OTBS

3a R_1 = OEt; R_2 = H; R_3 = Ph; R_4 = OH
3b R_1 = H; R_2 = OEt; R_3 = OH; R_4 = Ph
3c R_1 = OEt; R_2 = H; R_3 = Ph; R_4 = OMe
3d R_1 = H; R_2 = OEt; R_3 = OMe; R_4 = Ph
R = CH_2OTBS

(*R*)-(+)-**2** R_3 = Ph; R_4 = OMe
(*S*)-(-)-**2** R_3 = OMe; R_4 = Ph

[a](i) MeC≡CMgBr, THF, −78 °C (>99%). (ii) NaH, MeI, THF, rt (>95%). (iii) (a) NCS, $AgNO_3$, $MeCN/H_2O$; (b) CrO_3, H_2SO_4/H_2O. (*R*)-(+)-**2**: $[\alpha]^{25}_D$ = +42.6° (*c* 1.51, $CHCl_3$); (*S*)-(−)-**2**: $[\alpha]^{25}_D$ = −42.4° (*c* 1.65, $CHCl_3$).

(CrO_3 in H_2O/H_2SO_4) and easily purified by conversion to the sodium salt, washing with Et_2O/hexanes (1:1) and back-conversion to the free acid using 10% aq HCl solution.

It must be mentioned that preparation of the corresponding esters from (*R*)-MPPA or (*S*)-MPPA gave a diastereomeric mixture ranging from 79:21 to 97:3 and 87:13 to 97:3, respectively, as can be observed in their corresponding ^{1}H NMR spectra (Supporting Information). This result must be either in direct connection with the combined optical purity[5] of both tested carbinols and amines (sold as 95−99% purum, labeled as the sum of enantiomers) and MPPA acids (*R*)-(+)-**2** and (*S*)-(−)-**2**, as well as the presence of some level of kinetic resolution. For instance, the later event was particularly pronounced in the preparation of (*R*)-MPPA and (*S*)-MPPA bornyl esters **12a** (dr 87:13) and **12b** (dr 79:21).

According to the protocol for determining the absolute configuration of secondary alcohols via the double derivatization Mosher method,[1,2,6] the relative sign of the chemical shift difference for ligands L_1 and L_2 ($\Delta\delta^{SR}$), obtained from ^{1}H NMR spectra of the R*O-(*S*)-MPPA and R*O-(*R*)-MPPA esters (**4**−**23**), will indicate the absolute configuration of the chiral carbinol. As can be seen, these alcohols comprise a wide structural diversity including cyclic, open chain, and benzylic secondary alcohols. The numbers attached to structures (**4**−**23**) in Table 1 reveal all $\Delta\delta^{SR}$ values obtained from the synthesized R*O-(*S*)-MPPA and R*O-(*R*)-MPPA pairs of esters, where blue (positive) values are those resulting from $\Delta\delta^{SR}(L_2)$ = $[\delta_{(L2)}$ R*O-(*S*)-MPPA] − $[\delta_{(L2)}$ R*O-(*R*)-MPPA] and red (negative) values result from $\Delta\delta^{SR}(L_1)$ = $[\delta_{(L1)}$ R*O-(*S*)-MPPA] − $[\delta_{(L1)}$ R*O-(*R*)-MPPA].

Complete consistency between the known absolute configuration of the tested carbinols and the $\Delta\delta^{SR}$ values for ligands L_1 and L_2 belonging to their respective esters is the first point that should be highlighted from Table 1. In addition, the size and systematic relative signs of the $\Delta\delta^{SR}$ values, which range from 0.1 to ca. 0.4 ppm for the α positions at ligands L_1 and L_2, allowed for a very reliable assignment of the absolute configuration of the tested carbinols. Two additional facts must be emphasized: (a) when L_1 or L_2 is or possesses an aromatic group, this is mostly under the protective anisotropic effect of the MPPA's phenyl group (structures **4**−**6**), as was corroborated through NOE experiments (Supporting Information), making these CDAs especially effective for this kind of alcohol, and (b) in cases where no hydrogen atom is present at the α position, the protective anisotropic effect of the phenyl group of the MPPA moiety was efficiently transmitted to the β, γ, or even more remote positions (structures **4**, **6**, **12**, **13**, and **16**). Just to provide a graphical example, Figure 2 illustrates sections of the ^{1}H NMR spectra for esters prepared by condensing (3*R*)-hydroxytetrahydrofuran with the (*R*)- and (*S*)-MPPAs (upper and lower traces, respectively). As can be seen, the chemical shifts ($\Delta\delta^{SR}$) pattern obtained from both compounds clearly correlates with the absolute configuration of the alcohol used. The same trend was observed for all esters synthesized in this work; the full set of NMR spectra is provided in the Supporting Information.

In addition, we consider it useful to extend the scope of this method to determine the absolute configuration of chiral primary amines, since they represent an important group of compounds widely found in pharmaceutical formulations and in nature (i.e., alkaloids, amino acids) or even as frequent targets in asymmetric synthesis. In this case, the available chiral primary amines were methylbenzyl amine, norbornyl amine, and the methyl esters of L-valine and L-serine, whose corresponding amides **24**−**27** were prepared using BOP as coupling reagent and DEA as a catalyst. It is important to note that

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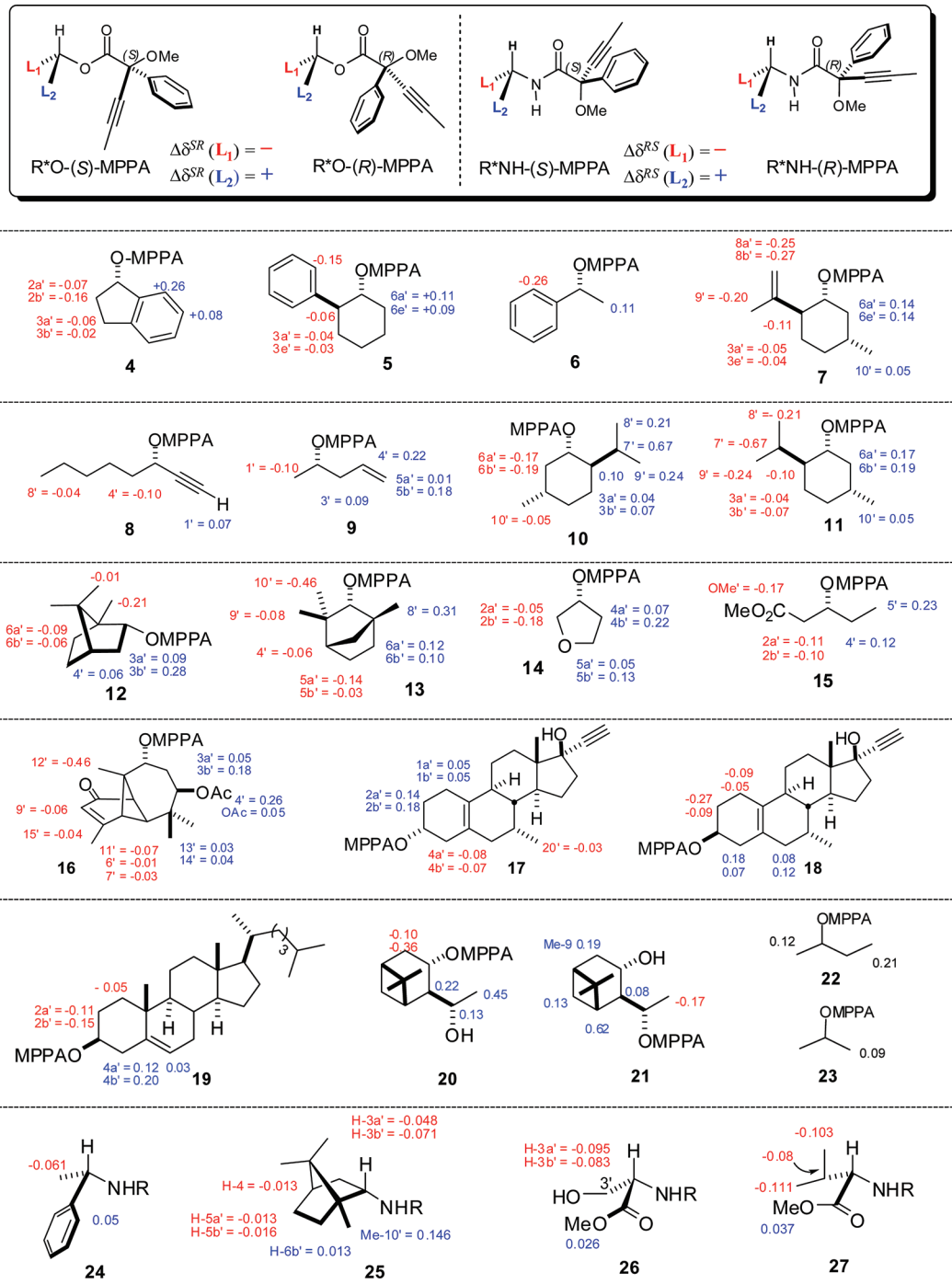
Table 1. Representative MPPA Esters and Amides of Chiral Alcohols and Amines, of Known Absolute Configuration[a]



[a]Negative (red) and positive (blue) values are $\Delta\delta^{SR}$ values for molecular regions representing ligands L_1 and L_2, respectively, which systematically agree with the absolute configuration of tested chiral alcohols and amines. Projections of esters R*O-(*S*)-MPPA and R*O-(*R*)-MPPA **4**–**23**, as well as amides R*NH-(*S*)-MPPA and R*NH-(*R*)-MPPA **24**–**27**, are shown in the more stable *syn*-periplanar (*spO*, vide infra) and *anti*-periplanar (*ap-Z*)[2] conformations, respectively. All chemical shifts were recorded in $CDCl_3$ at rt.

conformational analysis of Mosher amides reveals (vide infra) that the main conformer corresponds to an *anti*-periplanar (*ap-Z*) arrangement (Figure 1).[2] Consequently, to maintain $\Delta\delta$ negative values in ligand L_1 and positive in ligand L_2, NMR data must be interpreted as $\Delta\delta^{RS}(L_1) = [\delta_{(L1)}$ R*NH-(*R*)-MPPA$] - [\delta_{(L1)}$ R*NH-(*S*)-MPPA] and $\Delta\delta^{RS}(L_2) = [\delta_{(L2)}$ R*NH-(*R*)-MPPA$] - [\delta_{(L2)}$ R*NH-(*S*)-MPPA], respectively, since in the resulting *ap-Z* conformation the relative orientation of phenyl and propynyl groups, in relation to ligands L_1 and L_2, are opposite as compared with the main conformer of the corresponding esters (Figure 1).

The last row in Table 1 shows the resulting amides along with their $\Delta\delta^{RS}$ values. In this case, these values are smaller than the corresponding $\Delta\delta^{SR}$ values for esters as the distance between the anisotropic groups and ligands L_1 and L_2 is larger in the *ap-Z* conformation in comparison with the corresponding *sp* conformation. However, all $\Delta\delta^{RS}$ values were completely consistent with the known absolute configuration of the used amines and amino acids.

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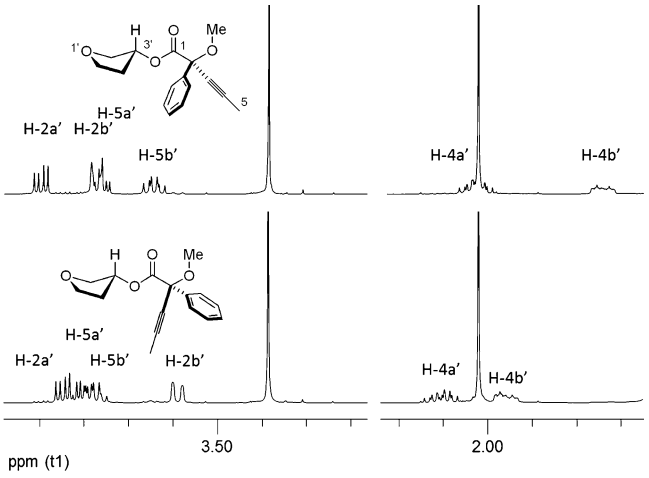
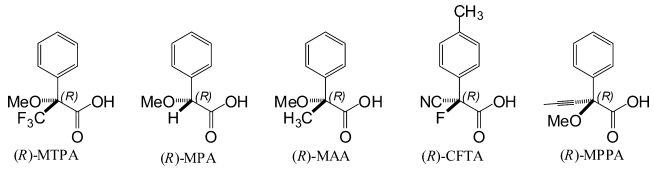


Figure 2. Spectral regions for esters **14a** and **14b** formed with (3*R*)-3-hydroxyfurane and (*R*)-MPPA (top) and (*S*)-MPPA (bottom) acids, respectively. See Table 1 for the corresponding $\Delta\delta^{SR}$ values.

Table 2 shows a comparison between the $\Delta\delta^{SR}$ values obtained in this work and those $\Delta\delta^{SR}$ values obtained by using the most known phenyl-derived CDAs bearing the same carbinol and amine moiety: (*R*)-menthol-R* **10**, (*R*)-phenetole-R* **6**, (*R*)-borneol-R* **12**, *s*-BuO-R* **22**, *i*-PrO-R* **23**, methylbenzyl amine-R* **24**, (+)-2-bornyl amine-R* **25**, L-serine-R* **26**, and L-valine-R* **27**, where R* is the corresponding CDA to be used for comparison. It should be noted that the absolute $\Delta\delta$ values are shown for convenience, thus comparing only their magnitudes. As can be seen, the absolute values induced by MPPA are very similar to those obtained when using its analogues MPA[2] and CFTA[7] and clearly improve the values obtained when using MTPA[2,8] and MAA.[2,9]

It is well-known that the success of this methodology for the assignment of absolute configuration relies on the assumption that conformers such as those shown in Figure 1 are the predominant ones within the overall conformational distribution of esters and amides.[2,6] For instance, MTPA esters give rise to six conformers out of which the *syn*- (*sp1*) and *anti*-periplanar (*ap1*) are the most abundant ones.[2] According to previous theoretical studies of MTPA esters,[2−6] a thorough conformational search was carried out on (*S*)-*s*-Bu-(*R*)-MPPA and (*S*)-*s*-Bu-(*S*)-MPPA esters (**22**).[10] The search showed that the *sec*-butyl fragment conformation in both esters is essentially the same as that shown in Figure 1, that is, the C−H bond of the secondary carbon is coplanar and *syn* with respect to the carbonyl C=O bond. In addition, it was found that rotation of the OC−Cα bond in each ester leads to two distinct sets of conformers (Figure 3). The most stable set corresponds to the approximately *syn*-periplanar arrangement of the methoxy group with respect to the carbonyl group, which is designated as the *sp*(*O*) conformer (Figure 3).

Table 2. $\Delta\delta^{SR}$ or $\Delta\delta^{RS}$ Absolute Values for Esters and Amides Derived from Some of the Most Common Described Phenyl-Containing CDAs and Their Comparison with $\Delta\delta^{SR}$ and $\Delta\delta^{RS}$ Values Obtained in This Work



		CDA, $\Delta\delta^{SR}$ or $\Delta\delta^{RS}$ (ppm)[a]				
alcohol/amine	substituent	MTPA	MPA[b]	MAA[c]	CFTA	MPPA
i-PrOH	Me	0.07	0.12	0.05 (0.082)		0.09
s-BuOH	H-1	0.08	0.13	0.006 (0.093)	0.14	0.12
	H-3	0.05/0.04	0.11		0.10/0.11	
	H-4	0.11	0.23	0.009 (0.147)	0.22	0.21
(*R*)-menthol	Me-8	0.17	0.21	0.024 (0.183)	0.21	0.21
	Me-9	0.04	0.26	0.019 (0.154)	0.25	0.24
	Me-10	0.07	0.05	0.003 (0.035	0.06	0.05
(*R*)-phenetol	Me	0.06	0.15	0.005 (0.074)	0.10	0.11
	H-*ortho*	0.03			0.25	0.26
(*R*)-borneol	H-3	0.10	0.39		0.33	0.28
	H-4	0.03	0.06	(0.043)	0.10	0.06
	Me-10	0.08	0.27	0.0035 (0.134)	0.22	0.21
(+)-2-bornyl amine	H-3	0.07				0.048/0.071
	H-4	0.02				0.013
	Me-8	0.022				
	Me-10	0.078				0.0146
L-valine methyl ester	OMe	0.017				0.037
	H-3	0.084				0.08
	Me (*i*-Pr)	0.189				0.111
	Me (*i*-Pr)	0.08				0.103
L-serine methyl ester	OMe	0.022				0.026
	H-3	0.07				0.095/0.083

[a]All $\Delta\delta^{SR}$ and $\Delta\delta^{RS}$ values were obtained in $CDCl_3$ and are expressed as absolute values. Comparative values of CDAs other than MPPA were taken from ref 2. [b]Values for MPA correspond to $\Delta\delta^{RS}$. [c]Values in brackets were obtained in CCl_4.

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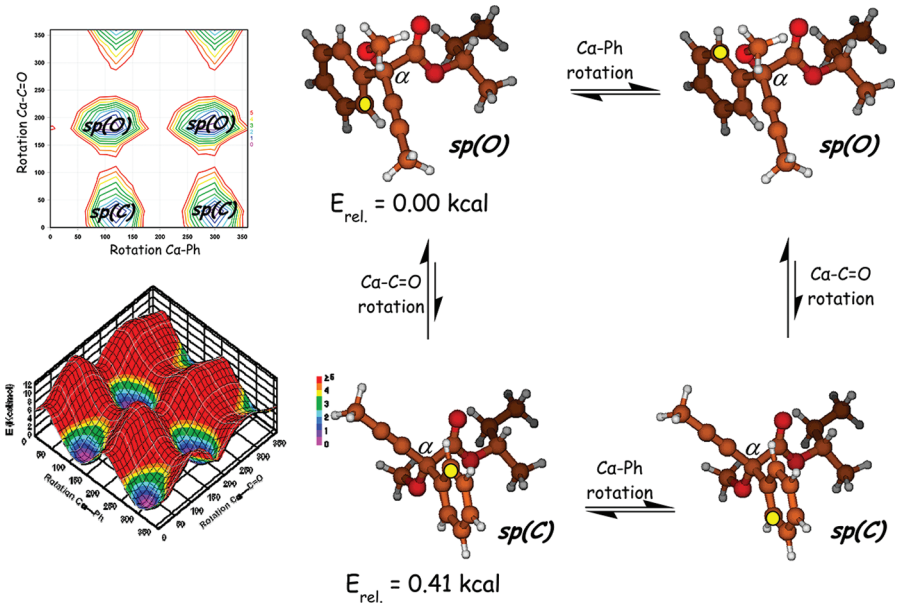

Figure 3. Relative energies (kcal/mol) between *syn*-periplanar *sp*(*O*) and *sp*(*C*) conformers of (*S*)-*s*-Bu-(*R*)-MPPA ester obtained through C*α*-C═O and C*α*-Ph rotations. The aromatic carbon labeled with a yellow dot shows the equivalence between both conformers *sp*(*O*), as well as between both conformers *sp*(*C*), in the range 0−180° and 180−360°. The relative stability of these four conformers is also shown in the contour plots of the potential energy surface illustrated at the left-hand side of this figure.

In the second set, the 1-propynyl group also attains a *syn*-periplanar position with respect to the carbonyl, and therefore this one was designated as the *sp*(*C*) conformer. Although in both conformations the phenyl group would exert similar shielding effects on both L_1 and L_2 groups, a fact that would lead to poor $\Delta\delta^{SR}$ values and to an inaccurate assignment of the absolute configuration, the relative stability of the *sp*(*O*) and *sp*(*C*) conformers is such that, according to B3LYP/6-31G(d) relative energies, the total population of the *sp*(*O*) conformers of the (*S*)-*s*-Bu-(*R*)-MPPA is 90%. For the (*S*)-*s*-Bu-(*S*)-MPPA diastereomer, the population of the *sp*(*C*) conformers is lower, about 71%. The predominance of the *sp*(*O*) conformers in both derivatives would lead to sufficiently large $\Delta\delta^{SR}$ values with the expected sign, which would be expected to correlate with the correct absolute configuration of the carbinol moiety. Figure 3 also shows the relative stability between *sp*(*O*) and *sp*(*C*) conformers (0.41 kcal/mol), which were generated by rotating C_α−Ph and C_α−CO bonds while maintaining the conformation of the carbinol moiety unchanged;[11] the resulting potential energy surface from this conformational search are also illustrated in both 3D and contour plots perspectives. Interestingly, the corresponding *anti*-periplanar conformers where the OMe group is *anti* to the carbonyl (Figure 1) are almost negligible in this case, resulting in a clear contrast with CDAs bearing OMe group at C_α, for instance, MPA.

Concerning amides, a conformational search of the amide derived from (*R*)-*sec*-butyl amine and (*R*)-MPPA acid, by using the Monte Carlo method and the Molecular Mechanics Force Field MMFF94 (Spartan 10, V1.0.1), afforded 15 conformers under 10 kcal/mol, from which ca. 19% adopt an *ap*-*Z* conformation in a similar way as MPA amide derivatives behave,[2] while the remaining ca. 81% takes an *sp*(*C*) arrangement related to the *sp*(*C*) conformer found for MPPA esters (Figure 3). In Figure 4 are shown the structures of both conformers; in the former one the OMe and C═O groups are *anti*-periplanar, while in the later the propynyl and C═O groups are *syn*-periplanar. It can be observed that the anisotropic

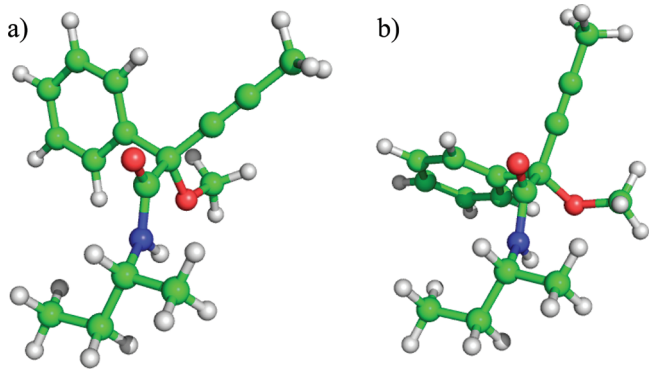

Figure 4. (a) *ap*-*Z* and (b) *sp*(*C*) conformers found for MPPA-amides. MMFF (Monte Carlo) calculations showed that *sp*(*C*) is the major conformer.

contribution of the propynyl group should be lower in conformer *sp*(*C*); however, the phenyl group orientation is always on the same side of ligand L_1 in both conformers, thus maintaining a consistent shielding effect. No *sp*(*O*) conformer similar to that for esters was found under the above energy range.

■ CONCLUSIONS

Although currently there are growing alternatives to determine the absolute configuration of chiral compounds, e.g., vibrational circular dichroism (VCD),[12] the combined double derivatization and NMR measurements so far remains one of the most reliable methodologies to accomplish this task. In this sense, this work contributes with a robust protocol for the synthesis of novel (*R*)- and (*S*)-MPPAs and introduces their use as CDAs in the assignment of the absolute configuration of a representative number of chiral secondary alcohols. The $\Delta\delta^{SR}$ values were all in agreement with the correct absolute configuration of the carbinol moiety. The magnitude of the $\Delta\delta^{SR}$ values found (0.1−0.4 ppm) for all R*O-(*S*)-MPPA and R*O-(*R*)-MPPA esters

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(**4**−**23**) is very similar to those described for the most recommended CDA, MPA[2] and CFTA.[7] However, it must be emphasized that synthesis of the latter involves a more elaborated protocol, comprising resolution of a racemic mixture, than preparation of MPPA and, in contrast to MPA, MPPA esters were successfully prepared under different reaction conditions without racemization because of their lack of "racemizable" alpha protons. Our acids are particularly suitable for the assignment of absolute configuration of chiral α-aryl secondary alcohols in cases where other CDA fails[2,9b,13] and are comparable with CFTA in this regard. Finally, all above results strongly indicate that the structural features of MPPA acids, bearing the two divergent anisotropic phenyl and propynyl groups, ensures an $sp(O)$ conformational predominance, thus rendering easily measurable $\Delta\delta^{SR}$ values with the correct signs, which in turn allows for the unequivocal assignment of the absolute configuration of secondary alcohols. The shown MPPA amine derivatives **24**−**27** also demonstrated that the present method offers a reliable alternative to determine the absolute configuration of chiral primary amines.

EXPERIMENTAL SECTION

General Information. All reactions were carried out under a nitrogen atmosphere in oven- or flame-dried glassware, unless the reaction procedure states otherwise. Tetrahydrofuran (THF) and ether (Et_2O) were distilled from sodium−benzophenone in a continuous still under an atmosphere of nitrogen. Dichloromethane was distilled from calcium hydride in a still under an atmosphere of nitrogen. Room temperature reactions were carried out between 20 and 25 °C, and reactions at −78 °C were carried out in an acetone−dry ice bath. Analytical thin-layer chromatography (TLC) was performed using precoated TLC plates with Silica Gel 60 F254 and visualized using combinations of UV, anisaldehyde, and ceric ammonium molybdate (CAM) staining. Flash column chromatography was performed using silica gel (230−400 mesh) as the stationary phase. Proton magnetic resonance spectra were recorded at 300 and 500 MHz, as specified. Carbon magnetic resonance spectra were recorded at 75 and 125 MHz, as specified. Chemical shifts were reported in δ units relative to tetramethylsilane using the residual solvent signal for reference ($CDCl_3$ $\Delta\delta$ 7.27 and 77.0 ppm for proton and carbon, respectively). Peak assignments of the ^{1}H and ^{13}C NMR spectra were confirmed by using 2D NMR experiments (gCOSY, NOESY-1D, gHSQC, and gHMBC). IR spectral data were obtained using CH_2Cl_2 as solvent. Optical rotations were measured in solutions of $CHCl_3$ using the sodium D line (589 nm). High resolution mass spectral data were obtained using either of the following ionization methods: HREIMS, HRESIMS (Micro-TOF), or HRFABMS.

Preparation of *S,O*-Acetals 3a and 3b. A solution of *S,O*-acetals **1a** and **1b** (3.75 g, 8.0 mmol) in dry THF (32 mL) at −78 °C was treated with propynylmagnesium bromide (32 mL, 0.5 M in THF, 16.1 mmol) and stirred at −78 °C for 2 h. The reaction mixture was quenched with aqueous NH_4Cl (3 mL). The resulting mixture was allowed to warm to room temperature, diluted with saturated solution of NaCl, and extracted with diethyl ether. The ethereal layer was dried (Na_2SO_4) and concentrated to give the corresponding pure alcohols **3a** or **3b** (3.88 g, >99%, dr > 99:<1) as colorless oils. When the reaction was performed with the mixture of both *S,O*-acetals **1a** and **1b**, a mixture of the above carbinols was obtained. The two products were separated by flash column chromatography (silica gel 230−400, hexane/diethyl ether 93:7).

(1*S*,2*R*,3*S*,5*R*)-2-(*O*-*tert*-Butyldimethylsilyloxymethylen)-6,6-dimethyl-3-[(1*R*,2*R*)-1-ethoxy-2-phenyl-2-hydroxy-3-pentyn-1-sulfanyl)]-bicyclo-[3.1.1]-heptane (3a). Obtained in 96% yield (>99:<1 dr) as colorless syrup (R_f 0.44, hexane/ethyl ether 9:1). $[\alpha]^{23}_D$ = +35.6 (*c* 0.535, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.70 (m, 2H, H-*o*), 7.31 (m, 3H, H-*m*,*p*), 4.47 (s, 1H, H-11), 3.83 (dd, 1H, *J* = 9.9, 5.1 Hz, H-10a), 3.76 (dq, 1H, *J* = 9.6, 7.1 Hz, H-1′a), 3.71 (s, 1H, OH), 3.61 (t, 1H, *J* = 9.9 Hz, H-10b), 3.41 (ddd, 1H, *J* = 9.5, 8.7. 5.7 Hz, H-3), 3.22 (dq, 1H, *J* = 9.6, 7.1 Hz, H-1′b), 2.59 (m, 1H, H-4e), 2.41 (dtd, 1H, *J* = 9.8, 6.1, 2.1 Hz, H-7e), 2.24 (td, 1H, *J* = 6.1, 1.8 Hz, H-1), 2.12 (ddd, 1H, *J* = 13.4, 5.7, 2.5 Hz, H-4a), 2.12 (m, 1H, H-2), 2.94 (tt, 1H, *J* = 6.1, 2.5 Hz, H-5), 1.93 (s, 3H, Me-15), 1.21 (s, 3H, Me-9), 1.02 (d, 1H, *J* = 9.8 Hz, H-7a), 0.96 (t, 3H, *J* = 7.1 Hz, H-2′), 0.96 (s, 3H, Me-8), 0.89 (s, 9H, *t*-Bu), 0.06 (s, 6H, Me_2-Si). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 141.5 (C-*i*), 127.8 (C-*p*), 127.6 (C-*m*), 126.6 (C-*o*), 94.5 (C-11), 82.6 (C-13), 80.1 (C-14), 73.9 (C-12), 65.7 (C-1′), 65.6 (C-10), 52.6 (C-2), 42.2 (C-1), 42.2 (C-5), 39.3 (C-4), 38.4 (C-6), 35.7 (C-3), 33.4 (C-7), 27.6 (Me-9), 26.0 (*t*-Bu), 23.4 (Me-8), 18.4 (C-Si), 14.4 (Me-2′), 4.0 (Me-15), −5.2 (Me-Si), −5.3 (Me-Si). IR (CH_2Cl_2) ν_{max}: 3446, 3060, 2928, 2855, 1470, 1449, 1385, 1361, 1254, 108, 837, 777, 698 cm^{-1}. MS (EI) *m*/*z* (%): 485 ([M − OH]$^+$·, 6.2), 456 ([M − EtOH]$^+$·, 12.1), 357 ([M − PhC(OH)-CCMe]$^+$·, 24), 265 (44), 135 (100). HRFABMS calcd for $C_{29}H_{46}O_3SSi$ + Na: 525.2835, found 525.2825.

(1*S*,2*R*,3*S*,5*R*)-2-(*O*-*tert*-Butyldimethylsilyloxymethylen)-6,6-dimethyl-3-[(1*S*,2*S*)-1-ethoxy-2-phenyl-2-hydroxy-3-pentyn-1-sulfanyl)]-bicyclo-[3.1.1]-heptane (3b). Obtained in 98% yield (>99:<1 dr) as colorless syrup (R_f 0.32, hexane/ethyl ether 9:1). $[\alpha]^{23}_D$ = +36.6 (*c* 0.624, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.71 (m, 2H, H-*o*), 7.33 (m, 3H, H-*m*,*p*), 4.47 (s, 1H, H-11), 3.84 (dq, 1H, *J* = 9.4, 7.1 Hz, H-1′a), 3.73 (s, 1H, OH), 3.62 (dd, 1H, *J* = 9.6, 5.3 Hz, H-10a), 3.43 (t, 1H, *J* = 9.6 Hz, H-10b), 3.25 (dq, 1H, *J* = 9.4, 7.1 Hz, H-1′b), 2.77 (ddd, 1H, *J* = 9.8, 7.9, 5.7 Hz, H-3), 2.58 (m, 1H, H-4e), 2.38 (dtd, 1H, *J* = 9.8, 6.1, 1.7 Hz, H-7e), 2.16 (ddd, 1H, *J* = 11.1, 5.7, 2.7 Hz, H-4a), 2.04 (m, 1H, H-1), 2.04 (m, 1H, H-2), 1.93 (tt, 1H, *J* = 6.1, 2.7 Hz, H-5), 1.91 (s, 3H, Me-15), 1.18 (s, 3H, Me-9), 1.04 (d, 1H, *J* = 9.8 Hz, H-7a), 1.03 (t, 3H, *J* = 7.1 Hz, Me-2′), 0.90 (s, 9H, *t*-Bu), 0.87 (s, 3H, Me-8), 0.07 (s, 3H, Me-Si), 0.06 (s, 3H, Me-Si). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 141.4 (C-*i*), 127.7 (C-*p*), 127.5 (C-*m*), 126.6 (C-*o*), 94.9 (C-11), 82.0 (C-13), 80.0 (C-14), 74.8 (C-12), 65.7 (C-10), 65.3 (C-1′), 52.7 (C-2), 42.3 (C-1), 42.1 (C-5), 39.1 (C-4), 38.1 (C-6), 36.9 (C-3), 33.1 (C-7), 27.5 (Me-9), 26.0 (*t*-Bu), 23.3 (Me-8), 18.4 (C-Si), 14.4 (Me-2′), 3.9 (Me-15), −5.2 (Me-Si), −5.3 (Me-Si). IR (CH_2Cl_2) ν_{max}: 3460, 3060, 2927, 2855, 1472, 1450, 1385, 1361, 1254, 1079, 837, 777, 699 cm^{-1}. MS (EI) *m*/*z* (%): 485 ([M − OH]$^+$·, 3.5), 456 ([M − EtOH]$^+$·, 8.8), 357 ([M − PhC(OH)-CCMe]$^+$·, 41.8), 265 (42.4), 135 (100). HRFABMS calcd for $C_{29}H_{46}O_3SSi$ + Na: 525.2835, found 525.2839.

Preparation of *S,O*-Acetals 3c and 3d. To a solution of alcohol **3a** (4.05 g, 8.0 mmol) and methyl iodide (3.43 g, 24.2 mmol) in dry THF (20 mL) was added sodium hydride (644 mg, 60% dispersion in mineral oil, 16.1 mmol) under N_2 atmosphere. The reaction mixture was stirred for 2 h at room temperature and quenched with methanol. Saturated aqueous NH_4Cl and NaCl were added successively and extracted with ethyl ether. The ethereal layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude mixture was filtered through a silica gel column (hexane/ethyl ether 9:1) affording methyl ether **3c** (4.04 g, >95%) as a colorless oil.

(1*S*,2*R*,3*S*,5*R*)-2-(*O*-*tert*-Butyldimethylsilyloxymethylen)-6,6-dimethyl-3-[(1*R*,2*R*)-2-methoxy-1-ethoxy-2-phenyl-3-pentyn-1-sulfanyl)]-bicyclo-[3.1.1]-heptane (3c). Obtained in 97% yield (>99:<1 dr) as colorless syrup (R_f 0.54, hexane/ethyl ether 9:1). $[\alpha]^{25}_D$ = +53.3 (*c* 0.59, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.63 (m, 2H, H-*o*), 7.33 (m, 3H, H-*m*,*p*), 4.64 (s, 1H, H-11), 3.80 (dd, 1H, *J* = 9.8, 4.3 Hz, H-10a), 3.58 (dq, 1H, *J* = 9.6, 7.1 Hz, H-1′a), 3.56 (t, 1H, *J* = 9.8 Hz, H-10b), 3.23 (dq, 1H, *J* = 9.6, 7.1 Hz, H-1′b), 3.23 (s, 3H, OMe), 3.06 (ddd, 1H, *J* = 9.5, 8.3, 5.8 Hz, H-3), 2.46 (m, 1H, H-4e), 2.35 (dtd, 1H, *J* = 9.6, 6.0, 1.9 Hz, H-7e), 2.24 (td, 1H, *J* = 6.0, 2.0 Hz, H-1), 2.11 (ddd, 1H, *J* = 13.8, 5.8, 2.7 Hz, H-4a), 2.05 (m, 1H, H-2), 2.01 (s, 3H, Me-15), 1.90 (tt, 1H, *J* = 6.0, 2.7 Hz, H-5), 1.18 (s, 3H, Me-9), 1.06 (d, 1H, *J* = 9.6 Hz, H-7a), 0.92 (s, 3H, Me-8), 0.92 (t, 3H, *J* = 7.1 Hz, Me-2′), 0.87 (s, 9H, *t*-Bu), 0.04 (s, 6H, Me_2-Si). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 139.6 (C-*i*), 127.9 (C-*p*), 127.8 (C-*m*), 127.7 (C-*o*), 92.3 (C-11), 86.1 (C-13), 82.9 (C-14), 76.2 (C-12), 65.6 (C-1′), 65.3 (C-10), 52.2 (OMe), 52.1 (C-2), 42.2 (C-5), 41.9 (C-1), 38.5 (C-6), 34.4 (C-4), 34.9 (C-3), 33.0 (C-7), 27.6 (Me-9), 26.0

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(*t*-Bu), 23.3 (Me-8), 18.3 (C-Si), 14.8 (Me-2′), 4.0 (Me-15), −5.1 (Me-Si), −5.3 (Me-Si). IR (CH_2Cl_2) ν_{max}: 3060, 2928, 2855, 1471, 1447, 1387, 1362, 1255, 1075, 837, 775, 699 cm^{-1}. MS (EI) *m*/*z* (%): 485 ([M − OMe]$^{+\cdot}$, 5.3), 357 ([M − PhC(OMe)CCMe]$^{+\cdot}$, 42.6), 265 (52.8), 159 (100) 135 (99.1). HRFABMS calcd for $C_{30}H_{48}O_3SSi$ + Na: 539.2991, found 539.3011.

(1*S*,2*R*,3*S*,5*R*)-2-(*O*-*tert*-Butyldimethylsilyloxymethylen)-6,6-dimethyl-3-[(1*S*,2*S*)-2-methoxy-1-ethoxy-2-phenyl-3-pentyn-1-sulfanyl)]-bicyclo-[3.1.1]-heptane (3d). Obtained in 98% yield (>99:<1 dr) as colorless syrup starting from tertiary alcohol **3b** and following the methodology for the synthesis of ether **3c**. (R_f 0.51, hexane/ethyl ether 9:1). $[\alpha]^{25}_D$ = +186.8 (*c* 0.48, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.64 (m, 2H, H-*o*), 7.31 (m, 3H, H-*m*,*p*), 4.56 (s, 1H, H-11), 3.78 (dd, 1H, *J* = 10.1, 3.9 Hz, H-10a), 3.75, (dq, 1H, *J* = 9.4, 7.0 Hz, H-1′a), 3.50 (t, 1H, *J* = 10.1 Hz, H-10b), 3.31 (dq, 1H, *J* = 9.4, 7.0 Hz, H-1′b), 3.26 (s, 3H, OMe), 2.85 (ddd, 1H, *J* = 9.8, 8.3, 6.1 Hz, H-3), 2.54 (m, 1H, H-4e), 2.37 (tdt, 1H, *J* = 10.0, 6.0, 1.8 Hz, H-7e), 2.23 (td, 1H, *J* = 6.0, 1.9 Hz, H-1), 2.17 (ddd, 1H, *J* = 13.7, 6.1, 2.6 Hz, H-4a), 2.01 (m, 1H, H-2), 2.01 (s, 3H, Me-15), 1.92 (tt, 1H, *J* = 6.0, 2.6 Hz, H-5), 1.19 (s, 3H, Me-9), 1.01 (d, 1H, *J* = 10.0 Hz, H-7a), 1.00 (t, 3H, *J* = 7.0 Hz, Me-2′), 0.92 (s, 3H, Me-8), 0.90 (s, 9H, *t*-Bu), 0.06 (s, 6H, Me_2-Si). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 139.3 (C-*i*), 128.0 (C-*p*), 127.8 (C-*m*), 127.5 (C-*o*), 92.9 (C-11), 85.3 (C-13), 83.6 (C-14), 76.6 (C-12), 65.1 (C-10), 64.8 (C-1′), 52.8 (C-2); 52.1 (OMe), 42.3 (C-5), 41.9 (C-1), 38.8 (C-4), 38.4 (C-6), 37.0 (C-3), 33.4 (C-7), 27.7 (Me-9), 26.0 (*t*-Bu), 23.2 (Me-8), 18.4 (C-Si), 14.5 (Me-2′), 3.9 (Me-15), −5.1 (Me-Si), −5.2 (Me-Si). IR (CH_2Cl_2) ν_{max}: 3060, 2928, 2855, 1471, 1448, 1386, 1362, 1254, 1080, 837, 775, 706 cm^{-1}. MS (EI) *m*/*z* (%): 485 ([M − OMe]$^{+\cdot}$, 10.5), 357 ([M − PhC(OMe)CCMe]$^{+\cdot}$, 52.6), 265 (51.8), 159 (100) 135 (99.7). HRFABMS calcd for $C_{30}H_{48}O_3SSi$ + Na: 539.2991, found 539.3010.

Preparation of MTPA Acids (*R*)-(+)-2 and (*S*)-(−)-2. A suspension of NCS (1.9 g, 14.4 mmol) and $AgNO_3$ (2.5 g, 14.4 mmol) in CH_3CN/H_2O 1:1 (18.0 mL) cooled at 0 °C was added to a solution of adducts **3c** or **3d** (3.7 g, 7.2 mmol) in CH_3CN (18.0 mL) previously cooled at 0 °C. The reaction mixture was stirred for 10 min at 0 °C and quenched by successively adding saturated solutions of NaCl, Na_2SO_3, and $NaHCO_3$ (3.0 mL). The slurry was filtered in vacuo, solids were washed with cold diethyl ether, and then the filtrate was diluted with saturated $NaHCO_3$ and extracted with diethyl ether. The combined organic layers were washed with saturated aqueous NaCl and dried over Na_2SO_4, and the solvent was distilled in a rotary evaporator at 46 °C and atmospheric pressure. The residue was dissolved in 200 mL of acetone, cooled at 0 °C, and treated with Jones' reagent (10.6 mL, 1.16 M (7.0 g of CrO_3, 6.0 mL of H_2SO_4 and water to make up 60.0 mL of solution), 14.4 mmol). The reaction mixture was stirred for 1 h at the same temperature and quenched with isopropanol; the clear supernatant was decanted and evaporated to give the crude product. The residue was dissolved in ethyl ether and washed with water, and then the organic layer was dried (Na_2SO_4), filtered, and concentrated to dryness. The crude product was dissolved in hexane/ethyl ether 1:1 and transferred to a separatory funnel, saturated aqueous $NaHCO_3$ was added until no gas was produced, and if necessary water was added in order to make a suitable volume. Then the aqueous layer was washed with hexane/ethyl ether 1:1 (2 × 30 mL), acidified with concentrated HCl (pH = 3), and extracted with hexane/ethyl ether/dichloromethane 1:1:1. The organic layer was dried over Na_2SO_4, filtered, and concentrated to dryness to yield acid (*R*)-(+)-**2** (1.32 g, 90% yield) as a colorless syrup.

(*R*)-(+)-2-Methoxy-2-phenylpent-3-ynoic Acid. Obtained in 90% yield (91:09 er)[5] as colorless syrup $[\alpha]^{25}_D$ = +42.6 (*c* 1.51, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.22 (s, 1H, OH), 7.65 (m, 2H, H-*o*), 7.36 (m, 3H, H-*m*,*p*), 3.36 (s, 3H, OMe), 2.01 (s, 3H, Me-5). ^{13}C NMR (125 MHz, $CDCl_3$): δ 171.4 (C-1), 136.6 (C-*i*), 129.2 (C-*p*), 128.5 (C-*o*), 126.9 (C-*m*), 86.9 (C-3), 80.0 (C-4), 73.2 (C-2), 52.8 (OMe), 3.8 (Me-5). IR (CH_2Cl_2) ν_{max}: 2939.6, 1738.9, 1450.3, 1215.6, 1093.9, 698.6 cm^{-1}. MS (EI) *m*/*z* (%): 204 ([M]$^{+\cdot}$, 5.3), 189 ([M − Me]$^{+\cdot}$, 4.1), 173 ([M − OMe]$^{+\cdot}$, 42.9), 159 ([M − CO_2H]$^{+\cdot}$, 100), 115 (20.2). HRESIMS calcd for $C_{12}H_{12}O_3$ + H: 205.0864, found 205.0859.

(*S*)-(−)-2-Methoxy-2-phenylpent-3-ynoic Acid. Obtained in 91% yield (91:09 er)[5] as colorless syrup $[\alpha]^{25}_D$ = −42.4 (*c* 1.65, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.22 (s, 1H, OH), 7.65 (m, 2H, H-*o*), 7.36 (m, 3H, H-*m*,*p*), 3.36 (s, 3H, OMe), 2.01 (s, 3H, Me-5). ^{13}C NMR (125 MHz, $CDCl_3$): δ 171.4 (C-1), 136.6 (C-*i*), 129.2 (C-*p*), 128.5 (C-*o*), 126.9 (C-*m*), 86.9 (C-3), 80.0 (C-4), 73.2 (C-2), 52.8 (OMe), 3.8 (Me-5). IR (CH_2Cl_2) ν_{max}: 2939.4, 1737.7, 1450.3, 1215.2, 1093.8, 698.4 cm^{-1}. MS (EI) *m*/*z* (%): 204 ([M]$^{+\cdot}$, 4.1), 189 ([M − Me]$^{+\cdot}$, 2.6), 173 ([M − OMe]$^{+\cdot}$, 39.2), 159 ([M − CO_2H]$^{+\cdot}$, 100), 115 (16.1). HRESIMS calcd for $C_{12}H_{12}O_3$ + H: calcd 205.0864, found 205.0861.

Preparation of MPPA Esters 4−23. To a solution of acids (*R*)-(+)-**2** or (*S*)-(−)-**2** (1 equiv), the chiral alcohol (1.1 quiv), and DMAP (1.5 equiv) in dry dichloromethane (5 mL/50 mg of the acid) was added 1.1 equiv of DCC at room temperature. The reaction mixture was stirred for 24 h, then filtered, diluted with dichloromethane, and washed with aqueous 5% HCl. The organic layer was dried over Na_2SO_4, filtered, and evaporated to dryness to give the crude product. Column chromatography of the crude product on silica (230−400 mesh) and hexane/ethyl ether as eluant gave the corresponding esters R*O-(*S*)-MPPA and R*O-(*R*)-MPPA.

(1*S*)-1-Indanyl (*R*)-2-Methoxy-2-phenylpent-3-ynoate 4a. Obtained in 56% yield as colorless syrup (R_f 0.47 hexane/AcOEt/Et_2O 85:10:5); dr 95:5. $[\alpha]^{24}_D$ = −2.8 (*c* 0.29, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.64 (m, 2H, H-*o*), 7.30 (m, 3H, H-*m*,*p*), 7.22 (m, 2H, H-4′,5′), 7.10 (td, 1H, *J* = 6.9, 2.5 Hz, H-6′), 7.02 (d, 1H, *J* = 6.9 Hz, H-7′), 6.18 (dd, 1H, *J* = 7.1, 4.7 Hz, H-1′), 3.38 (s, 3H, OMe), 3.02 (ddd, 1H, *J* = 16.0, 8.6, 5.4 Hz, H-3a′), 2.82 (ddd, 1H, *J* = 16.0, 8.4, 5.4 Hz, H-3b), 2.48 (dddd, 1H, *J* = 13.8, 8.4, 7.1, 5.4 Hz, H-2a′), 2.02 (dddd, 1H, *J* = 13.8, 8.6, 5.9, 4.7 Hz, H-2b′), 1.98 (s, 3H, Me-5). ^{13}C NMR (125 MHz, $CDCl_3$): δ 169.4 (C-1), 144.0 (C-*i*′), 140.3 (C-*i*′), 138.2 (C-*i*), 128.8 (C-*p*), 128.5 (C-5′), 128.1 (C-*m*), 126.6 (C-*o*), 126.5 (C-6′), 125.2 (C-7′), 124.6 (C-4′), 85.7 (C-3), 80.5 (C-4), 80.0 (C-1′), 74.4 (C-2), 53.0 (OMe), 31.9 (C-2′), 30.0 (C-3′), 3.8 (Me-5). IR (CH_2Cl_2) ν_{max}: 1737, 1236, 1093, 756 cm^{-1}. MS (EI) *m*/*z* (%): 159 ([M − $CO_2C_9H_9$]$^{+\cdot}$, 100), 128 (2.7), 117 ([indanyl]$^{+\cdot}$, 20), 105 (5), 67 (2.5). HRESIMS: calcd for $C_{21}H_{20}O_3$ + Na: 343.1310, found 343.1316.

(1*S*)-1-Indanyl (*S*)-2-Methoxy-2-phenylpent-3-ynoate 4b. Obtained in 49% yield as colorless syrup (R_f 0.47 hexane/AcOEt/Et_2O 85:10:5); dr 93:7. $[\alpha]^{25}_D$ = +1.2 (*c* 0.31, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.66 (m, 2H, H-*o*), 7.32 (m, 3H, H-*m*,*p*), 7.28 (m, 2H, H-5′,7′), 7.23 (m, 1H, H-4′), 7.18 (m, 1H, H-6′), 6.21 (dd, 1H, *J* = 7.1, 4.4 Hz, H-1′), 3.39 (s, 3H, OMe), 2.96 (ddd, 1H, *J* = 16.1, 8.6, 5.6 Hz H-3a′), 2.80 (ddd, 1H, *J* = 16.0, 8.3, 5.8 Hz, H-3b′), 2.41 (dddd, 1H, *J* = 13.8, 8.3, 7.1, 5.6 Hz, H-2a′), 1.96 (s, 3H, Me-5), 1.86 (dddd, 1H, *J* = 13.8, 8.6, 5.8, 4.4 Hz, H-2b′). ^{13}C NMR (125 MHz, $CDCl_3$): δ 169.4 (C-1), 144.1 (C-*i*′), 140.4 (C-*i*′), 138.1 (C-*i*), 128.8 (C-*p*), 128.6 (C-5′), 128.1 (C-*m*), 126.7 (C-*o*), 126.6 (C-6′), 125.3 (C-7′), 124.6 (C-4′), 85.8 (C-3), 80.5 (C-4), 80.0 (C-1′), 74.4 (C-2), 53.0 (OMe), 31.8 (C-2′), 30.0 (C-3′), 3.7 (Me-5). IR (CH_2Cl_2) ν_{max}: 1737, 1236, 1093, 757 cm^{-1}. MS (EI) *m*/*z* (%): 159 ([M − $CO_2C_9H_9$]$^{+\cdot}$, 100), 128 (2.7), 117 ([indanyl]$^{+\cdot}$, 15), 105 (5), 67 (0.7). HRESIMS: calcd for $C_{21}H_{20}O_3$ + Na: 343.1310, found 343.1311.

(1*R*,2*S*)-1-(2-Phenyl)cyclohexanyl (*R*)-2-Methoxy-2-phenylpent-3-ynoate 5a. Obtained in 43% yield as colorless syrup (R_f 0.51 hexane-Et_2O 4:1) ; dr 97:3. $[\alpha]^{25}_D$ = −47.2 (*c* 0.37, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.41 (m, 2H, H-*o*), 7.23 (m, 3H, H-*m*,*p*), 7.23 (m, 3H, H-*m*′), 7.17 (m, 2H, H-*o*′,*p*′), 5.03 (td, 1H, *J* = 10.8, 4.4 Hz, H-1′), 3.17 (s, 3H, OMe), 2.69 (ddd, 1H, *J* = 12.7, 10.8, 3.8 Hz, H-2′), 1.97 (m, 1H, H-6e′), 1.90 (m, 1H, H-3e′), 1.84 (s, 3H, Me-5), 1.78 (m, 1H, H-4e′), 1.74 (m, 1H, H-5e′), 1.52 (qd, 1H, *J* = 12.7, 3.5 Hz, H-3a′), 1.43 (qt, 1H, *J* = 12.7, 3.2 Hz, H-5a′), 1.30 (qt, 1H, *J* = 12.7, 3.3 Hz, H-4a′), 1.25 (m, 1H, H-6a′). ^{13}C NMR (125 MHz, $CDCl_3$): δ 168.5 (C-1), 142.8 (C-*i*′), 138.2 (C-*i*), 128.3 (C-*p*′), 128.1 (C-*m*), 128.0 (C-*o*), 127.5 (C-*o*′), 126.4 (C-*m*′), 126.3 (C-*p*), 85.2 (C-3), 80.2 (C-4), 77.6 (C-1′) 74.2 (C-2), 52.8 (OMe), 49.3 (C-2′), 34.0 (C-3′), 31.5 (C-6′), 25.6 (C-4′), 24.5 (C-5′), 3.6 (Me-5). IR (CH_2Cl_2) ν_{max}: 2932, 1739, 1449, 1239, 1091, 757, 697 cm^{-1}. HREIMS calcd for $C_{24}H_{26}O_3$: 362.1882, found 362.1880.

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(1*R*,2*S*)-1-(2-Phenyl)cyclohexanyl (*S*)-2-Methoxy-2-phenylpent-3-ynoate 5b. Obtained in 40% yield as colorless syrup (R_f 0.51 hexane-Et_2O 4:1); dr 96:4. $[\alpha]^{24}_D = -34.3$ (*c* 0.36, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ 7.32 (m, 2H, H-*o*), 7.21 (m, 1H, H-*p*′), 7.14 (m, 3H, H-*m*,*p*), 7.14 (m, 2H, H-*m*′), 7.02 (m, 2H, H-*o*′), 5.03 (td, 1H, *J* = 10.8, 4.3 Hz, H-1′), 3.06 (s, 3H, OMe), 2.63 (ddd, 1H, *J* = 12.6, 10.8, 3.7 Hz, H-2′), 2.06 (m, 1H, H-6e′), 1.95 (m, 1H, Me-5), 1.87 (s, 3H, H-3e′), 1.81 (m, 1H, H-4e′), 1.74 (m, 1H, H-5e′), 1.48 (qd, 1H, *J* = 12.6, 3.7 Hz, H-3a′), 1.45 (qt, 1H, *J* = 12.6, 3.6 Hz, H-5a′), 1.36 (m, 1H, H-6a′), 1.30 (qt, 1H, *J* = 12.6, 3.6 Hz, H-4a′). ^{13}C NMR (125 MHz, $CDCl_3$): δ 168.7 (C-1), 142.7 (C-*i*′), 138.1 (C-*i*), 128.2 (C-*m*), 128.1 (C-*p*′), 127.9 (C-*o*), 127.2 (C-*o*′), 126.24 (C-*m*′), 126.18 (C-*p*), 85.2 (C-3), 80.4 (C-4), 77.7 (C-1′) 74.8 (C-2), 52.8 (OMe), 49.2 (C-2′), 34.2 (C-3′), 31.5 (C-6′), 25.6 (C-4′), 24.5 (C-5′), 3.7 (Me-5). IR (CH_2Cl_2) ν_{max}: 2932, 1739, 1239, 1091, 757, 697 cm^{-1}. HREIMS calcd for $C_{24}H_{26}O_3$: 362.1882, found 362.1894.

(1*R*)-1-(1-Phenyl)ethyl (*R*)-2-Methoxy-2-phenylpent-3-ynoate 6a. Obtained in 48% yield as colorless syrup (R_f 0.4, hexane/ethyl ether 4:1); dr 96:4. $[\alpha]^{24}_D = +15.1$ (*c* 0.56, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ 7.68 (m, 2H, H-*o*), 7.29 (m, 3H, H-*m*,*p*), 7.27 (m, 3H, H-*m*′,*p*′), 7.27 (m, 2H, H-*o*′), 5.88 (q, 1H, *J* = 6.6 Hz, H-1′), 3.39 (s, 3H, OMe), 2.01 (s, 3H, Me-5), 1.38 (d, 3H, *J* = 6.6 Hz, Me-2). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 168.1 (C-1), 141.1 (C-*i*́), 138.0 (C-*i*), 128.6 (C-*p*), 128.3 (C-*o*′ or C-*m*), 128.2 (C-*m* or C-*o*′), 127.6 (C-*p*′), 126.6 (C-*o*), 125.6 (C-*m*′), 85.8 (C-3), 80.4 (C-4), 74.4 (C-2), 73.7 (C-1′), 53.0 (OMe), 21.9 (C-2′), 3.7 (C-5). IR (CH_2Cl_2) ν_{max}: 1746.6, 1450.1, 1238.2, 1094.1, 697.7 cm^{-1}. MS (EI) *m*/*z* (%): 159 ($[M - CO_2C_8H_9]^{+\cdot}$, 100), 128 (2.9), 115 (2.9), 105 ($[PHCHMe]^{+\cdot}$, 15.7), 77 (2.6). HRESIMS calcd for $C_{20}H_{20}O_3$ + Na: 331.1310, found 331.1311.

(1*R*)-1-(1-Phenyl)ethyl (*S*)-2-Methoxy-2-phenylpent-3-ynoate 6b. Obtained in 44% yield as colorless syrup (R_f 0.4, hexane/ethyl ether 4:1); dr 95:05. $[\alpha]^{24}_D = +186.8$ (*c* 0.42, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ 7.63 (m, 2H, H-*o*), 7.32 (m, 3H, H-*m*,*p*), 7.19 (m, 3H, H-*m*′,*p*′), 7.01 (m, 2H, H-*o*′), 5.85 (q, 1H, *J* = 6.6 Hz, H-1′), 3.37 (s, 3H, OMe), 2.03 (s, 3H, Me-5), 1.48 (d, 3H, *J* = 6.6 Hz, Me-2′). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 168.4 (C-1), 140.9 (C-*i*́), 137.9 (C-*i*), 128.6 (C-*p*), 128.1 (C-*m*), 128.1 (C-*m*′), 127.5 (C-*p*′), 126.8 (C-*o*), 125.5 (C-*o*′), 85.8 (C-3), 80.3 (C-4), 74.3 (C-2), 73.8 (C-1′), 53.4 (OMe), 21.9 (C-2′), 3.8 (C-5). IR (CH_2Cl_2) ν_{max}: 1747.8, 1450.2, 1239.1, 1095.7, 697.7 cm^{-1}. MS (EI) *m*/*z* (%): 159 ($[M - CO_2C_8H_9]^{+\cdot}$, 100), 128 (2.8), 115 (2.8), 105 ($[PHCHMe]^{+\cdot}$, 16.2), 77 (2.4). HRESIMS calcd for $C_{20}H_{20}O_3$ + Na: 331.1310, found 331.1308.

(1*R*,2*S*,5*R*)-1-Isopulegoyl (*R*)-2-Methoxy-2-phenylpent-3-ynoate 7a. Obtained in 40% yield as colorless syrup (R_f 0.39 hexane-Et_2O 4:1); dr 97:3. $[\alpha]^{22}_D = -11.2$ (*c* 0.32, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ 7.64 (m, 2H, H-*o*), 7.31 (m, 3H, H-*m*,*p*), 4.79 (td, 1H, *J* = 11.0, 4.4 Hz, H-1′), 4.66 (m, 1H, H-8a′), 4.64 (m, 1H, H-8b′), 3.37 (s, 3H, OMe), 2.11 (ddd, 1H, *J* = 12.6, 11.0, 3.7 Hz, H-2′), 1.97 (s, 3H, Me-5), 1.81 (dtd, 1H, *J* = 12.2, 4.4, 1.8 Hz, H-6e′), 1.67 (m, 1H, H-3e′), 1.63 (m, 1H, H-4e′), 1.58 (dd, 3H, *J* = 1.4, 0.8 Hz, Me-9′), 1.49 (ddqd, 1H, *J* = 16.5, 13.2, 6.6, 4.4 Hz, H-5′), 1.34 (m, 1H, H-3a′), 0.87 (m, 1H, H-6a′), 0.87 (m, 1H, H-4a′), 0.85 (d, 3H, *J* = 6.6 Hz, Me-10′). ^{13}C NMR (125 MHz, $CDCl_3$): δ 168.7 (C-1), 145.6 (C-7′), 138.4 (C-*i*), 128.4 (C-*p*), 128.0 (C-*m*), 126.6 (C-*o*), 111.7 (C-8′), 85.3 (C-3), 80.4 (C-4), 75.6 (C-1′), 74.7 (C-2), 52.9 (OMe), 50.3 (C-2′), 39.5 (C-6′), 34.0 (C-4′), 31.2 (C-5′), 30.5 (C-3′), 21.9 (Me-10′), 19.5 (Me-9′), 3.7 (Me-5). IR (CH_2Cl_2) ν_{max}: 1927, 1738, 1241, 1093 cm^{-1}. MS (EI) *m*/*z* (%): 159 ($[M - CO_2C_{10}H_{17}]^{+\cdot}$, 100), 128 (2.7), 105 (5), 81 (5), 67 (6.7). HRESIMS: calcd for $C_{22}H_{28}O_3$ + Na: 363.1936, found 363.1946.

(1*R*,2*S*,5*R*)-1-Isopulegoyl (*S*)-2-Methoxy-2-phenylpent-3-ynoate 7b. Obtained in 38% yield as colorless syrup (R_f 0.42 hexane-Et_2O 4:1); dr 93:7. $[\alpha]^{24}_D = -11.6$ (*c* 0.08, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ 7.61 (m, 2H, H-*o*), 7.30 (m, 3H, H-*m*,*p*), 4.76 (td, 1H, *J* = 11.0, 4.4 Hz, H-1′), 4.41 (m, 1H, H-8a′), 4.37 (m, 1H, H-8b′), 3.36 (s, 3H, OMe), 2.01 (m, 1H, H-2′), 2.01 (s, 3H, Me-5), 1.95 (dtd, 1H, *J* = 12.0, 4.0, 1.6 Hz, H-6e′), 1.63 (m, 1H, H-3e′), 1.59 (m, 1H, H-4e′), 1.51 (m, 1H, H-5′), 1.38 (dd, 3H, *J* = 1.4, 0.8 Hz, Me-9′), 1.29 (m, 1H, H-3a′), 1.01 (q, 1H, *J* = 12.0 Hz, H-6a′). 0.90 (d, 3H, *J* = 6.5 Hz, Me-10′), 0.89 (m, 1H, H-4a′). ^{13}C NMR (125 MHz, $CDCl_3$): δ 168.8 (C-1), 145.3 (C-7′), 138.3 (C-*i*), 128.4 (C-*p*), 128.0 (C-*m*), 126.8 (C-*o*), 111.6 (C-8′), 85.4 (C-3), 80.4 (C-4), 75.6 (C-1′), 74.7 (C-2), 53.0 (OMe), 50.1 (C-2′), 39.7 (C-6′), 34.0 (C-4′), 31.3 (C-5′), 30.6 (C-3′), 22.0 (Me-10′), 19.4 (Me-9′), 3.8 (Me-5). IR (CH_2Cl_2) ν_{max}: 2926, 1737, 1240, 1095 cm^{-1}. MS (EI) *m*/*z* (%): 159 ($[M - CO_2C_{10}H_{17}]^{+\cdot}$, 100), 128 (2.5), 105 (5), 81 (5), 67 (5.7). HRESIMS: calcd for $C_{22}H_{28}O_3$ + Na: 363.1936, found 363.1945.

(3*S*)-3-Octinyl (*R*)-2-Methoxy-2-phenylpent-3-ynoate 8a. Obtained in 76% yield as colorless syrup (R_f 0.56 hexane/AcOEt/Et_2O 85:10:5); dr 95:5. $[\alpha]^{24}_D = -49.3$ (*c* 0.15, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ 7.68 (m, 2H, H-*o*), 7.36 (m, 3H, H-*m*,*p*), 5.33 (td, 1H, *J* = 6.6, 2.2 Hz, H-3′), 3.42 (s, 3H, OMe), 2.36 (d, 1H, *J* = 2.2 Hz, H-1′), 2.01 (s, 3H, Me-5), 1.74 (m, 2H, H-4′), 1.31 (m, 2H, H-5′), 1.24 (m, 2H, H-6′), 1.22 (m, 2H, H-7′), 0.86 (t, 3H, *J* = 6.7 Hz, H-8′). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 168.5 (C-1), 137.8 (C-*i*), 128.7 (C-*p*), 128.2 (C-*m*), 126.6 (C-*o*), 85.9 (C-3), 80.4 (C-4), 80.2 (C-2′), 74.3 (C-2), 73.9 (C-1′), 65.3 (C-3′), 53.1 (OMe), 34.2 (C-4′), 31.0 (C-6′), 24.2 (C-5′), 22.4 (C-7′), 13.9 (Me-8′), 3.8 (Me-5). IR (CH_2Cl_2) ν_{max}: 2954, 2931, 1747, 1215, 1093 cm^{-1}. HRESIMS: calcd for $C_{20}H_{24}O_3$: 312.1725, found 312.1726.

(3*S*)-3-Octinyl (*S*)-2-Methoxy-2-phenylpent-3-ynoate 8b. Obtained in 60% yield as colorless syrup (R_f 0.56 hexane/AcOEt/Et_2O 85:10:5); dr 94:6. $[\alpha]^{19}_D = -33.1$ (*c* 0.46, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ 7.68 (m, 2H, H-*o*), 7.35 (m, 3H, H-*m*,*p*), 5.33 (td, 1H, *J* = 6.5, 2.2 Hz, H-3′), 3.40 (s, 3H, OMe), 2.43 (d, 1H, *J* = 2.2 Hz, H-1′), 2.03 (s, 3H, Me-5), 1.64 (m, 2H, H-4′), 1.18 (m, 2H, H-7′), 1.16 (m, 2H, H-6′), 1.13 (m, 2H, H-5′), 0.81 (t, 3H, *J* = 6.7 Hz, H-8′). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 168.3 (C-1), 137.9 (C-*i*), 128.7 (C-*p*), 128.2 (C-*m*), 126.7 (C-*o*), 86.2 (C-3), 80.4 (C-4), 80.2 (C-2′), 73.9 (C-2), 73.9 (C-1′), 65.3 (C-3′), 53.3 (OMe), 34.2 (C-4′), 30.9 (C-6′), 24.0 (C-5′), 22.3 (C-7′), 13.8 (Me-8′), 3.8 (Me-5). IR (CH_2Cl_2) ν_{max}: 2954, 2932, 1748, 1210, 1094 cm^{-1}. HRESIMS: calcd for $C_{20}H_{24}O_3$: 312.1725, found 312.1727.

(2*S*)-2-Penten-4-yl (*R*)-2-Methoxy-2-phenylpent-3-ynoate 9a. Obtained in 45% yield as colorless syrup (R_f 0.50 hexane/AcOEt/Et_2O 85:10:5); dr 95:5. $[\alpha]^{21}_D = +13.0$ (*c* 0.24, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ 7.66 (m, 2H, H-*o*), 7.33 (m, 3H, H-*m*,*p*), 5.45 (m, 1H, H-4′), 4.95 (q, 1H, *J* = 6.2 Hz, H-2′), 4.89 (dd, 1H, *J* = 2.2, 1.1 Hz, H-5a′), 4.85 (m, 1H, H-5b′), 3.39 (s, 3H, OMe), 2.17 (m, 2H, H-3′), 2.02 (s, 3H, Me-5), 1.19 (d, 3H, *J* = 6.3 Hz, Me-1′). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 168.8 (C-1), 138.2 (C-*i*), 133.0 (C-4′), 128.5 (C-*p*), 128.1 (C-*m*), 126.7 (C-*o*), 117.7 (C-5′), 85.6 (C-3), 80.4 (C-4), 74.5 (C-2), 72.1 (C-2′), 53.0 (OMe), 39.8 (C-3′), 19.0 (Me-1′), 3.7 (Me-5). IR (CH_2Cl_2) ν_{max}: 1739, 1239, 1093 cm^{-1}. MS (EI) *m*/*z* (%): 159 ($[M - CO_2C_{10}H_{17}]^{+\cdot}$, 100), 128 (2.7), 115 (3.7), 105 (4.9), 67 (4.6). HRESIMS: calcd for $C_{17}H_{20}O_3$ + Na: 295.1310, found 295.1314.

(2*S*)-2-Penten-4-yl (*S*)-2-Methoxy-2-phenylpent-3-ynoate 9b. Obtained in 52% yield as colorless syrup (R_f 0.50 hexane/AcOEt/Et_2O 85:10:5); dr 94:6. $[\alpha]^{23}_D = +9.1$ (*c* 0.12, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ 7.66 (m, 2H, H-*o*), 7.34 (m, 3H, H-*m*,*p*), 5.67 (ddt, 1H, *J* = 17.1, 10.2, 7.0 Hz, H-4′), 5.03 (ddt, 1H, *J* = 10.2, 1.9, 1.5 Hz, H-5b′), 4.99 (m, 1H, H-5a′), 4.96 (q, 1H, *J* = 6.3 Hz, H-2′), 3.39 (s, 3H, OMe), 2.26 (m, 2H, H-3′), 2.00 (s, 3H, Me-5), 1.08 (d, 3H, *J* = 6.3 Hz, Me-1′). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 168.8 (C-1), 138.2 (C-*i*), 133.2 (C-4′), 128.2 (C-*p*), 128.1 (C-*m*), 126.6 (C-*o*), 117.7 (C-5′), 85.5 (C-3), 80.4 (C-4), 74.6 (C-2), 72.0 (C-2′), 53.0 (OMe), 39.9 (C-3′), 18.9 (Me-1′), 3.7 (Me-5). IR (CH_2Cl_2) ν_{max}: 1740, 1241, 1094 cm^{-1}. MS (EI) *m*/*z* (%): 159 ($[M - CO_2C_{10}H_{17}]^{+\cdot}$, 100), 128 (3.0), 115 (2.2), 105 (5.3), 67 (6.4). HRESIMS: calcd for $C_{17}H_{20}O_3$ + Na: 295.1310, found 295.1316.

(1*S*,2*R*,5*S*)-Menthyl (*R*)-2-Methoxy-2-phenylpent-3-ynoate 10a. Obtained in 45% yield as colorless syrup (R_f 0.54, hexane/ethyl ether 4:1); dr 95:5. $[\alpha]^{24}_D = +63.9$ (*c* 0.52, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ 7.65 (m, 2H, H-*o*), 7.32 (m, 3H, H-*m*,*p*), 4.60 (td, 1H, *J* = 11.6, 4.3 Hz, H-1′), 3.38 (s, 3H, OMe), 2.03 (s, 3H, Me-5), 1.96 (tdt, 1H, *J* = 11.6, 4.2, 1.9 Hz, H-6a′), 1.63 (m, 1H, H-4a′), 1.56 (dq, 1H, *J* = 13.2, 3.3 Hz, H-3a′), 1.45 (m, 1H, H-5′), 1.26 (tt, 1H, *J* = 11.6, 2.6 Hz, H-2′), 1.09 (sept-d, 1H, *J* = 7.0, 2.6 Hz, H-7′), 0.98 (q, 1H, *J* = 11.6 Hz,

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H-6b′), 0.93 (dq, 1H, J = 13.2, 3.0 Hz, H-3b′), 0.88 (d, 3H, J = 6.6 Hz, Me-10′), 0.82 (m, 1H, H-4b′), 0.61 (d, 3H, J = 7.0 Hz, Me-8′), 0.43 (d, 3H, J = 7.0 Hz, Me-9′). ^{13}C NMR (125 MHz, $CDCl_3$): δ 168.8 (C-1), 138.2 (C-*i*), 128.5 (C-*p*), 128.0 (C-*m*), 126.8 (C-*o*), 85.7 (C-3), 80.3 (C-4), 76.1 (C-1′), 74.4 (C-2), 52.9 (OMe), 46.8 (C-2′), 40.1 (C-6′), 34.1 (C-4′), 31.3 (C-5′), 25.3 (C-7′), 22.9 (C-3′), 21.9 (C-10′), 20.5 (C-9′), 15.6 (C-8′), 3.8 (Me-5). IR (CH_2Cl_2) ν_{max}: 2953.2, 1741.1, 1449.5, 1240−5, 1096.4, 1012.9 cm^{-1}. MS (EI) m/z (%): 311 ([M − OMe]$^{+\cdot}$, 2.4), 159 ([M − $CO_2C_{10}H_{19}$]$^{+\cdot}$, 100), 128 (2.3), 115 (2.5), 105 (3.1). HRESIMS calcd for $C_{22}H_{30}O_3$ + Na: 365.2092, found 365.2098.

(1*S*,2*R*,5*S*)-Menthyl (*S*)-2-Methoxy-2-phenylpent-3-ynoate 10b. Obtained in 50% yield as colorless syrup (R_f 0.54, hexane/ethyl ether 4:1); dr 91:9. $[\alpha]^{26}_D$ = +63.0 (c 0.24, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.65 (m, 2H, H-*o*), 7.33 (m, 3H, H-*m*,*p*), 4.67 (td, 1H, J = 10.9, 4.4 Hz, H-1′), 3.39 (s, 3H, OMe), 1.99 (s, 3H, Me-5), 1.79 (m, 1H, H-6a′), 1.76 (sept-d, 1H, J = 7.0, 2.8 Hz, H-7′), 1.62 (m, 1H, H-4a′), 1.60 (m, 1H, H-3a′), 1.43 (m, 1H, H-5′), 1.36 (tt, 1H, J = 11.7, 3.1 Hz, H-2′), 1.00 (qd, 1H, J = 13.0, 3.3 Hz, H-3b′), 0.83 (d, 3H, J = 6.5 Hz, Me-10′), 0.82 (d, 3H, J = 7.0 Hz, Me-8′), 0.79 (m, 1H, H-6b′), 0.79 (m, 1H, H-4b′), 0.67 (d, 3H, J = 7.0 Hz, Me-9′). ^{13}C NMR (125 MHz, $CDCl_3$): δ 168.8 (C-1), 138.3 (C-*i*), 128.5 (C-*p*), 128.1 (C-*m*), 126.5 (C-*o*), 85.4 (C-3), 80.4 (C-4), 76.1 (C-1′), 74.8 (C-2), 52.9 (OMe), 47.0 (C-2′), 39.9 (C-6′), 34.1 (C-4′), 31.3 (C-5′), 25.9 (C-7′), 23.3 (C-3′), 21.9 (C-10′), 20.6 (C-9′), 16.1 (C-8′), 3.6 (Me-5). IR (CH_2Cl_2) ν_{max}: 2954, 1739, 1450, 1240, 1095, cm^{-1}. HREIMS calcd for $C_{22}H_{30}O_3$: 342.2195, found 342.2207.

(1*R*,2*S*,5*R*)-Menthyl (*R*)-2-Methoxy-2-phenylpent-3-ynoate 11a. Obtained in 53% yield as colorless syrup (R_f 0.54, hexane/ethyl ether 4:1); dr 97:3. $[\alpha]^{24}_D$ = −51.4 (c 0.53, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.65 (m, 2H, H-*o*), 7.33 (m, 3H, H-*m*,*p*), 4.67 (td, 1H, J = 11.3, 4.4 Hz, H-1′), 3.39 (s, 3H, OMe), 1.99 (s, 3H, Me-5), 1.79 (m, 1H, H-6a′), 1.76 (sept-d, 1H, J = 7.0, 2.5 Hz, H-7′), 1.62 (m, 1H, H-4a′), 1.60 (m, 1H, H-3a′), 1.43 (m, 1H, H-5′), 1.36 (tt, 1H, J = 11.3, 2.5 Hz, H-2′), 1.00 (qd, 1H, J = 13.0, 3.3 Hz, H-3b′), 0.83 (d, 3H, J = 6.5 Hz, Me-10′), 0.82 (d, 3H, J = 7.0 Hz, Me-8′), 0.79 (m, 1H, H-6b′), 0.79 (m, 1H, H-4b′), 0.67 (d, 3H, J = 7.0 Hz, Me-9′). ^{13}C NMR (125 MHz, $CDCl_3$): δ 168.8 (C-1), 138.3 (C-*i*), 128.5 (C-*p*), 128.1 (C-*m*), 126.5 (C-*o*), 85.4 (C-3), 80.4 (C-4), 76.1 (C-1′), 74.8 (C-2), 52.9 (OMe), 47.0 (C-2′), 39.9 (C-6′), 34.1 (C-4′), 31.3 (C-5′), 25.9 (C-7′), 23.3 (C-3′), 21.9 (C-10′), 20.6 (C-9′), 16.1 (C-8′), 3.6 (Me-5). IR (CH_2Cl_2) ν_{max}: 29534.7 1740.4 1450.5, 1240.4, 1095.9, 999.0 cm^{-1}. MS (EI) m/z (%): 311 ([M − OMe]$^{+\cdot}$, 2.3), 159 ([M − $CO_2C_{10}H_{19}$]$^{+\cdot}$, 100), 128 (2.8), 115 (2.3), 105 (2.6). HRESIMS calcd for $C_{22}H_{30}O_3$ + Na: 365.2092, found 365.2084.

(1*R*,2*S*,5*R*)-Menthyl (*S*)-2-Methoxy-2-phenylpent-3-ynoate 11b. Obtained in 48% yield as colorless syrup (R_f 0.54, hexane/ethyl ether 4:1); dr 93:7. $[\alpha]^{23}_D$ = −65.2 (c 0.18, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.65 (m, 2H, H-*o*), 7.32 (m, 3H, H-*m*,*p*), 4.60 (td, 1H, J = 11.6, 4.2 Hz, H-1′), 3.38 (s, 3H, OMe), 2.03 (s, 3H, Me-5), 1.96 (dtd, 1H, J = 11.6, 4.2, 1.9 Hz, H-6a′), 1.63 (m, 1H, H-4a′), 1.56 (dq, 1H, J = 13.2, 3.3 Hz, H-3a′), 1.45 (m, 1H, H-5′), 1.26 (tt, 1H, J = 11.6, 3.2 Hz, H-2′), 1.09 (sept-d, 1H, J = 7.0, 2.8 Hz, H-7′), 0.98 (q, 1H, J = 11.6 Hz, H-6b′), 0.93 (qd, 1H, J = 13.1, 3.0 Hz, H-3b′), 0.88 (d, 3H, J = 6.6 Hz, Me-10′), 0.82 (m, 1H, H-4b′), 0.61 (d, 3H, J = 7.0 Hz, Me- 8′), 0.43 (d, 3H, J = 7.0 Hz, Me-9′). ^{13}C NMR (125 MHz, $CDCl_3$): δ 186.8 (C-1), 138.2 (C-*i*), 128.5 (C-*p*), 128.1 (C-*m*), 126.8 (C-*o*), 85.7 (C-3), 80.3 (C-4), 76.1 (C-1′), 74.4 (C-2), 52.9 (OMe), 46.8 (C-2′), 40.1 (C-6′), 34.1 (C-4′), 31.3 (C-5′), 25.3 (C-7′), 23.0 (C-3′), 22.0 (C-10′), 20.5 (C-9′), 15.6 (C-8′), 3.8 (Me-5). IR (CH_2Cl_2) ν_{max}: 1254, 1740, 1450, 1240, 1096 cm^{-1}. HREIMS calcd for $C_{22}H_{30}O_3$: 342.2195, found 342.2184.

(1*S*,2*R*)-Bornyl (*R*)-2-Methoxy-2-phenylpent-3-ynoate 12a. Obtained in 41% yield as colorless syrup (R_f 0.42, hexane/ethyl ether 4:1); dr 87:13. $[\alpha]^{24}_D$ = −7.4 (c 0.53, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.69 (m, 2H, H-*o*), 7.34 (m, 3H, H-*m*,*p*), 4.85 (ddd, 1H, J = 10.1, 3.1, 1.9 Hz, H-2′), 3.42 (s, 3H, OMe), 2.20 (m, 1H, H-3a′), 2.02 (s, 3H, Me-5), 1.81 (ddd, 1H, J = 13.1, 9.3, 3.9 Hz, H-6a′), 1.63 (m, 1H, H-5a′), 1.57 (m, 1H, H-4′), 1.20 (m, 1H, H-6b′), 0.92 (m, 1H, H-5b′), 0.84 (s, 3H, Me-9′), 0.82 (s, 3H, Me-8′), 0.79 (s, 3H, Me-10′), 0.63 (dd, 1H, J = 13.9, 3.79 Hz, H-3b′). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 169.4 (C-1), 138.3 (C-*i*), 128.5 (C-*p*), 128.1 (C-*m*), 126.6 (C-*o*), 85.4 (C-3), 81.4 (C-2′), 80.3 (C-4), 74.6 (C-2), 53.0 (OMe), 49.0 (C-7′), 47.7 (C-1′), 44.7 (C-4′), 36.0 (C-3′), 27.7 (C-6′), 26.8 (C-5′), 19.5 (Me-9′), 18.8 (Me-8′), 13.3 (Me-10′), 3.7 (Me-5). IR (CH_2Cl_2) ν_{max}: 2953.8, 1741.9, 1450.8, 1241.2, 1097.8, 1021.4 cm^{-1}. MS (EI) m/z (%): 159 ([M − $CO_2C_{10}H_{17}$]$^{+\cdot}$, 100), 128 (3.5), 115 (3.1), 105 (3.7), 81 (5.5), 67 (4.7). HRESIMS calcd for $C_{22}H_{28}O_3$ + Na: 363.1936, found 363.1940.

(1*S*,2*R*)-Bornyl (*S*)-2-Methoxy-2-phenylpent-3-ynoate 12b. Obtained in 49% yield as colorless syrup (R_f 0.42, hexane/ethyl ether 4:1); dr 71:29. $[\alpha]^{24}_D$ = −28.8 (c 0.56, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.70 (m, 2H, H-*o*), 7.34 (m, 3H, H-*m*,*p*), 4.81 (ddd, 1H, J = 10.0, 3.0, 2.0 Hz, H-2′), 4.42 (s, 3H, OMe), 2.29 (m, 1H, H-3a′), 2.03 (s, 3H, Me-5), 1.72 (m, 1H, H-6a′), 1.63 (m, 1H, H-5a′), 1.63 (m, 1H, H-4′), 1.14 (m, 1H, H-5b′), 1.14 (m, 1H, H-6b′), 0.91 (dd, 1H, J = 13.7, 3.8 Hz, H-3b′), 0.84 (s, 3H, Me-9′), 0.81 (s, 3H, Me-8′), 0.58 (s, 3H, Me-10′). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 169.4 (C-1), 138.4 (C-*i*), 128.5 (C-*p*), 128.1 (C-*m*), 126.1 (C-*o*), 85.5 (C-3), 81.5 (C-2′), 80.4 (C-4), 74.5 (C-2), 53.0 (OMe), 48.9 (C-7′), 47.7 (C-1′), 44.7 (C-4′), 36.2 (C-3′), 27.8 (C-6′), 26.7 (C-5′), 19.5 (Me-9′), 18.8 (Me-8′), 13.1 (Me-10′), 3.7 (Me-5). IR (CH_2Cl_2) ν_{max}: 2953.8, 1741.9, 1450.9, 1241.9, 1097.7, 1021.5 cm^{-1}. MS (EI) m/z (%): 159 ([M − $CO_2C_{10}H_{17}$]$^{+\cdot}$, 100) 128 (2.3), 105 (2.6), 81 (2.2), 67 (2.3). HRESIMS calcd for $C_{22}H_{28}O_3$ + Na: 363.1936, found 363.1935.

(1*R*,2*S*,4*S*)-2-Fenchyl (*R*)-2-Methoxy-2-phenylpent-3-ynoate 13a. Obtained in 42% yield as colorless syrup (R_f 0.56 hexane/Et_2O 4:1); dr 88:12. $[\alpha]^{23}_D$ = +21.5 (c 0.28, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.70 (m, 2H, H-*o*), 7.32 (m, 3H, H-*m*,*p*), 4.27 (d, 1H, J = 1.9 Hz, H-2′), 3.42 (s, 3H, OMe), 2.01 (s, 3H, Me-5), 1.67 (m, 1H, H-4′), 1.62 (m, 1H, H-5a′), 1.51 (m, 1H, H-6a′), 1.49 (m, 1H, H-7a′), 1.38 (tdd, 1H, J = 12.4, 5.7, 4.0 Hz, H-5b′), 1.09 (dd, 1H, J = 10.4, 1.5 Hz, H-7b′), 1.06 (s, 3H, Me-9′), 0.90 (tdd, 1H, J = 12.4, 3.4, 2.0 Hz, H-6b′), 0.71 (s, 3H, Me-10′), 0.69 (s, 3H, Me-8′). ^{13}C NMR (125 MHz, $CDCl_3$): δ 169.6 (C-1), 138.6 (C-*i*), 128.5 (C-*p*), 128.1 (C-*m*), 126.7 (C-*o*), 87.6 (C-2′), 85.5 (C-3), 80.3 (C-4), 74.7 (C-2), 53.0 (OMe), 48.4 (C-1′), 48.3 (C-4′), 41.1 (C-7′), 39.7 (C-3′), 29.5 (Me-9′), 26.2 (C-6′), 25.7 (C-5′), 19.9 (Me-10′), 18.9 (Me-8′), 3.6 (Me-5). IR (CH_2Cl_2) ν_{max}: 2956, 1743, 1242, 1098 cm^{-1}. MS (EI) m/z (%): 188 (4.3), 159 ([M − $CO_2C_{10}H_{17}$]$^{+\cdot}$, 100), 128 (3.2), 105 (4.6), 81 (7.7), 67 (6.7). HRESIMS: calcd for $C_{22}H_{28}O_3$ + Na: 363.1936, found 363.1946.

(1*R*,2*S*,4*S*)-2-Fenchyl (*S*)-2-Methoxy-2-phenylpent-3-ynoate 13b. Obtained in 40% yield as colorless syrup (R_f 0.56 hexane/Et_2O 4:1); dr 87:13. $[\alpha]^{22}_D$ = −8.1 (c 0.12, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.70 (m, 2H, H-*o*), 7.33 (m, 3H, H-*m*,*p*), 4.32 (d, 1H, J = 1.9 Hz, H-2′), 3.41 (s, 3H, OMe), 2.01 (s, 3H, Me-5), 1.63 (m, 1H, H-6a′), 1.61 (m, 1H, H-4′), 1.51 (m, 1H, H-7a′), 1.48 (m, 1H, H-5a′), 1.35 (tdd, 1H, J = 12.4, 5.9, 4.0 Hz, H-5b′), 1.12 (dd, 1H, J = 10.3, 1.5 Hz, H-7b′), 1.003 (tdd, 1H, J = 12.4, 3.3, 2.1 Hz, H-6b′), 0.999 (s, 3H, Me-8′), 0.98 (s, 3H, Me-9′), 0.25 (s, 3H, Me-10′). RMN ^{13}C (125 MHz, $CDCl_3$): δ 169.6 (C-1), 138.4 (C-*i*), 128.5 (C-*p*), 128.1 (C-*m*), 126.9 (C-*o*), 87.7 (C-2′), 85.5 (C-3), 80.3 (C-4), 74.8 (C-2), 53.0 (OMe), 48.6 (C-1′), 48.2 (C-4′), 41.1 (C-7′), 39.5 (C-3′), 29.5 (Me-9′), 26.3 (C-6′), 25.6 (C-5′), 19.5 (Me-10′), 19.1(Me-8′), 3.6 (Me-5). IR (CH_2Cl_2) ν_{max}: 2956, 17343, 1242, 1098 cm^{-1}. MS (EI) m/z (%): 188 (4.2), 159 ([M − $CO_2C_{10}H_{17}$]$^{+\cdot}$, 100), 128 (3.0), 105 (4.9), 81 (7.5), 67 (6.5). HRESIMS: calcd for $C_{22}H_{28}O_3$ + Na: 363.1936, found 363.1943.

(3*R*)-3-Tetrahydrofuranyl (*R*)-2-Methoxy-2-phenylpent-3-ynoate 14a. Obtained in 21% yield as colorless syrup (R_f 0.16 hexane/AcOEt/CH_2Cl_2 8:1:1); dr 95:5. $[\alpha]^{23}_D$ = +17.0 (c 0.08, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.66 (m, 2H, H-*o*), 7.35 (m, 3H, H-*m*,*p*), 5.30 (ddt, 1H, J = 6.3, 4.7, 1.7 Hz, H-3′), 3.90 (dd, 1H, J = 10.6, 4.7 Hz, H-2a′), 3.77 (dd, 1H, J = 10.6, 1.7 Hz, H-2b′), 3.76 (td, 1H, J = 8.4, 3.8 Hz, H-5a′), 3.64 (td, 1H, J = 8.4, 6.5 Hz, H-5b′), 3.38 (s, 3H, OMe), 2.03 (m, 1H, H-4a′), 2.02 (s, 3H, Me-5), 1.74 (m, 1H, H-4b′). ^{13}C NMR (125 MHz, $CDCl_3$): δ 169.1 (C-1), 137.9 (C-*i*), 128.7 (C-*p*), 128.3 (C-*m*), 126.7 (C-*o*), 86.0 (C-3), 80.3 (C-4), 76.4 (C-3′), 74.1 (C-2), 72.6 (C-2′), 66.9 (C-5′), 53.0 (OMe), 32.6 (C-4′),

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3.8 (C-5). IR (CH_2Cl_2) ν_{max}: 1741, 1239, 1088 cm^{-1}. HREIMS calcd for $C_{16}H_{18}O_4$: 274.1205, found 274.1213.

(3*R*)-3-Tetrahydrofuranyl (*S*)-2-Methoxy-2-phenylpent-3-ynoate 14b. Obtained in 21% yield as colorless syrup (R_f 0.16 hexane/AcOEt/CH_2Cl_2 8:1:1); dr 96:4. $[\alpha]^{26}_D$ = −5.0 (*c* 0.13, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ 7.66 (m, 2H, H-*o*), 7.35 (m, 3H, H-*m*,*p*), 5.29 (m, 1H, H-3′), 3.85 (dd, 1H, *J* = 10.6, 4.8 Hz, H-2a′), 3.81 (td, 1H, *J* = 8.5, 3.9 Hz, H-5a′), 3.77 (td, 1H, *J* = 8.5, 6.5 Hz, H-5b′), 3.59 (dd, 1H, *J* = 10.6, 0.6 Hz, H-2b′), 3.39 (s, 3H, OMe), 2.10 (m, 1H, H-4a′), 2.02 (s, 3H, Me-5), 1.96 (m, 1H, H-4b′). ^{13}C NMR (125 MHz, $CDCl_3$): δ 169.2 (C-1), 137.8 (C-*i*), 128.7 (C-*p*), 128.3 (C-*m*), 126.7 (C-*o*), 86.9 (C-3), 80.3 (C-4), 76.4 (C-3′), 74.2 (C-2), 72.6 (C-2′), 66.9 (C-5′), 53.0 (OMe), 32.7 (C-4′), 3.7 (C-5). IR (CH_2Cl_2) ν_{max}: 1740, 1218, 1085 cm^{-1}. HREIMS calcd for $C_{16}H_{18}O_4$: 274.1205, found 274.1212.

(2*R*)-2-(1-Methyloxycarbonyl)butyl (*R*)-2-Methoxy-2-phenylpent-3-ynoate 15a. Obtained in 20% yield as colorless syrup (R_f 0.16 hexane/acetone 9:1); 94:6. $[\alpha]^{20}_D$ = −1.4 (*c* 0.24, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ 7.66 (m, 2H, H-*o*), 7.33 (m, 3H, H-*m*,*p*), 5.18 (tt, 1H, *J* = 7.7, 5.3 Hz, H-3′), 3.60 (s, 3H, OMe′), 3.39 (s, 3H, OMe), 2.59 (dd, 1H, *J* = 15.6, 7.7 Hz, H-2a′), 2.50 (dd, 1H, *J* = 15.6, 5.3 Hz, H-2b′), 2.01 (s, 3H, Me-5′), 1.51 (m, 2H, H-4′), 0.62 (t, 3H, *J* = 7.4 Hz, Me-5′). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.4 (C-1′), 168.7 (C-1), 138.2 (C-*i*), 128.6 (C-*p*), 128.2 (C-*m*), 126.7 (C-*o*), 85.7 (C-3), 80.3 (C-4), 74.3 (C-2), 73.6 (C-3′), 53.0 (OMe), 51.6 (OMe′), 38.5 (C-2′), 26.6 (C-4′), 8.8 (C-5′), 3.7 (C-5). IR (CH_2Cl_2) ν_{max}: 1742, 1237, 1091 cm^{-1}. HREIMS calcd for $C_{18}H_{22}O_5$: 318.1467, found 318.1472.

(2*R*)-2-(1-Methyloxycarbonyl)butyl (*S*)-2-Methoxy-2-phenylpent-3-ynoate 15b. Obtained in 20% yield as colorless syrup (R_f 0.17 hexane/acetone 9:1); 91:9. $[\alpha]^{25}_D$ = −32.5 (*c* 0.06, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ 7.65 (m, 2H, H-*o*), 7.33 (m, 3H, H-*m*,*p*), 5.19 (tt, 1H, *J* = 7.8, 5.2 Hz, H-3′), 3.43 (s, 3H, OMe′), 3.38 (s, 3H, OMe), 2.48 (dd, 1H, *J* = 15.7, 7.8 Hz, H-2a′), 2.40 (dd, 1H, *J* = 15.7, 5.2 Hz, H-2b′), 2.01 (s, 3H, Me-5′), 1.63 (m, 2H, H-4′), 0.85 (t, 3H, *J* = 7.4 Hz, Me-5′). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.3 (C-1′), 168.6 (C-1), 138.1 (C-*i*), 128.5 (C-*p*), 128.1 (C-*m*), 126.7 (C-*o*), 85.6 (C-3), 80.3 (C-4), 74.5 (C-2), 73.3 (C-3′), 52.9 (OMe), 51.6 (OMe′), 38.2 (C-2′), 26.7 (C-4′), 8.9 (C-5′), 3.7 (C-5). IR (CH_2Cl_2) ν_{max}: 1740, 1238, 1091 cm^{-1}. HREIMS calcd for $C_{18}H_{22}O_5$: 318.1467, found 318.1473.

Longipinenoyl (*R*)-2-Methoxy-2-phenylpent-3-ynoate 16a. Obtained in 14% yield as colorless syrup (R_f 0.22 hexane/acetone 4:1); dr 93:7. $[\alpha]^{25}_D$ = +60.0 (*c* 0.03, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ 7.72 (m, 2H, H-*o*), 7.36 (m, 2H, H-*m*), 7.30 (m, 1H, H-*p*), 5.75 (q, 1H, *J* = 1.5 Hz, H-9′), 5.00 (t, 1H, *J* = 3.4 Hz, H-2′), 4.86 (dd, 1H, *J* = 11.9, 1.8 Hz, H-4′), 3.46 (s, 3H, OMe), 3.04 (dd, 1H, *J* = 6.7, 0.9 Hz, H-7′), 2.57 (d, 1H, *J* = 6.7 Hz, H-11′), 2.24 (s, 1H, H-6′), 2.15 (ddd, 1H, *J* = 15.1, 11.9, 3.4 Hz, H-3a′), 2.02 (s, 3H, Me-5), 2.00 (d, 3H, *J* = 1.5 Hz, Me-15′), 1.98 (s, 3H, OAc′), 1.85 (ddd, 1H, *J* = 15.1, 3.4, 1.8 Hz, H-3b′), 0.96 (s, 3H, Me-13′), 0.84 (s, 3H, Me-14′), 0.78 (s, 3H, Me-12′). ^{13}C NMR (125 MHz, $CDCl_3$): δ 202.5 (C-8′), 170.0 (O<u>CO</u>Me), 169.2 (C-10′), 169.1 (C-1′), 137.8 (C-*i*), 128.6 (C-*p*), 128.3 (C-*m*), 126.8 (C-*o*), 122.8 (C-9′), 86.2 (C-3), 80.7 (C-4), 76.9 (C-2′), 74.6 (C-2), 72.1(C-4′), 65.7 (C-6′), 56.0 (C-1′), 53.40 (C-7′), 53.36 (OMe), 48.3 (C-11′), 37.5 (C-5′), 32.4 (C-3′), 26.3 (Me-14′), 23.3 (Me-15′), 21.0 (OCO<u>Me</u>), 20.5 (Me-12′), 19.3 (Me-13′), 3.7 (Me-5). HREIMS calcd for $C_{29}H_{34}O_6$: 478.2355, found 478.2358.

Longipinenoyl (*S*)-2-Methoxy-2-phenylpent-3-ynoate 16b. Obtained in 14% yield as colorless syrup (R_f 0.22 hexane/acetone 4:1); dr 95:5. $[\alpha]^{23}_D$ = +86.7 (*c* 0.11, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ 7.71 (m, 2H, H-*o*), 7.34 (m, 2H, H-*m*), 7.28 (tt, 1H, *J* = 7.3, 1.3 Hz, H-*p*), 5.69 (q, 1H, *J* = 1.5 Hz, H-9′), 5.12 (dd, 1H, *J* = 12.0, 1.8 Hz, H-4′), 4.86 (t, 1H, *J* = 3.1 Hz, H-2′), 3.44 (s, 3H, OMe), 3.01 (dd, 1H, *J* = 6.8 Hz, H-7′), 2.52 (d, 1H, *J* = 6.8 Hz, H-11′), 2.23 (s, 1H, H-6′), 2.20 (ddd, 1H, *J* = 15.1, 12.0, 3.1 Hz, H-3a′), 2.07 (s, 3H, Me-5), 2.05 (s, 3H, OAc′), 2.03 (ddd, 1H, *J* = 15.1, 3.1, 1.8 Hz, H-3b′), 1.96 (d, 3H, *J* = 1.5 Hz, Me-15′), 0.99 (s, 3H, Me-13′), 0.88 (s, 3H, Me-14′), 0.32 (s, 3H, Me-12′). ^{13}C NMR (125 MHz, $CDCl_3$): δ 202.4 (C-8′), 169.9 (O<u>CO</u>Me), 169.4 (C-10′), 168.7 (C-1), 137.9 (C-*i*), 128.7 (C-*p*), 128.3 (C-*m*), 126.8 (C-*o*), 122.6 (C-9′), 86.6 (C-3), 80.1 (C-4), 76.6 (C-2′), 73.5 (C-2), 71.9 (C-4′), 65.7 (C-6′), 55.6 (C-1′), 53.3 (C-7′), 53.0 (OMe), 48.2 (C-11′), 37.5 (C-5′), 32.6 (C-3′), 26.3 (Me-14′), 23.2 (Me-15′), 21.1 (OCO<u>Me</u>), 20.2 (Me-12′), 19.0 (Me-13′), 3.7 (Me-5). HREIMS calcd for $C_{29}H_{34}O_6$: 478.2355, found 478.2351.

3α-Tibolol-3-yl (*R*)-2-Methoxy-2-phenylpent-3-ynoate 17a. Obtained in 14% yield as colorless syrup (R_f 0.23 hexane/acetone 4:1); dr 97:3. $[\alpha]^{26}_D$ = +178.0 (*c* 0.08, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ 7.67 (m, 2H, H-*o*), 7.34 (m, 3H, H-*m*,*p*), 4.90 (dddd, 1H, *J* = 11.4, 9.1, 5.7, 3.4 Hz, H-3′), 3.39 (s, 3H, OMe), 2.57 (s, 1H, H-19′), 2.29 (ddd, 1H, *J* = 13.8, 9.5, 5.6 Hz, H-16a′), 2.19 (m, 1H, H-4a′), 2.09 (m, 1H, H-1a′), 2.02 (s, 3H, Me-5), 1.97 (m, 1H, H-16b′), 1.92 (m, 1H, H-1b′), 1.78 (m, 1H, H-2a′), 1.55 (m, 1H, H-4b′), 1.40 (m, 1H, H-2b′), 1.13 (qd, 1H, *J* = 13.0, 3.9 Hz, H-11b′), 0.85 (s, 3H, Me-21′), 0.76 (d, 3H, *J* = 7.0 Hz, Me-20′). ^{13}C NMR (125 MHz, $CDCl_3$): δ 169.0 (C-1), 138.4 (C-*i*), 128.6 (C-10′), 128.5 (C-*p*), 128.2 (C-*m*), 126.7 (C-*o*), 123.4 (C-5′), 87.6 (C-18′), 85.6 (C-3), 80.5 (C-4), 79.9 (C-17′), 74.6 (C-2), 73.8 (C-19′), 72.8 (C-3′), 53.0 (OMe), 47.4 (C-13′), 46.2 (C-14′), 41.6 (C-8′), 39.7 (C-9′), 39.0 (C-16′), 38.5 (C-4′), 36.0 (C-6′), 33.0 (C-12′), 28.0 (C-2′), 27.1 (C-7′), 26.0 (C-1′), 25.2 (C-11′), 22.0 (C-15′), 12.81 (Me-20′), 12.79 (Me-21′), 3.8 (Me-5). HREIMS calcd for $C_{33}H_{40}O_4$: 500.2927, found 500.2946.

3α-Tiboloyl (*S*)-2-Methoxy-2-phenylpent-3-ynoate 17b. Obtained in 15% yield as colorless syrup (R_f 0.22 hexane/acetone 4:1). $[\alpha]^{25}_D$ = +28.0 (*c* 0.10, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ 7.67 (m, 2H, H-*o*), 7.34 (m, 3H, H-*m*,*p*), 4.89 (dddd, 1H, *J* = 11.4, 9.1, 5.7, 3.4 Hz, H-3′), 3.39 (s, 3H, OMe), 2.57 (s, 1H, H-19′), 2.29 (ddd, 1H, *J* = 13.8, 9.5, 5.6 Hz, H-16a′), 2.14 (m, 1H, H-1a′), 2.11 (m, 1H, H-4a′), 2.02 (s, 3H, Me-5), 1.95 (m, 1H, H-1b′), 1.92 (m, 1H, H-2a′), 1.58 (m, 1H, H-2b′), 1.48 (m, 1H, H-4b′), 1.14 (qd, 1H, *J* = 13.0, 3.8 Hz, H-11b′), 0.84 (s, 3H, Me-21′), 0.73 (d, 3H, *J* = 7.0 Hz, Me-20′). ^{13}C NMR (125 MHz, $CDCl_3$): δ 169.0 (C-1), 138.4 (C-*i*), 128.6 (C-10′), 128.5 (C-*p*), 128.2 (C-*m*), 126.7 (C-*o*), 123.5 (C-5′), 87.6 (C-18′), 85.6 (C-3), 80.5 (C-4), 79.9 (C-17′), 74.7 (C-2), 73.8 (C-19′), 72.8 (C-3′), 53.0 (OMe), 47.4 (C-13′), 46.2 (C-14′), 41.6 (C-8′), 39.7 (C-9′), 39.0 (C-16′), 38.5 (C-4′), 35.8 (C-6′), 33.0 (C-12′), 28.1 (C-2′), 27.1 (C-7′), 26.1 (C-1′), 25.2 (C-11′), 22.0 (C-15′), 12.81 (Me-20′), 12.79 (Me-21′), 3.8 (Me-5). IR (CH_2Cl_2) ν_{max}: 3293, 2935, 1738, 1245, 1094 cm^{-1}. HREIMS calcd for $C_{33}H_{40}O_4$: 500.2927, found 500.2909.

3β-Tiboloyl (*R*)-2-Methoxy-2-phenylpent-3-ynoate 18a. ^1H NMR (500 MHz, $CDCl_3$): δ 7.68 (m, 2H, H-*o*), 7.36 (m, 3H, H-*m*,*p*), 5.12 (m, 1H, H-3′), 3.44 (s, 3H, OMe), 2.61 (s, 1H, H-19′), 2.34 (m, 1H, H-16a′), 2.03 (m, 1H, H-6a′), 2.18 (m, 1H, H-1a′), 2.05 (s, 3H, Me-5), 2.04 (m, 1H, H-4a′), 2.01 (m, 1H, H-16′), 2.00 (m, 1H, H-11′), 2.03 (m, 1H, H-6a′), 1.95 (m, 1H, H-2a′), 1.80 (m, 1H, H-4b′), 1.78 (m, H-7b′), 1.76 (m, 1H, H-1b′), 1.61−1.72 (m, 4H, H-14′, H-15a′, H-9′, H-12b′), 1.61 (m, 1H, H-2b′), 1.42 (H-6b′), 1.37 (m, 1H, H-8), 1.36 (m, 1H, H-15b′), 1.14 (m, 1H, H-11b′), 0.95 (s, 3H, Me-21′), 0.77 (d, 3H, *J* = 7.0 Hz, Me-20′). ^{13}C NMR (125 MHz, $CDCl_3$): δ 168.95 (C-1), 138.54 (C-*i*), 128.39 (C-10′), 128.23 (C-*p*), 128.08 (C-*m*), 126.58 (C-*o*), 121.87 (C-5′), 87.58 (C-18′), 85.25 (C-3), 80.39 (C-2), 79.89 (C-17′), 74.63 (C-4), 73.90 (C-19′), 70.94 (C-3′), 53.05 (OMe), 47.42 (C-13′), 46.20 (C-14′), 41.69 (C-8′), 39.64 (C-9′), 38.99 (16′), 38.55 (C-6′), 35.16 (C-4′), 33.10 (C-12′), 27.10 (C-7′), 26.58 (C-1′), 25.27 (C-11′), 22.53 (C-2′), 22.05 (C-5′), 12.90 (Me-20′,21′), 3.78 (Me-5). HREIMS calcd for $C_{33}H_{40}O_4$: 500.2927, found 500.2929.

3β-Tiboloyl (*S*)-2-Methoxy-2-phenylpent-3-ynoate 18b. Obtained in 18% yield as colorless syrup. ^1H NMR (500 MHz, $CDCl_3$): δ 7.68 (m, 2H, H-*o*), 7.36 (m, 3H, H-*m*,*p*), 5.10 (m, 1H, H-3′), 3.43 (s, 3H, OMe), 2.61 (s, 1H, H-19′), 2.34 (m, 1H, H-16a′), 2.15 (m, 1H, H-6a′), 2.11 (m, 1H, H-4a′), 2.05 (s, 3H, Me-5), 1.99 (m, 1H, H-16b′), 1.91 (m, 1H, H-1a′), 1.91 (m, 1H, H-11a′), 1.86 (m, 1H, H-2a′), 1.98 (m, 1H, H-4b′), 1.80 (m, H-7b′), 1.76 (m, 1H, H-1b′), 1.61−1.75 (m, 4H, H-14′, H-15a′, H-9′, H-12b′), 1.56 (m, 1H, H-2b′), 1.50 (H-6b′), 1.42 (m, 1H, H-8), 1.35 (m, 1H, H-15b′), 1.08 (m, 1H, H-11b′), 0.93 (s, 3H, Me-21′), 0.78 (d, 3H, *J* = 7.0 Hz, Me-20′). ^{13}C NMR (125 MHz, $CDCl_3$): δ 169.05 (C═O), 138.52 (C-*i*), 128.47 (C-10′),

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128.37 (C-*p*), 128.11 (C-*m*), 126.69 (C-*o*), 121.99 (C-5′), 87.57 (C-18′), 85.49 (C-3), 80.57 (C-2), 79.90 (C-17′), 74.63 (C-4), 73.91 (C-19′), 71.21 (C-3′), 53.06 (OMe), 47.40 (C-13′), 46.19 (C-14′), 41.80 (C-8′), 39.52 (C-9′), 38.98 (C-16′), 38.72 (C-6′), 35.38 (C-4′), 33.06 (C-12′), 27.15 (C-7′), 26.52 (C-1′), 25.35 (C-11′), 22.51 (C-2′), 22.06 (C-15′), 12.97 (Me-20′), 12.86 (C-21′), 3.82 (Me-5). HREIMS calcd for $C_{33}H_{40}O_4$: 500.2927, found 500.2929.

3β-Cholesteryl (*R*)-2-Methoxy-2-phenylpent-3-ynoate 19a. Obtained in 32% yield as colorless syrup. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.67 (m, 2H, H-*o*), 7.34 (m, 3H, H-*o*, H-*p*), 5.31 (m, 1H, H-6′), 4.63 (m, 1H, H-3′), 2.19 (m, 1H, H-4a′), 2.17 (m, 1H, H-4b′), 1.89−2.04 (m, 2H, H-7a′, H12a′), 1.84 (m, 1H, H-16a), 1.80 (m, 1H, H-2a′), 1.58 (m, 1H, H-2b′), 1.29−1.60 (m, 9H, H-1′a, H-15′a,b, H-7′b, H-25′, H-8′, H-20′, H-11′a,b), 1.24 (m, 1H, H-16b), 0.89−1.19 (m, 9H, H-1′b, H-12b′, H-23′a,b, H-24′a,b, H-17′, H-14′, H-9′), 0.97 (s, 3H, Me-19′), 0.90 (d, 3H, *J* = 7.0 Hz, Me-21′), 0.87 (d, 3H, *J* = 7.1 Hz, Me-26′), 0.86 (d, 3H, *J* = 7.1 Hz, Me-27′), 0.66 (s, 3H, Me-18′). ^{13}C NMR (125 MHz, $CDCl_3$): 168.84 (C-1), 139.34 (C-5′), 138.40 (C-*i*), 128.56 (C-*p*), 128.18 (C-*o*), 126.67 (C-*m*), 122.81 (C-6′), 85.62 (C-3), 80.54 (C-2), 75.82 (C-3′), 74.69 (C-4), 56.66 (C-14′), 56.12 (C-17′), 49.97 (C-9′), 42.30 (C-13′), 39.71 (C-12′), 39.51 (C-24′), 37.52 (C-4′), 36.86 (C-10′), 36.54 (C-1′), 36.17 (C-22′), 35.78 (C-20′), 31.87 (C-7′), 31.82 (C-8′), 28.21 (C-16′), 28.01 (C-25′), 27.34 (C-2′), 24.26 (C-15′), 23.82 (C-23′), 22.81 (C-26′), 22.55 (C-27′), 21.02 (C-11′), 19.31 (C-19′), 18.71 (C-21′), 11.84 (C-18′), 3.84 (C-5). HREIMS calcd for $C_{33}H_{40}O_4$: 572.4230, found 572.4214.

3β-Cholesteryl (*S*)-2-Methoxy-2-phenylpent-3-ynoate 19b. Obtained in 32% yield as colorless syrup. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.67 (m, 2H, H-*o*), 7.34 (m, 3H, H-*o*, H-*p*), 5.34 (m, 1H, H-6′), 4.64 (m, 1H, H-3′), 2.31 (m, 1H, H-4a′), 2.27 (m, 1H, H-4b′), 1.89−2.04 (m, 2H, H-7a′, H12a′), 1.84 (m, 1H, H-16a), 1.69 (m, 1H, H-2a′), 1.43 (m, 1H, H-2b′), 1.29−1.60 (m, 9H, H-1′a, H-15′a,b, H-7′b, H-25′, H-8′, H-20′, H-11′a,b), 1.24 (m, 1H, H-16b), 0.89−1.19 (m, 9H, H-1′b, H-12b′, H-23′a,b, H-24′a,b, H-17′, H-14′, H-9′), 0.97 (s, 3H, Me-19′), 0.90 (d, 3H, *J* = 7.0 Hz, Me-21′), 0.87 (d, 3H, *J* = 7.1 Hz, Me-26′), 0.86 (d, 3H, *J* = 7.1 Hz, Me-27′), 0.66 (s, 3H, Me-18′). ^{13}C NMR (125 MHz, $CDCl_3$): 168.82 (C-1), 139.41 (C-5′), 138.39 (C-*i*), 128.55 (C-*p*), 128.17 (C-*o*), 126.67 (C-*m*), 122.79 (C-6′), 85.63 (C-3), 80.52 (C-2), 75.78 (C-3′), 74.67 (C-4), 56.66 (C-14′), 56.12 (C-17′), 49.96 (C-9′), 42.30 (C-13′), 39.70 (C-12′), 39.51 (C-24′), 37.61 (C-4′), 36.82 (C-10′), 36.54 (C-1′), 36.17 (C-22′), 35.77 (C-20′), 31.88 (C-7′), 31.83 (C-8′), 28.21 (C-16′), 28.00 (C-25′), 27.25 (C-2′), 24.26 (C-15′), 23.82 (C-23′), 22.81 (C-26′), 22.55 (C-27′), 21.01 (C-11′), 19.31 (C-19′), 18.70 (C-21′), 11.84 (C-18′), 3.84 (C-5). HREIMS calcd for $C_{39}H_{56}O_3$: 572.4230, found 572.4244.

3-[10-Methyl-3,10-dihydroxy]-pinanyl (*R*)-2-Methoxy-2-phenylpent-3-ynoate 20a. Obtained in 27% yield as colorless syrup. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.67 (m, 2H, H-*o*), 7.28−7.37 (m, 3H, H-*m*, H-*p*), 4.89 (m, 1H, H-3′), 3.59 (m, 1H, H-10′), 3.38 (s, 3H, OMe), 2.63 (m, 1H, H-4′ec), 2.40 (m, 1H, H-7*ec*), 2.30 (m, 1H, H-1′), 2.03 (s, 3H, CCMe), 1.91 (m, 1H, H-5′), 1.75 (m, 1H, H-2′), 1.63 (m, 1H, H-4′ax), 1.21 (s, 3H, Me-9′), 1.04 (d, 1H, *J* = 9.7 Hz, H-7′ax), 0.86 (s, 3H, Me-8′), 0.57 (d, 3H, *J* = 7.1 Hz, Me-11′). ^{13}C NMR (125 MHz, $CDCl_3$): δ 168.57 (C═O), 137.83 (C-*i*), 128.64 (C-*p*), 128.16 (C-*m*), 126.88 (C-*o*), 85.87 (C-3), 80.30 (C-4), 74.30 (C-2), 70.73 (C-3′), 69.23 (10′), 55.91 (C-2′), 52.94 (OMe), 41.35 (C-5′), 41.02 (C-1′), 37.86 (C-6′), 35.92 (C-4′), 32.18 (C-7′), 27.09 (Me-9′), 23.78 (Me-8′), 21.45 (m-11′), 3.74 (CCMe). HREIMS calcd for $C_{23}H_{30}O_4$: 370.2144, found 370.2158.

10-[10-Methyl-3,10-dihydroxy]-pinanyl (*R*)-2-Methoxy-2-phenylpent-3-ynoate 21a. Obtained in 29% yield as colorless syrup. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.68 (m, 2H, H-*o*), 7.31−7.40 (m, 3H, H-*m*, H-*p*), 4.96 (m, 1H, H-10′), 3.97 (m, 1H, H-3′), 3.38 (s, 3H, OMe), 2.51 (m, 1H, H-4′ec), 2.13 (m, 1H, H-7*ec*), 2.04 (s, 3H, CCMe), 1.89 (m, 1H, H-2′), 1.83 (m, 1H, H-5′), 1.69 (m, 1H, H-4′ax), 1.33 (d, 3H, *J* = 7.1 Hz, Me-11′), 1.28 (m, 1H, H-1′), 0.90 (s, 3H, Me-9′), 0.89 (d, 1H, *J* = 9.7 Hz, H-7′ax), 0.76 (s, 3H, Me-8′). ^{13}C NMR (125 MHz, $CDCl_3$): δ 168.60 (C═O), 138.00 (C-*i*), 128.63 (C-*p*), 128.25 (C-*m*), 126.84 (C-*o*), 85.83 (C-3), 80.27 (C-4), 74.42 (C-10′), 74.28 (C-2), 65.74 (C-3′), 57.27 (C-2′), 53.39 (OMe), 41.29 (C-1′), 41.15 (C-5′), 39.39 (C-4′), 37.11 (C-6′), 32.46 (C-7′), 26.79 (M2−9′), 18.75 (Me-8′), 3.77 (Me′5). HREIMS calcd for $C_{23}H_{30}O_4$: 370.2144, found 370.2144.

10-[10-Methyl-3,10-dihydroxy]-pinanyl (*S*)-2-Methoxy-2-phenylpent-3-ynoate 21b and 3-[10-Methyl-3,10-dihydroxy]-pinanyl (*S*)-2-Methoxy-2-phenylpent-3-ynoate 20b. Obtained in 16% yield as a mixture of esters at C-3 and C-10 position (colorless syrup), which were difficult to separate by column chromatography; therefore, their ^{1}H data were assigned without previous separation by performing homonuclear 2D NMR experiments. Data for compound **21b**: ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.62−7.69 (m, 2H, H-*o*), 7.29−7.39 (m, 3H, H-*m*, H-*p*), 5.00 (m, 1H, H-10′), 4.01 (m, 1H, H-3′), 3.40 (s, 3H, OMe), 2.53 (m, 1H, H-4′ec), 2.32 (m, 1H, H-7*ec*), 2.01 (s, 3H, CCMe), 1.97 (m, 1H, H-2′), 1.90 (m, 1H, H-1′), 1.83 (m, 1H, H-5′), 1.72 (m, 1H, H-4′ax), 1.16 (d, 3H, *J* = 7.1 Hz, Me-11′), 1.07 (s, 3H, Me-9′), 1.01 (d, 1H, *J* = 9.7 Hz, H-7′ax), 0.83 (s, 3H, Me-8′). Data for compound **20b**: ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.62−7.69 (m, 2H, H-*o*), 7.29−7.39 (m, 3H, H-*m*, H-*p*), 4.97 (m, 1H, H-3′), 3.72 (m, 1H, H-10′), 3.38 (s, 3H, OMe), 2.54 (m, 1H, H-4′ec), 2.30 (m, 1H, H-7*ec*), 2.03 (s, 3H, CCMe), 1.95 (m, 1H, H-2′), 1.82 (m, 1H, H-5′), 1.27 (m, 1H, H-4′ax), 1.16 (d, 3H, *J* = 7.1 Hz, Me-11′), 1.20 (s, 3H, Me-9′), 1.01 (d, 1H, *J* = 9.7 Hz, H-7′ax), 0.87 (s, 3H, Me-8′). HREIMS calcd for $C_{23}H_{30}O_4$: 370.2144, found 370.2155.

2-Butyl (*R*)-2-Methoxy-2-phenylpent-3-ynoate 22a. Obtained in 54% yield as colorless syrup (R_f 0.46, hexane/ethyl ether 4:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.67 (m, 2H, H-*o*), 7.33 (m, 3H, H-*m*,*p*), 4.84 (sext, 1H, *J* = 6.2 Hz, H-2′), 3.39 (s, 3H, OMe), 2.02 (s, 3H, Me-5), 1.49 (m, 2H, H-3′), 1.06 (d, 3H, *J* = 6.2 Hz, H-1′), 0.83 (t, 3H, *J* = 7.5 Hz, H-4′). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 169.1 (C-1), 138.3 (C-*i*), 128.5 (C-*p*), 128.1 (C-*m*), 126.6 (C-*o*), 85.5 (C-3), 80.4 (C-4), 74.5 (C-2), 74.2 (C-2′), 52.9 (OMe), 28.5 (C-3′), 19.0 (C-1′), 9.2 (C-4′), 3.8 (C-5).

2-Butyl (*R*)-2-methoxy-2-phenylpent-3-ynoate 22b. Obtained in 54% yield as epimer of **22a** at the carbinol moiety; colorless syrup (R_f 0.46, hexane/ethyl ether 4:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.67 (m, 2H, H-*o*), 7.33 (m, 3H, H-*m*,*p*), 4.84 (sext, 1H, *J* = 6.2 Hz, H-2′), 3.39 (s, 3H, OMe), 2.01 (s, 3H, Me-5), 1.49 (m, 2H, H-3′), 1.18 (d, 3H, *J* = 6.2 Hz, H-1′), 0.62 (t, 3H, *J* = 7.5 Hz, H-4′). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 169.1 (C-1), 138.3 (C-*i*), 128.5 (C-*p*), 128.1 (C-*m*), 126.7 (C-*o*), 85.6 (C-3), 80.4 (C-4), 74.7 (C-2), 74.3 (C-2′), 52.9 (OMe), 28.6 (C-3′), 19.1 (C-1′), 9.4 (C-4′), 3.8 (C-5).

Isopropyl (*R*)-2-Methoxy-2-phenylpent-3-ynoate 23. Obtained in 48% yield as colorless syrup (R_f 0.43, hexane/ethyl ether 4:1). $[\alpha]^{24}_D$ = +7.2 (*c* 0.37, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.67 (m, 2H, H-*o*), 7.37 (m, 3H, H-*m*,*p*), 5.02 (sept, 1H, *J* = 6.2 Hz, H-2′), 3.39 (s, 3H, OMe), 2.02 (s, 3H, Me-5), 1.21 (d, 3H, *J* = 6.2 Hz, Me-1′), 1.12 (d, 3H, *J* = 6.2 Hz, Me-3′). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 168.9 (C-1), 138.2 (C-*i*), 128.5 (C-*p*), 128.1 (C-*m*), 126.6 (C-*o*), 74.5 (C-2), 69.8 (C-2′), 52.9 (OMe), 21.4 (Me-1′), 21.2 (Me-3′), 3.8 (Me-5). IR (CH_2Cl_2) ν_{max}: 2981.9, 1740.8, 1450.7, 1243.6, 1094.5 cm^{-1}. MS (EI) *m*/*z* (%): 215 ([M − OMe]$^+$·, 15.4), 159 ([M − $CO_2CH(CH_3)_2$]$^+$·, 100), 128 (3.6), 115 (3.4), 105 (3.7). HRESIMS calcd for $C_{15}H_{18}O_3$ + Na: 269.1150, found 269.1153.

Preparation of MPPA Amides 24−27. To a solution of (*R*)-(+)-**2** or (*S*)-(−)-**2** (1 equiv), the chiral amine (1.1 quiv), and TEA (1.1 equiv) in dry dichloromethane (5 mL/50 mg of the acid) was added 1.1 equiv of BOP at room temperature. The reaction mixture was stirred for 24 h, diluted with dichloromethane, and washed with aqueous 5% HCl. The organic layer was dried over Na_2SO_4, filtered, and evaporated to dryness to give the crude product, which was purified by silica gel (230−400 mesh) column chromatography using hexane/ethyl ether as eluent to give the corresponding R*NH-(*S*)-MPPA and R*NH-(*R*)-MPPA amides.

Amide of Methylbenzyl Amine and (*R*)-2-Methoxy-2-phenylpent-3-ynoic 24a. Obtained in 64% yield as colorless syrup. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.61 (2H, m, H-o), 7.33 (3H, m, H-m,p), 7.33 (5H, m, H-*o*′,*m*′,*p*′), 7.18 (1H, d, *J* = 8.0 Hz, NH), 5.08 (1H, dq, *J* = 8.0, 6.9 Hz, H-1′), 3.27 (3H, s, OMe), 1.98 (3H, s, Me-5), 1.48 (3H, d, *J* = 6.9 Hz, Me-2′). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 168.4 (CO), 142.8 (C), 138.1 (C), 128.6 (CH), 128.4 (CH), 128.2 (CH),

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127.2 (CH), 126.8 (CH), 126.2 (CH), 85.7 (C), 81.0 (C), 74.8 (C), 52.4 (OCH3), 48.6 (CH), 21.5 (CH3), 3.8 (CH3). HRESI calcd for $C_{20}H_{21}O_2$ + Na: 330.1470, found 330.1474.

Amide of Methylbenzyl Amine and (*S*)-2-Methoxy-2-phenylpent-3-ynoic Acid 24b. Obtained in 48% yield as colorless syrup. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.54 (2H, m, H-*o*), 7.30 (3H, m, H-*m*,*p*), 7.30 (5H, m, H-*o*′,*m*′,*p*′), 7.19 (1H, d, J = 8.2 Hz, NH), 5.09 (1H, dq, J = 8.2, 6.9 Hz, H-1′), 3.27 (3H, s, OMe), 2.02 (3H, s, Me-5), 1.54 (3H, d, J = 6.9 Hz, Me-2′). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 168.4 (CO), 142.9 (C), 138.0 (C), 128.5 (CH), 128.4 (CH), 128.2 (CH), 127.2 (CH), 126.8 (CH), 126.1 (CH), 85.7 (C), 81.1 (C), 74.9 (C), 52.3 (OCH3), 48.6 (CH), 21.5 (CH3), 3.9 (CH3). HRESI calcd for $C_{20}H_{21}NO_2$ + Na: 330.1470, found 330.1474.

Amide of 3-Norbornyl Amine and (*R*)-2-Methoxy-2-phenylpent-3-ynoic Acid 25a. Obtained in 38% yield as colorless syrup. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.18 (m, 1H, H-3a′), 2.01 (s, 3H, CCMe), 1.78 (m, 1H, H-6a′), 1.65 (m, 1H, H-4′), 1.55 (m, 1H, H-5a′), 1.43 (m, 1H, H-6b′), 1.23 (m, 1H, H-5b′), 0.91 (s, 3H, Me-9′), 0.87 (s, 3H, Me-8′), 0.83 (s, 3H, Me-10′), 0.78 (dd, 1H, J = 4.1, 9.3 Hz, H-3b′). HRESI calcd for $C_{22}H_{29}NO_2$: 339.2198, found 339.2193.

Amide of 3-Norbornyl Amine and (*S*)-2-Methoxy-2-phenylpent-3-ynoic Acid 25b. Obtained in 43% yield as colorless syrup. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.34 (1H, m, H-3a′), 2.02 (s, 3H, CCMe), 1.78 (m, 1H, H-6a′), 1.67 (m, 1H, H-4′), 1.53 (m, 1H, H-5a′), 1.40 (m, 1H, H-6b′), 1.24 (m, 1H, H-5b′), 0.91 (s, 3H, Me-9′), 0.86 (s, 3H, Me-8′), 0.85 (s, 3H, Me-10′), 0.69 (dd, 1H, J = 4.1, 9.3 Hz, H-3b′). HRESI calcd for $C_{22}H_{29}NO_2$: 339.2198, found 339.2205.

Amide of L-valine and (*R*)-2-Methoxy-2-phenylpent-3-ynoic Acid 27a. Obtained in 62% yield as colorless syrup. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.64 (2H, m, H-o), 7.43 (1H, d, J = 9.1 Hz, NH), 7.37 (3H, m, H-m,p), 4.51 (1H, dd, J = 9.1, 4.8 Hz, H-1′), 3.71 (3H, s, CO2Me), 3.31 (3H, s, OMe), 2.23 (1H, m, H-2′), 2.02 (3H, s, Me-5), 0.97 (3H, d, J = 6.9 Hz, Me-4′), 0.94 (3H, d, J = 6.9 Hz, Me-5′). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 172.1 (CO), 169.4 (CO), 137.9 (C), 128.5 (CH), 128.2 (CH), 127.0 (CH), 85.9 (C), 81.1 (C), 74.9 (C), 57.0 (CH), 52.5 (CH_3), 52.0 (CH_3), 31.4 (CH), 18.9 (CH_3), 17.7 (CH_3), 3.8 (CH_3). R_f = 0.61, 5% acetone/chloroform. HRESI calcd for $C_{18}H_{23}NO_4$ + H: 318.1705, found 318.1705.

Amide of L-valine and (*S*)-2-Methoxy-2-phenylpent-3-ynoic Acid 27a. Obtained in 71% yield as colorless syrup. *Rf* = 0.61 in 5% acetone/chloroform. 318.1709. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.62 (2H, m, H-*o*), 7.36 (3H, m, H-*m*,*p*), 7.36 (1H, d, J = 9.1 Hz, NH), 4.51 (1H, dd, J = 9.1, 4.9 Hz, H-1′), 3.75 (3H, s, CO2Me), 3.35 (3H, s, OMe), 2.15 (1H, m, H-2′), 2.01 (3H, s, Me-5), 0.86 (3H, d, J = 6.9 Hz, Me-4′), 0.83 (3H, d, J = 6.9 Hz, Me-5′). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 172.1 (CO), 169.3 (CO), 138.4 (C), 128.5 (CH), 128.2 (CH), 126.6 (CH), 85.9 (C), 81.3 (C), 74.7 (C), 56.9 (CH), 52.6 (CH3), 52.1 (CH3), 31.6 (CH), 18.8 (CH3), 17.6 (CH3), 3.9 (CH3). HRESI calcd for $C_{18}H_{23}NO_4$ + H: 318.1705, found 318.1709.

Amide of L-serine (*R*)-2-Methoxy-2-phenylpent-3-ynoic Acid 26a. Obtained in 32% yield as colorless syrup. ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.51 (m, 1H, H-2′), 3.92 (1H, dd, J = 3.0, 9.1 Hz, 3-a′), 3.85 (1H, dd, J = 3.0, 9.1 Hz, H-3b′), 3.78 (s, 3H, COOMe), 3.31 (s, 3H, OMe), 2.44 (bs, 1H, OH), 2.01 (s, 3H, CCMe). HRESI calcd for $C_{16}H_{18}NO_4 - H_2O$: 288.1236, found 288.1250.

Amide of L-serine (*S*)-2-Methoxy-2-phenylpent-3-ynoic Acid 26b. Obtained in 27% yield as colorless syrup. ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.51 (m, 1H, H-2′), 4.02 (1H, dd, J = 3,0, 9.1 Hz, 3-a′), 3.93 (1H, dd, J = 3.0, 9.1 Hz, H-3b′), 3.75 (s, 3H, COOMe), 3.28 (s, 3H, OMe), 2.44 (bs, 1H, OH), 2.01 (s, 3H, CCMe), 1.90 (bs, 1H, OH). HRESI calcd for $C_{16}H_{20}NO_5$: 306.1341, found 306.1352.

■ ASSOCIATED CONTENT

Supporting Information

^{1}H and ^{13}C NMR spectra for all relevant compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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(5) (1*R*)-(−)-Myrtenal ($[\alpha]^{20}_D$ = −15.0, neat) is commercially available from two providers: (1) Penta Manufacturing Corp. (Fairfield, NJ, USA) and (2) Aldrich-Aldrich Co, (St. Louis, MO, USA). Only (1*R*)-(−)-myrtenal from the first provider was used to synthesize S,O-acetals **1a** and **1b**. All commercial carbinols and amines used to prepare R*O-(*R*)-MPPA **4a−23a** and R*O-(*S*)-MPPA **4b−23b** esters and R*NH-(*R*)-MPPA **24a−27a** and R*NH-(*S*)-MPPA **24b−27b** amides are sold as 95−99% purum (sum of enantiomers, GC) whose enantiomeric purity is not specified.

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(10) The conformational search was carried out in both esters by systematic rotation of all pertinent bonds at the HF/3-21G level of *ab initio* theory. The resulting geometries were further optimized at the HF/6-31G(d) and B3LYP/6-31G(d) levels of theory. Vibrational frequencies were obtained on the minima thus obtained; only real frequencies were obtained in all cases. Relative B3LYP/6-31G(d) energies (ΔE_0) were obtained considering the electronic energies of the minima corrected by inclusion of zero-point energies (E_0).

Conformational populations were estimated from ΔE_0 values of the relevant conformers according to their Boltzmann distribution.
(11) The conformational search also showed that the phenyl group in the acid moiety prefers a conformation in which the ring is coplanar with the methoxy group. In the particular case of esters **22** there are three *sp*(*O*) and three *sp*(*C*) conformers that differ mainly in the conformation of the ethyl group of the *sec*-butyl fragment.
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