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Synthesis of Enantiopure Aliphatic Acetylene Alcohols and Determination of Their Absolute Configurations by ^{1}H NMR Anisotropy and/or X-ray Crystallography

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The MαNP acid method has been applied to racemic aliphatic acetylene alcohols in order to simultaneously prepare enantiopure alcohols and to determine their absolute configurations by ^{1}H NMR anisotropy. Racemic acetylene alcohols **6**–**8**, **11**, and **20** were esterified with MαNP acid (*S*)-(+)-**1** to yield diastereomeric MαNP esters which were efficiently separated by HPLC on silica gel with separation factors a in the range 1.60–1.93. The ^{1}H NMR anisotropy factors $\Delta\delta$ [= δ(2nd fr.) – δ(1st fr.)] were calculated from the data of the first- (**22a**–**27a**) and second-eluted MαNP esters (**22b**–**27b**). The absolute configurations of the first-eluted esters were determined from the distribution of $\Delta\delta$ values in the MαNP sector rule. In the case of MαNP ester **26b**, the assigned absolute configuration was confirmed by X-ray crystallography. The solvolysis of MαNP esters yielded enantiopure acetylene alcohols **5**–**8** with established absolute configurations.

Introduction

Chiral acetylene alcohols have been extensively used as chiral synthons for the total synthesis of natural products, as in the case of (*S*)-(–)-1-octyn-3-ol used for the synthesis of prostaglandin[1] and others.[2] Various approaches have been developed to prepare chiral acetylene alcohols including asymmetric[1d,3] and biochemical reactions,[4] the use of natural chiral pools,[5] resolution with chiral acids,[6] and co-crystallization methods with chiral auxiliaries.[7] In such methods, the greatest problem is how to increase the enantiomeric purity of the products. Recently, it became possible to obtain chiral acetylene alcohols in more than 99% *ee* by selected synthetic[3a,3b,5] or biochemical[4c,4d] reactions under optimized conditions. However, there is still uncertainty as to whether these methods are generally applicable to a variety of acetylene alcohols to synthesize enantiopure alcohols. Furthermore, there is a serious problem of how to determine the absolute configurations (ACs) of the products. For compounds with known ACs, it is easy to assign the ACs of products by comparison of their $[a]_D$ values. However, if ACs are unknown, tedious chemical correlation reactions or pertinent spectroscopic analyses have to be carried out. Therefore, we have developed general and convenient methods that enable one to prepare various enantiopure alcohols and determine their ACs simultaneously.

One such method involves the use of chiral CSP (camphorsultam-phthalic) and CSDP (camphorsultam-dichlorophthalic) acids; diastereomeric esters formed from a racemic alcohol and an enantiopure acid were easily separated by HPLC on silica gel, and their ACs were determined by X-ray crystallography.[8–10] Another method that does not require crystals, involves the use of MαNP [2-methoxy-2-(1-naphthyl)propionic] acid (**1**, Figure 1) which has been widely applied to various secondary alcohols, especially to aliphatic alcohols.[9–12] By application of this method, a variety of chiral synthetic and natural compounds have been synthesized in enantiopure forms and/or their ACs have been determined: For example, a thyroid hormone analogue KAT-2003,[11i] (*R*)-(+)-[VCD(+)945]-4-ethyl-4-methyloctane (the simplest chiral saturated hydrocarbon with a quaternary chirality center),[11u] synthetic precursors of 5-lipoxygenase inhibitors[13a] and mispyric acid (an inhibitor of DNA polymerase β),[13b] pheromones,[13c,13d] hydroxy metabolites of blonanserin AD-5423 in humans,[13e] inherently chiral *anti-O,O′*-dialkylated calix[4]arenes,[13f] and antibiotic PF1140[13g] are interesting applications of the MαNP acid method.

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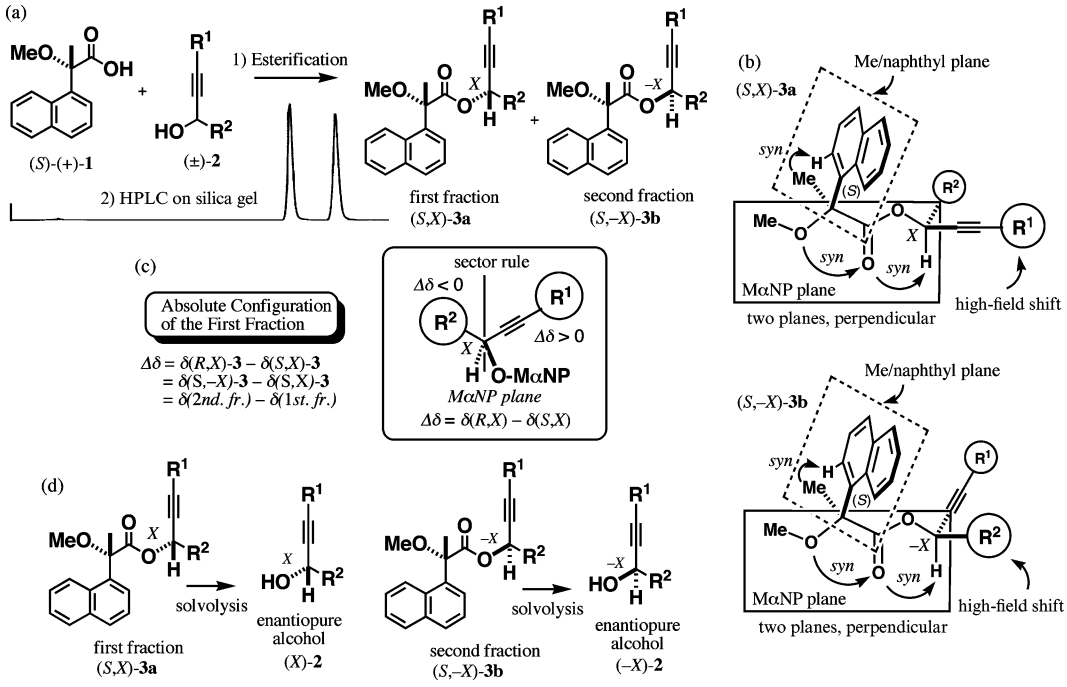


Figure 1. General scheme for the preparation of enantiopure acetylene alcohols **2** and simultaneous determination of their absolute configurations by the use of chiral MαNP acid (*S*)-(+)-**1**, a chiral resolving and ^{1}H NMR anisotropy reagent (CAR). In all the cases reported in this paper, the first-eluted ester **3a** takes the absolute configuration as illustrated.

We have previously reported the preparation of some enantiopure acetylene alcohols and the determination of their ACs by application of the MαNP acid method.[11m,11o] By this method, aliphatic acetylene alcohol **4** (Figure 2) was more efficiently enantioresolved as MαNP ester than aromatic acetylene alcohols. We have now extended this method to aliphatic acetylene alcohols **5**–**8** with longer alkyl chains and obtained excellent results, as will be discussed below.

Results and Discussion

Synthesis of Racemic Long-Chain Acetylenic Alcohols

To study the general applicability of the MαNP acid method to aliphatic acetylene alcohols, racemic alcohols with various chain lengths were synthesized as shown in Scheme 1: C_8 chain, 2-octyn-4-ol (**11**); C_{12} chain, 1-dodecyn-3-ol (**5**) and 1-trimethylsilyl-1-dodecyn-3-ol (**20**); C_{18}

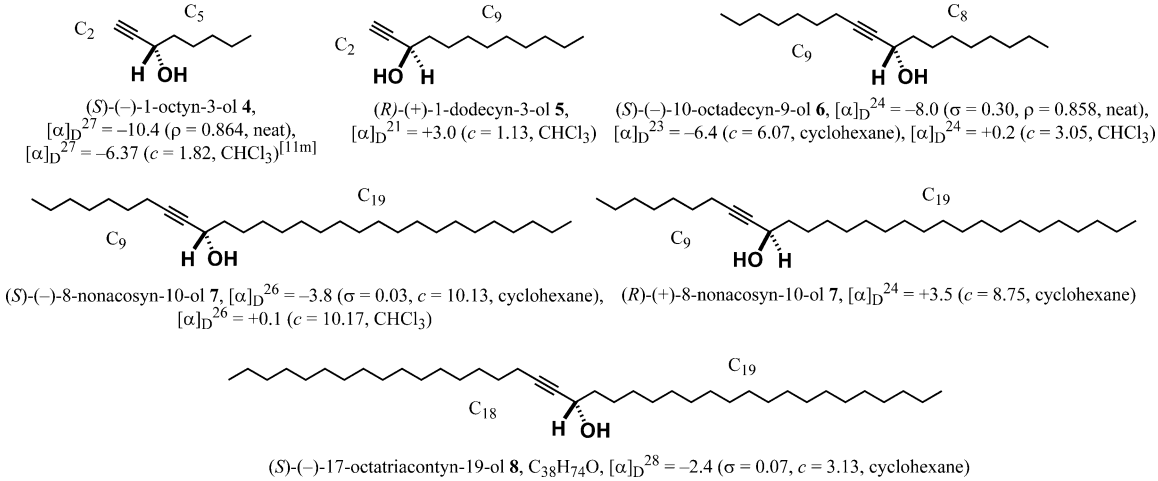
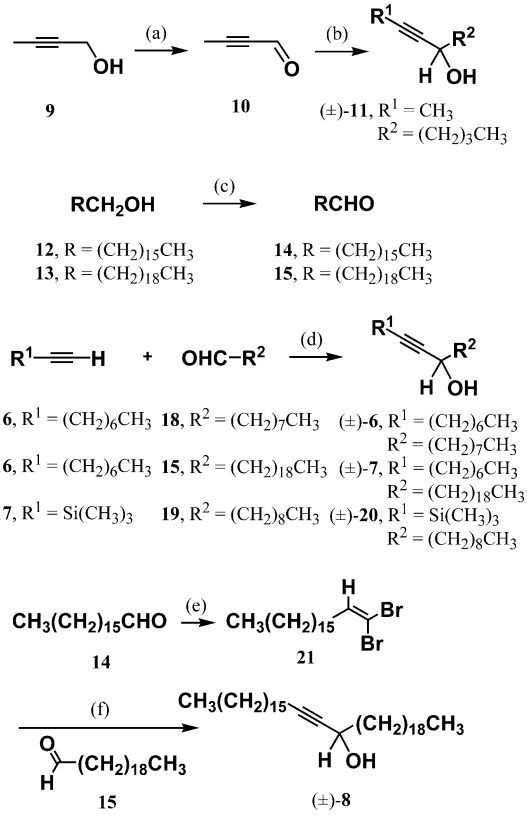


Figure 2. Absolute configurations and optical rotation data of enantiopure aliphatic acetylene alcohols, where σ is the standard deviation of the observed $[\alpha]_D$ value; the data for (*S*)-(–)-**4** are taken from ref.[11m]

chain, 10-octadecyn-9-ol (**6**); C_{29} chain, 8-nonacosyn-10-ol (**7**); C_{38} chain, 17-octatriacontyn-19-ol (**8**). 2-Butyn-1-ol (**9**) was oxidized with pyridinium chlorochromate (PCC) to yield 2-butynal (**10**), which was treated with *n*-butyllithium in hexane. After workup, the organic layer was distilled in a Kugelrohr apparatus to give alcohol **11** (9% for two steps). The low yield may be due to the volatility of the product. 1-Heptadecanol (**12**) was oxidized with PCC to afford heptadecanal (**14**) in good yield. Similarly, 1-icosanol (**13**) was converted into icosanal (**15**). 1-Nonyne (**16**) was treated with *n*-butyllithium in hexane, and nonanal (**18**) was added. After workup, the oily residue was purified by short-column chromatography on silica gel to give acetylene alcohol **6** in good yield. In a similar manner, alcohol **7** was prepared from acetylene compound **16** and aldehyde **15**. Ethynyltrimethylsilane (**17**) was treated with *n*-butyllithium in hexane, and decanal (**19**) was added to give alcohol **20**.

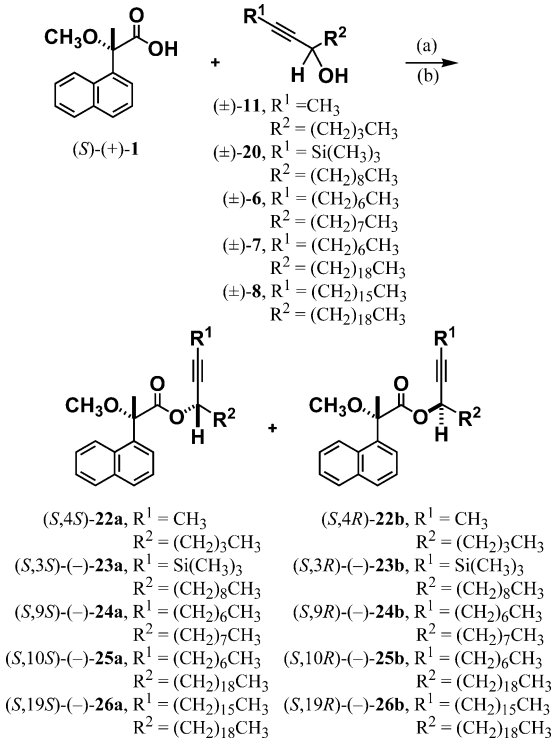


Scheme 1. Preparation of racemic acetylene alcohols. (a) PCC/CH_2Cl_2. (b) *n*BuLi/hexane, THF, 9% for 2 steps. (c) PCC/CH_2Cl_2, 80–81%. (d) *n*BuLi/hexane, THF, 49–77%. (e) CBr_4, PPh_3/CH_2Cl_2, 85%. (f) *n*BuLi/hexane, THF, and then **15**, 32%.

Triphenylphosphane was added to a solution of CBr_4 in CH_2Cl_2, followed by aldehyde **14** prepared as above. After workup, the oily residue was purified by short-column chromatography on silica gel to yield 1,1-dibromo-1-octadecene (**21**). Compound **21** was treated with *n*-butyllithium in hexane, and icosanal (**15**), prepared as above, was added. After workup, the residue was purified by short-column chromatography on silica gel to give the long-chain acetylene alcohol **8**. The structures of the obtained products were confirmed by spectroscopic and elemental analyses.

Preparation of Diastereomeric Esters from Racemic Acetylene Alcohols with (*S*)-(+)-MαNP Acid and HPLC Separation

Racemic acetylene alcohols **11**, **20**, and **6**–**8** were easily esterified with MαNP acid (*S*)-(+)-**1** to give diastereomeric esters, which were separated by HPLC on silica gel (Scheme 2). For example, a mixture of alcohol (±)-**8**, MαNP acid (*S*)-(+)-**1**, 1,3-dicyclohexylcarbodiimide (DCC), 4-(dimethylamino)pyridine (DMAP), and 10-camphorsulfonic acid (CSA) in CH_2Cl_2 was stirred at room temperature overnight to yield a diastereomeric mixture of esters **26a** and **26b**. The mixture was well separated by HPLC on silica gel (hexane/EtOAc = 50:1) with a large elution interval, as shown in Figure 3: Separation factor α = 1.78; resolution factor R_s = 4.10 (Table 1). The first-eluted ester (–)-**26a** {47%, $[\alpha]_D^{29}$ = –26.0 (c = 1.36, $CHCl_3$)} and the second-eluted ester (–)-**26b** {49%, $[\alpha]_D^{29}$ = –2.7 (c = 10.9, $CHCl_3$)} were obtained.



Scheme 2. Preparation of the diastereomeric MαNP esters and separation by HPLC. (a) DCC, DMAP, CSA/CH_2Cl_2. (b) HPLC on silica gel: first-eluted ester **a**, 20–49%; second-eluted ester **b**, 21–50%.

To obtain MαNP esters **27a** and **27b**, a diastereomeric mixture of esters **23a**/**23b** bearing trimethylsilyl groups was treated with tetrabutylammonium fluoride (TBAF) in THF, and the deprotected esters were separated by HPLC on silica gel: Separation factor α = 1.93; resolution factor R_s = 3.19 (Scheme 3 and Table 1). As shown in Table 1, all the MαNP esters were efficiently separated with a separation factor α = 1.60–1.93. Such large α values indicate that acetylene alcohol MαNP esters are separable on a large scale. This is an advantage of the MαNP acid method for

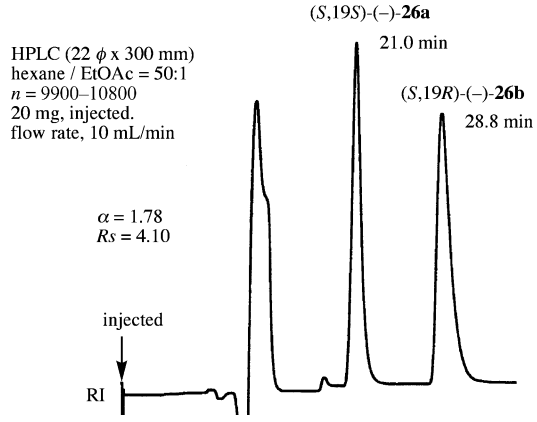


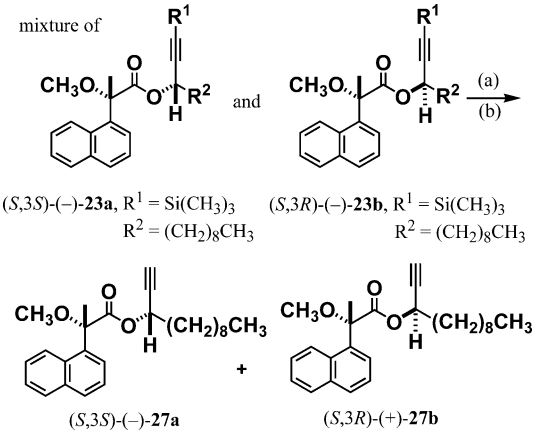
Figure 3. HPLC separation of the diastereomeric MαNP esters **26a/26b**.

Table 1. HPLC separation of the diastereomeric esters formed from racemic acetylene alcohol and MαNP acid (*S*)-(+)-**1**.

Entry[a]	Diastereomers	H/EA ratio[b]	α	R_s	1st-eluted fr.
1	**22a/22b**	20:1	1.76	2.88	(*S*,4*S*)-**22a**
2	**23a/23b**	20:1	1.60	1.63	(*S*,3*S*)-(–)-**23a**
3	**24a/24b**	20:1	1.61	1.93	(*S*,9*S*)-(–)-**24a**
4	**25a/25b**	20:1	1.88	1.65	(*S*,10*S*)-(–)-**25a**
5	**26a/26b**	50:1	1.78	4.10	(*S*,19*S*)-(–)-**26a**
6	**27a/27b**	20:1	1.93	3.19	(*S*,3*S*)-(–)-**27a**

[a] Glass column (22 $\phi \times$ 300 mm) of silica gel (particle size 5–10 μm). [b] Solvent: H = hexane, EA = ethyl acetate.

the preparation of enantiopure acetylene alcohols because the (*S*)-(+)-MαNP acid **1** used is enantiopure[14] and therefore the separated esters are also enantiopure. In the HPLC separation of esters **26a/26b**, a less polar mixed solvent (hexane/EtOAc, 50:1) was used reflecting the less polar nature of these esters, which results from their long-chain alkyl groups (Table 1). Note also that the α values remain in a narrow range, that is, 1.60–1.93, despite the large differences in the alkyl chain lengths. This implies that the HPLC separation is mostly controlled by the shape and polarity of the acetylene-MαNP ester moiety, the contribution from the alkyl chains being relatively negligible.



Scheme 3. Deprotection of the TMS group and HPLC separation of the diastereomeric MαNP. (a) TBAF/THF. (b) HPLC on silica gel: first-eluted ester **a**, 38%; second-eluted ester **b**, 38%.

Determination of the Absolute Configurations of MαNP Esters by ^{1}H NMR Anisotropy

The absolute configurations of the separated MαNP esters were determined by ^{1}H NMR anisotropy as follows. In the case of 2-octyn-4-ol (C_8 chain) esters **22a** and **22b**, all ^{1}H NMR signals were fully assigned by ^{1}H, ^{13}C, ^{1}H–^{1}H COSY, HMQC, and HMBC methods. The ^{1}H NMR anisotropy effect of the MαNP esters is expressed by the $\Delta\delta$ value, originally defined as $\Delta\delta = \delta(R,X) - \delta(S,X)$, where *R*, *S*, and *X* denote the absolute configurations of MαNP acids (*R*)-**1** and (*S*)-**1**, and the alcohol moiety, respectively. When (*S*)-(+)-MαNP acid **1** is used for the resolution of the racemic alcohol, the equation is expressed as $\Delta\delta = \delta(R,X) - \delta(S,X) = \delta(S,-X) - \delta(S,X) = \delta$(2nd fr.) – δ(1st fr.), where *X* and *–X* denote the absolute configurations of the alcohol parts of the first- and second-eluted esters, respectively (Figure 1).[11] Thus, subtraction of the chemical shifts of the first-eluted fraction δ(1st fr.) from those of the second-eluted fraction δ(2nd fr.) gives the values of $\Delta\delta$. By placing substituent R^1 with a positive $\Delta\delta$ value on the right-side in the sector rule shown in Figure 1 and R^2 with a negative $\Delta\delta$ value on the left-hand side, the absolute configuration *X* of the first-eluted ester can be determined. As seen in Figure 4, in the case of MαNP esters **22a/22b**, the methyl group attached to the acetylene moiety shows a positive $\Delta\delta$ value, whereas the butyl group shows negative $\Delta\delta$ values leading to the (*S*) absolute configuration of the first-eluted ester **22a**. The second-eluted MαNP ester **22b** naturally has the opposite (*R*) absolute configuration.

As listed in the Exp. Sect. and shown in Figure S1 of the Supporting Information, the proton signals of the butyl group of ester **22b** are widely distributed and high-field-shifted compared with those of ester **22a**. This fact is explained well by the conformations depicted in Figure 1. In the second-eluted ester (*S*,*–X*)-**3b**, the substituent R^2, that is, the butyl group in **22b**, is located on the same side of the MαNP plane as the naphthyl group. Namely, the butyl group is placed above the naphthalene ring, and the diamagnetic anisotropy leads to the high-field shift. On the other hand, in the first-eluted ester (*S*,*X*)-**3a**, the substituent R^2, that is, the butyl group in ester **22a**, is located on the opposite side of the MαNP plane to the naphthyl group. Therefore, the protons of the butyl group are not affected by the diamagnetic anisotropy. The ^{1}H NMR behavior of esters **22a** and **22b** is thus explained.

In the case of 1-trimethylsilyl-1-dodecyn-3-ol (C_{12} chain) esters **23a/23b** with a longer alkyl chain, it was difficult to assign all the proton signals because of the extensive overlapping of proton signals of the alkyl chain, especially those of the central part. Starting from the alcohol methine proton at the 3-position, we investigated the connectivity of

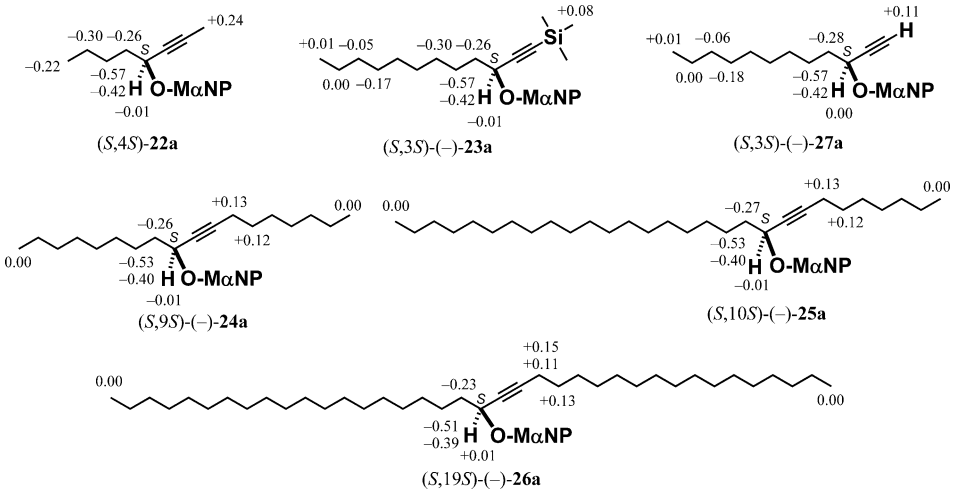


Figure 4. Observed $\Delta\delta$ values and absolute configurations of the acetylene alcohol MαNP esters as determined by the ^{1}H NMR anisotropy method ($\Delta\delta$ values are given in ppm, 600 MHz in $CDCl_3$).

protons and carbon atoms by analyzing the two-dimensional spectra and assigned the protons at the 4-, 5-, and 6-positions which allowed the $\Delta\delta$ values shown in Figure 4 to be determined. In a similar manner, starting from the terminal methyl group, the protons at the 9-, 10-, and 11-positions were assigned, and the $\Delta\delta$ values were calculated. Most of the protons of the C_9H_{19} group show negative $\Delta\delta$ values, whereas the protons of the TMS group show a positive $\Delta\delta$ value. Therefore, the AC of the first-eluted ester (–)-**23a** was unambiguously determined to be (*S*). In the ^{1}H NMR spectra of **23a**/**23b**, the alkyl chain signals of the second-eluted ester **23b** are widely distributed and high-field-shifted compared with those of the first-eluted ester **23a** (see Figures S2 and S3 of the Supporting Information).

In the case of 1-dodecyn-3-ol (C_{12} chain) MαNP esters **27a**/**27b**, a similar distribution of $\Delta\delta$ values was obtained, as shown in Figure 4, with the acetylene proton signal showing a positive $\Delta\delta$ value. The (*S*) absolute configuration was hence assigned to ester (–)-**27a**. The alkyl chain signals of the second-eluted ester **27b** are widely distributed and high-field-shifted (Figures S4 and S5).

The assignment of the ^{1}H NMR signals becomes much more difficult with increasing alkyl chain length. In the case of 10-octadecyn-9-ol (C_{18} chain) MαNP esters **24a**/**24b**, the protons at the 7- and 8-positions were assigned by correlation with the alcohol methine proton at the 9-position, leading to negative $\Delta\delta$ values for the left-hand alkyl chain. On the other hand, the protons of the right-hand alkyl chain appear isolated from the alcohol methine proton and others, and therefore it will be difficult to make a clear correlation between these protons. However, we have found that long-range coupling (J = 2.0–2.1 Hz) through a triple bond, that is, coupling between the 9-H methine proton and the 12-H methylene protons, is very useful for the assignment of the right-hand alkyl chain protons. Based on these results, the $\Delta\delta$ values of **24a**/**24b** were obtained, as shown in Figure 4, and the (*S*) absolute configuration was determined for the first-eluted ester (–)-**24a**. It is again true that in the second-eluted MαNP esters **24b**, the alkyl methylene proton signals are widely distributed and high-field-shifted compared with those of the first-eluted ester **24a** (Figure S6).

In a similar manner, the ACs of 8-nonacosyn-10-ol (C_{29} chain) MαNP esters **25a**/**25b** were determined. The 7-H methylene protons show a long-range coupling (J = 2.0–2.1 Hz) with the 10-H methine proton and could be easily assigned. The analysis of the two-dimensional spectra led to the assignment of protons 6-H, 11-H, and 12-H, and the $\Delta\delta$ values were thus calculated, as shown in Figure 4. Note that the $\Delta\delta$ values assigned to esters **25a**/**25b** are very similar to those of esters **24a**/**24b**. The (*S*) absolute configuration was thus assigned to the first-eluted ester (–)-**25a**. The alkyl methylene proton signals of **25b** are also widely distributed and high-field-shifted compared with those of the first-eluted ester **25a** (Figure S7).

This MαNP acid method has been successfully applied to 17-octatriacontyn-19-ol (C_{38} chain), an acetylene alcohol with a much longer chain structure. In MαNP esters **26a**/**26b**, most proton signals overlap with one another. However, we could assign the 20-H and 21-H methylene protons in the two-dimensional spectra starting from the alcohol 19-H methine proton. Furthermore, the long-range coupling (J = 1.9–2.0 Hz) through the acetylene bond between the methylene and methine protons was again useful for the assignment of 16-H and 15-H, and the $\Delta\delta$ values were calculated, as shown in Figure 4, leading to the (*S*) absolute configuration of the first-eluted ester (–)-**26a**. Therefore the (*R*) absolute configuration was naturally assigned to the second-eluted ester (–)-**26b**. Note that the alkyl methylene proton signals of **26b** are widely distributed and high-field-shifted compared with those of the first-eluted ester **26a** (Figure S8).

As shown in Figure 4, the first-eluted MαNP esters **22a**–**26a** have (*S*) absolute configurations, and hence the second-

eluted esters **22b**–**26b** have (*R*) absolute configurations. The general relationship between the HPLC elution order and the AC of the acetylene alcohol moiety is rationalized as depicted in Figure 1.

X-ray Crystallographic Analysis of MαNP Ester (–)-26b

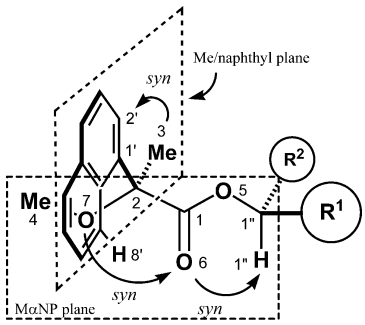
Most MαNP esters **22**–**26** were obtained as syrups or amorphous solids except for the ester (–)-**26b** which was recrystallized from *i*PrOH as thin plates. However, because they were thin crystals with only a 5 μm thickness, conventional X-ray machines could not be used. Therefore, the strong X-ray of synchrotron radiation was used for the X-ray diffraction experiment. The X-ray data are compiled in Table 2. The structure was solved by direct methods and refined by full-matrix least squares, and all hydrogen atoms were placed at their idealized positions: $R = 0.0814$. The AC of ester (–)-**26b** was unambiguously determined to be (*S*,19*R*) by using the (*S*) absolute configuration of the MαNP acid moiety as an internal reference (Figure 5). The result was in agreement with the AC determined by ^{1}H NMR anisotropy and thus proved that the ^{1}H NMR anisotropy method using MαNP acid gives the correct AC.

Table 2. X-ray crystallographic data for 17-octatriacontyn-19-ol MαNP ester (*S*,19*R*)-(–)-**26b**.

Compound	(–)-**26b**
Empirical formula	$C_{52}H_{86}O_3$
Formula mass [amu]	759.237
Solvent	*i*PrOH
Crystal size [mm]	$0.2 \times 0.02 \times 0.005$
Radiation wavelength [Å]	1.45460
Crystal system	orthorhombic
Space group	$P2_12_12_1$ (#19)
a [Å]	6.9470(1)
b [Å]	8.4830(2)
c [Å]	84.4530(15)
V [Å^3]	4976.93(16)
Z	4
$D_{calcd.}$ [g/cm^3]	1.013
No. of independent reflections, $F_o > 2.0\sigma(F_o)$	3599
No. of variables	500
Goodness of fit, *S*	1.043
Absolute configuration	(*S*,19*R*)
R (R_w)	0.0814 (0.2368)

As seen in Figure 5, MαNP ester **26b** adopts the so-called *syn*,*syn*,*syn* conformation[11s] in which the methoxy oxygen atom O-7 is synperiplanar to the ester carbonyl oxygen atom O-6, the carbonyl oxygen atom O-6 is synperiplanar to the 1′′-H methine proton, and the methyl group of the propionic acid moiety is synperiplanar to the naphthalene proton at the 2′-position (see value in Table 3). Table 3 lists the data of the crystalline-state conformation and intramolecular bifurcated hydrogen bond[11s] of ester (–)-**26b**, which represents a typical *syn*,*syn*,*syn* conformation of the MαNP ester.

Table 3. Selected data for the crystalline-state conformation and intramolecular bifurcated hydrogen bond of MαNP ester (–)-**26b**.[a]

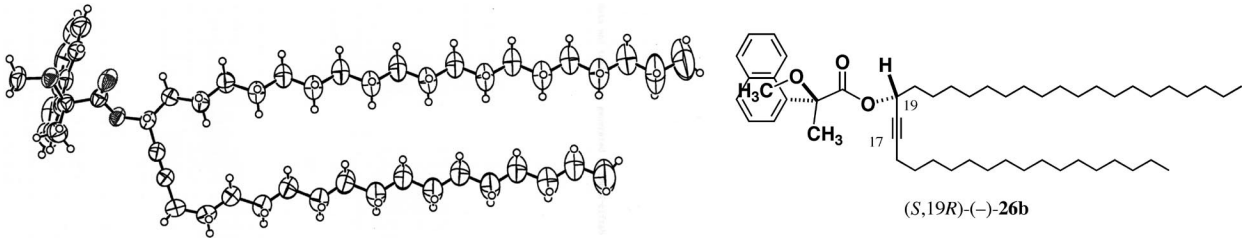


two planes, perpendicular

Compound	(–)-**26b**
Dihedral angle [°]	
C2′–C1′–C2–C3	–5.1
C1–C2–O7–C4	+175.8
C1′–O5–C1–C2	–161.6
C1′′–O5–C1–O6	+13.6
O6–C1–C2–O7	+17.5
H1′′–C1′′–O5–C1	33
Interatomic distance [Å]	
C8′–H8′	0.93
H8′–O6 (= d_1)	2.83
H8′–O7 (= d_2)	2.40
Interatomic angle [°]	
C8′–H8′–O6 (= θ_1)	140.3
C8′–H8′–O7 (= θ_2)	115.8
O6–H8′–O7 (= θ_3)	59.4

[a] The hydrogen atoms 1′′-H and 8′-H were placed at the calculated positions, and so the data regarding these atoms are not purely observed ones.

The molecular packing in the crystal of ester (–)-**26b** is shown in Figure 6, with four molecules contained in the unit lattice. It is very interesting that the two long alkyl chains (n-$C_{16}H_{33}$ and n-$C_{19}H_{39}$) of the first molecule in the unit lattice are parallel to each other and that these two alkyl chains form a pair with those of the second molecule in the unit lattice. These alkyl chain pairs are arranged so as to form an aliphatic bilayer in the crystal, and the third



(*S*,19*R*)-(–)-**26b**

Figure 5. X-ray view of 17-octatriacontyn-19-ol MαNP ester (*S*,19*R*)-(–)-**26b**.

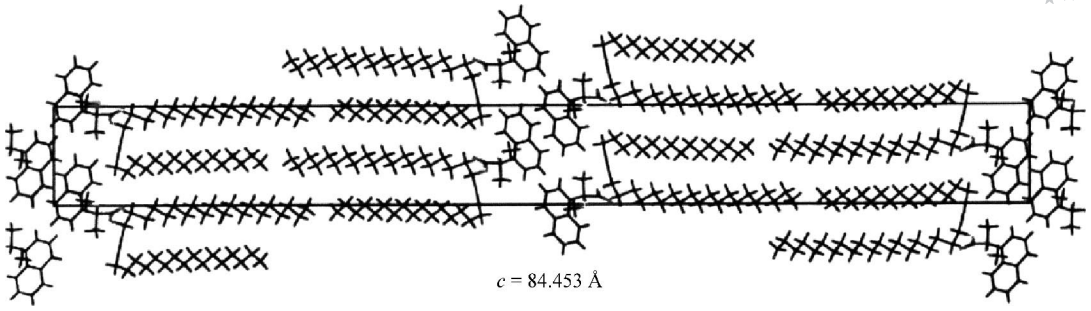
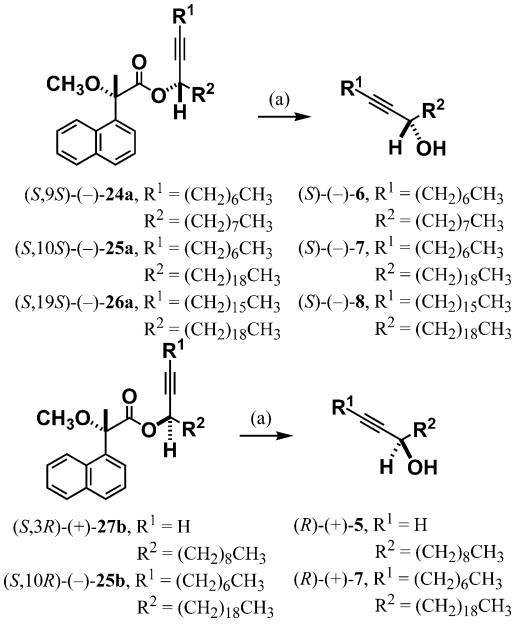


Figure 6. Crystal packing of 17-octatriacontyn-19-ol MαNP ester (*S*,19*R*)-(–)-**26b**. View along the *a* axis; the rectangle shows a unit lattice.

and fourth molecules also form an aliphatic bilayer. These aliphatic bilayer structures are similar to those of cell membranes. It is interesting that the interaction between aliphatic chains is operative not only in aqueous solutions but also in crystals.

Recovery of Enantiopure Acetylene Alcohols with Established Absolute Configurations and Their Chiroptical Properties

The MαNP esters were hydrolyzed to yield enantiopure acetylene alcohols (Scheme 4). For example, the first-eluted MαNP ester (*S*,*S*)-(–)-**26a** was treated with KOH/EtOH to yield enantiopure (*S*)-(–)-17-octatriacontyn-19-ol (**8**, 91%) as a colorless solid: $[\alpha]_D^{28}$ = –2.4 (σ = 0.07, *c* = 3.13, cyclohexane). Other acetylene alcohols were similarly obtained: (*R*)-(+)-1-dodecyn-3-ol (**5**), colorless oil, $[\alpha]_D^{21}$ = +3.0 (*c* = 1.13, $CHCl_3$); (*S*)-(–)-10-octadecyn-9-ol (**6**), colorless oil, $[\alpha]_D^{24}$ = –8.0 (σ = 0.30, ρ = 0.858, neat); (*S*)-(–)-8-nonacosyn-10-ol (**7**), colorless solid, $[\alpha]_D^{26}$ = –3.8 (σ = 0.03, *c* = 10.1, cyclohexane).



Scheme 4. Recovery of the enantiopure acetylene alcohols by hydrolysis. (a) KOH/EtOH, 83–99%.

As expected, these acetylene alcohols show small $[\alpha]_D$ values (Figure 2). In the case of alcohol (*S*)-(–)-**6**, the dependence of the $[\alpha]_D$ value on the sample state and the solvents used was studied. The observed $[\alpha]_D$ values decrease in the order of neat, solution in cyclohexane, and solution in $CHCl_3$: $[\alpha]_D^{24}$ = –8.0 (σ = 0.30, ρ = 0.858, neat), $[\alpha]_D^{23}$ = –6.4 (*c* = 6.07, cyclohexane), and $[\alpha]_D^{24}$ = +0.2 (*c* = 3.05, $CHCl_3$). Therefore, the neat measurement is better for liquid or oil samples. In the case of solid samples, nonpolar solvents such as cyclohexane are suitable.

When comparing the chiroptical properties of compounds, molar rotation $[M]_D$ is suitable, but not specific rotation $[\alpha]_D$. Thus, the $[M]_D$ values of acetylene alcohols were calculated and are listed in Table 4. Note that alcohols **6**–**8** show similar absolute values of $[M]_D$ in cyclohexane, that is, from 17.1 to 13.7. This implies that the chiroptical properties of these alcohols are mostly governed by the acetylene alcohol moiety. On the other hand, the $[M]_D$ values decrease remarkably in $CHCl_3$ solution.

Table 4. Molar rotation values of the enantiopure acetylene alcohols.

Entry	Alcohol	$[M]_D$(neat)	$[M]_D$(cyclohexane)	$[M]_D$($CHCl_3$)
1	(*S*)-(–)-**4**	–13.1	–	–8.0
2	(*R*)-(+)-**5**	–	–	+5.5
3	(*S*)-(–)-**6**	–21.3	–17.1	+0.5
4	(*S*)-(–)-**7**	–	–16.0	+0.4
5	(*R*)-(+)-**7**	–	+14.7	–
6	(*S*)-(–)-**8**	–	–13.7	–

Conclusions

The MαNP acid method has been applied to the preparation of enantiopure compounds from racemic acetylene alcohols with long alkyl chains and also to the determination of their absolute configurations by ^{1}H NMR anisotropy. It was found that diastereomeric MαNP esters were efficiently separated by HPLC on silica gel with large elution intervals. The absolute configurations of these MαNP esters were determined by the MαNP diamagnetic anisotropy method. One of these MαNP esters was obtained as single crystals, the synchrotron radiation X-ray crystallography of which confirmed the absolute configuration determined by ^{1}H NMR anisotropy. The ^{1}H NMR anisotropy

method using MαNP acid has thus been established. Hydrolysis of the MαNP esters yielded enantiopure acetylene alcohols with established absolute configurations. This method should be applicable to a variety of acetylene alcohols, and further applications are being investigated.

Experimental Section

General Methods: Melting points are uncorrected. IR spectra were obtained neat, as film on KBr, or as KBr disks with a Jasco FT/IR-410 spectrometer. ^{1}H and ^{13}C NMR spectra were recorded with a JEOL JNM-LA400 (400 and 100 MHz) and/or a JEOL JNM-LA600 (600 and 150 MHz) spectrometer. All NMR spectroscopic data are reported in ppm (δ) downfield from TMS. In the long-chain aliphatic compounds described below, the ^{13}C NMR peaks heavily overlap each other, like the ^{1}H NMR signals, and therefore it was difficult to identify the peaks of all the carbon atoms. The ^{13}C NMR spectroscopic data reported below are those obtained by peak-picking and therefore the peak numbers do not always agree with those of the carbon atoms. Optical rotations $[\alpha]_D$ were measured with a Jasco DIP-1000 spectropolarimeter, where σ is the standard deviation of the observed $[\alpha]_D$ value. The starting materials **9**, **12**, **13**, and **16**–**19** were commercially available. Silica gel 60 F_{254} precoated plates on glass from Merck Ltd. were used for thin-layer chromatography (TLC). HPLC separation and purification were performed using a prepacked glass column (Kusano 22 $\phi \times$ 300 mm, or 25 $\phi \times$ 400 mm, silica gel particle size 5–10 μm), a pump (Jasco PRC-70S, pressure 25–30 kgf cm^{-2}, flow rate 10 mL min^{-1}) and a UV/RI detector (Shimamura YRU-880). The purities of the title compounds were shown to be ≥99% by ^{1}H NMR, TLC, HPLC, and/or elemental analysis.

X-ray Crystallography of MαNP Ester (*S*,19*R*)-(–)-26b: As the single crystals of MαNP ester (–)-**26b** obtained by recrystallization from *i*PrOH are thin plates, the strong X-ray of synchrotron radiation at SPring-8 in Hyogo, Japan, was employed in the X-ray diffraction experiment: λ = 1.45460 Å; monochromator Si_111; data collected at 293 K; see Table 2 for other crystallographic data. The structure was solved by direct methods and refined by full-matrix least squares, with all hydrogen atoms placed at their idealized positions: R = 0.0814 for 3599 reflections with $I > 2\sigma(I)$ and 500 parameters (Figure 4 and Table 2). The absolute configuration of (*S*,19*R*)-(–)-**26b** was determined by using the (*S*)-MαNP acid moiety as the internal reference of absolute configuration. CCDC-671893 contains the supplementary crystallographic data for ester (–)-**26b**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Preparation of Racemic 2-Octyn-4-ol (11): A mixture of 2-butyn-1-ol (**9**) (0.561 g, 8.0 mmol) and pyridinium chlorochromate (PCC, 2.59 g, 12.0 mmol) in CH_2Cl_2 (13 mL) was stirred at room temperature for 4 h. After filtration through Celite, the filtrate was distilled to give 2-butynal (**10**) containing some CH_2Cl_2. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.08 (d, J = 1.0 Hz, 3 H), 9.16 (q, J = 1.0 Hz, 1 H) ppm. A solution of *n*-butyllithium in hexane (1.54 M, 5.64 mL, 8.69 mmol) was added dropwise to a solution of the crude product **10** in THF (10 mL) at 0 °C, and the mixture was stirred at room temperature overnight. After addition of aqueous NH_4Cl solution, the mixture was extracted three times with diethyl ether. The combined organic layers were washed with brine, dried with anhydrous $MgSO_4$, and distilled with a Kugelrohr apparatus to yield alcohol **11**. Yield 0.092 g, 9% for two steps; colorless liquid; b.p. 85 °C/28 Torr. IR (neat): $\tilde{\nu}_{max}$ = 3363, 2957, 2932, 2861, 1466, 1379, 1151, 1104, 1038, 891 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.92 (t, J = 7.1 Hz, 3 H), 1.30–1.46 (m, 4 H), 1.62–1.70 (m, 2 H), 1.85 (d, J = 2.2 Hz, 3 H), 4.33 (m, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 3.5, 14.0, 22.3, 27.3, 37.8, 62.7, 80.5, 80.9 ppm.

Preparation of Long-Chain Aldehydes 14 and 15: For example, a mixture of 1-heptadecanol (**12**) (0.500 g, 1.95 mmol) and pyridinium chlorochromate (PCC, 0.500 g, 2.32 mmol) in CH_2Cl_2 (10 mL) was stirred at room temperature overnight. After filtration through Celite, the filtrate was concentrated, and the residue was subjected to HPLC on silica gel (hexane/EtOAc = 20:1) to yield aldehyde **14**.

1-Heptadecanal (14): Yield 0.400 g, 80%; colorless solid. IR (film): $\tilde{\nu}_{max}$ = 2915, 2849, 1713, 1473 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88 (t, J = 6.8 Hz, 3 H), 1.26 (m, 26 H), 1.63 (tt, J = 7.4, 7.4 Hz, 2 H), 2.42 (td, J = 7.4, 1.9 Hz, 2 H), 9.77 (t, J = 1.9 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 22.0, 22.7, 29.1, 29.3, 29.3, 29.4, 29.5, 29.6–29.7 (m), 31.9, 43.9, 203.0 ppm.

1-Icosanal (15): Yield 1.62 g, 81%; colorless solid. IR (film): $\tilde{\nu}_{max}$ = 2953, 2917, 2848, 2357, 2331, 1770, 1702, 1463, 719 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88 (t, J = 6.8 Hz, 3 H), 1.19–1.30 (m, 32 H), 1.63 (tt, J = 7.3, 7.3 Hz, 2 H), 2.42 (td, J = 7.3, 1.9 Hz, 2 H), 9.77 (t, J = 1.9 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 22.1, 22.7, 29.2, 29.4, 29.4, 29.6–29.7 (m), 31.9, 43.9, 203.0 ppm.

Preparation of Acetylene Alcohols 6, 7, and 20: For example, a solution of *n*-butyllithium in hexane (1.54 M, 5.52 mL, 8.5 mmol) was added dropwise to a solution of 1-nonyne (**16**, 0.994 g, 8.0 mmol) in dried THF (35 mL) at 0 °C, followed by the dropwise addition of nonanal (**18**, 1.14 g, 8.0 mmol) at 0 °C, and then the mixture was stirred at room temperature overnight. After addition of an aqueous NH_4Cl solution, the mixture was extracted four times with EtOAc. The combined organic layers were washed with brine, dried with anhydrous $MgSO_4$, and the solvents evaporated to dryness. The oily residue was purified by short-column chromatography on silica gel (hexane/EtOAc = 10:1) to yield alcohol **6**.

10-Octadecyn-9-ol (6): Yield 1.64 g, 77%; colorless oil. IR (neat): $\tilde{\nu}_{max}$ = 3346, 2927, 2856, 1466, 1379, 1333, 1142, 1115, 1022 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88 (t, J = 6.8 Hz, 3 H), 0.89 (t, J = 6.8 Hz, 3 H), 1.27–1.53 (m, 20 H), 1.61–1.72 (m, 4 H), 2.20 (td, J = 7.0, 2.0 Hz, 2 H), 4.35 (ddt, J = 9.9, 6.3, 2.0 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 14.1, 18.7, 22.6, 22.7, 25.2, 28.7, 28.8, 28.8, 29.2, 29.3, 29.5, 31.7, 31.9, 38.2, 62.8, 81.3, 85.6 ppm.

8-Nonacosyn-10-ol (7): Yield 1.43 g, 68%; colorless solid. IR (film): $\tilde{\nu}_{max}$ = 3365, 3303, 2954, 2915, 2872, 2848, 1464, 1145, 1080, 1064, 805, 723, 644 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88 (t, J = 6.8 Hz, 3 H), 0.89 (t, J = 6.8 Hz, 3 H), 1.19–1.53 (m, 44 H), 1.66 (m, 2 H), 2.20 (td, J = 7.1, 2.0 Hz, 2 H), 4.35 (tt, J = 6.6, 2.0 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.0, 14.1, 18.6, 22.6, 22.7, 25.2, 28.6, 28.8, 29.3–29.7 (m), 31.7, 31.9, 38.2, 62.8, 81.3, 85.5 ppm. $C_{29}H_{56}O$ (420.76): calcd. C 82.78, H 13.42; found C 82.55, H 13.46.

1-Trimethylsilyl-1-dodecyn-3-ol (20): Yield 1.26 g, 49%; colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.17 (s, 9 H), 0.88 (t, J = 7.0 Hz, 3 H), 1.27–1.34 (m, 12 H), 1.43 (m, 2 H), 1.68 (m, 2 H), 1.84 (d, J = 5.6 Hz, 1 H), 4.35 (dd, J = 10.2, 6.6 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 0.0, 14.2, 22.8, 25.2, 29.3, 29.4, 29.6, 29.6, 32.0, 37.8, 63.1, 89.4, 107.1 ppm.

Preparation of 1,1-Dibromo-1-octadecene (21): Triphenylphosphane (1.7 g, 6.5 mmol) was added portionwise to a solution of CBr_4 (1.0 g, 3.0 mmol) in CH_2Cl_2 (15 mL) at 0 °C, and the mixture was stirred for 10 min. Heptadecanal (**14**, 0.390 g, 1.5 mmol) was then added. After being stirred for 2 h, the mixture was filtered through Celite, and the filtrate was concentrated to dryness. The oily residue was purified by short-column chromatography on silica gel (hexane) to yield compound **21**. Yield 0.555 g, 85%; colorless oil. IR (neat): $\tilde{\nu}_{max}$ = 2924, 2853, 1466, 800, 721 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.88 (t, J = 6.8 Hz, 3 H), 1.26 (m, 26 H), 1.38–1.43 (m, 2 H), 2.09 (td, J = 7.3, 7.3 Hz, 2 H), 6.39 (t, J = 7.3 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 22.7, 27.8, 29.0, 29.3, 29.4, 29.5, 29.6, 29.7–29.8 (m), 31.9, 33.0, 88.4, 138.9 ppm.

Preparation of 17-Octatriacontyn-19-ol (8): A solution of *n*-butyllithium in hexane (1.54 M, 2.0 mL, 3.1 mmol) was added dropwise to a solution of 1,1-dibromo-1-octadecene (**21**, 0.550 g, 1.3 mmol) in dried THF (14 mL) at –78 °C, and the mixture was stirred for 20 min. A solution of icosanal (**15**, 0.400 g, 1.3 mmol) in THF (5 mL) was added dropwise, and then the mixture was stirred at room temperature for 2 h. After addition of an aqueous NH_4Cl solution, the mixture was extracted with EtOAc several times. The combined organic layers were washed with brine, dried with anhydrous $MgSO_4$, and the solvents evaporated to dryness. The residue was purified by short-column chromatography on silica gel (hexane/EtOAc = 10:1) to yield alcohol **8**. Yield 0.234 g, 32%; colorless solid. IR (film): $\tilde{\nu}_{max}$ = 2917, 2849, 1466, 722 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.88 (t, J = 7.0 Hz, 6 H), 1.23–1.73 (m, 64 H), 2.20 (td, J = 7.1, 2.0 Hz, 2 H), 4.32–4.37 (m, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 14.1, 18.6, 22.7, 22.7, 25.2, 28.6–29.7 (m), 31.9, 38.2, 62.8, 81.3, 85.5 ppm. $C_{38}H_{74}O$ (546.99): calcd. C 83.44, H 13.64; found C 82.74, H 13.30.

Preparation of Diastereomeric Acetylene Alcohol MαNP Esters 22–26 and HPLC Separation: For example, a solution of racemic alcohol (±)-**11** (0.0401 g, 0.320 mmol) in CH_2Cl_2 (0.4 mL) was added to a solution of (*S*)-(+)-2-methoxy-2-(1-naphthyl)propionic acid [MαNP acid (**1**), 0.081 g, 0.35 mmol], DCC (0.132 g, 0.64 mmol), DMAP (0.020 g, 0.16 mmol), and CSA (0.0149 g, 0.060 mmol) in CH_2Cl_2 (0.6 mL) at 0 °C, and the mixture was gently heated at reflux whilst being stirred overnight. After addition of a small amount of water, stirring for 1 h, and addition of diethyl ether and anhydrous $MgSO_4$, the mixture was filtered through Celite which was then washed with EtOAc. The combined organic layers were concentrated under reduced pressure, and the residue was subjected to HPLC on silica gel (22 $\phi \times$ 300 mm column, Table 1) to give the first- and second-eluted esters **22a** and **22b**, respectively.

(*S*,4*S*)-2-Octyn-4-ol MαNP Ester (22a): Yield 0.0219 g, 20%; colorless syrup. IR (neat): $\tilde{\nu}_{max}$ = 3050, 2955, 2935, 2871, 2830, 2361, 2341, 2246, 1733, 1510, 1458, 1370, 1237, 1133, 1051, 955, 806, 780 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ = 0.77 (t, J = 7.1 Hz, 3 H), 1.15 (m, 2 H), 1.16 (m, 2 H), 1.59 (m, 2 H), 1.64 (d, J = 2.0 Hz, 3 H), 1.99 (s, 3 H), 3.18 (s, 3 H), 5.31 (tq, J = 6.7, 2.0 Hz, 1 H), 7.45 (m, 3 H), 7.65 (dd, J = 7.4, 1.1 Hz, 1 H), 7.83 (m, 2 H), 8.36 (m, 1 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 3.4, 13.8, 22.0, 22.1, 27.0, 34.3, 51.3, 65.6, 76.1, 81.7, 81.8, 124.7, 125.3, 125.4, 125.5, 126.1, 128.7, 129.3, 131.1, 134.1, 135.5, 173.1 ppm. UV (EtOH): λ_{max} (ε) = 291.8 (4100), 281.2 (5900), 271.4 (4900), 224.0 (57600 $L\,mol^{-1}\,cm^{-1}$) nm. CD (EtOH): λ_{ext} ($\Delta\varepsilon$) = 283.4 (+0.4), 248.2 (–0.4), 237.8 (+0.5), 224.2 (–8.4), 222.8 (–9.1), 212.0 (–11.1 $L\,mol^{-1}\,cm^{-1}$) nm. $C_{22}H_{26}O_3$ (338.44): calcd. C 78.07, H 7.74; found C 78.01, H 7.80.

(*S*,4*R*)-2-Octyn-4-ol MαNP Ester (22b): Yield 0.0230 g, 21%; colorless syrup. IR (neat): $\tilde{\nu}_{max}$ = 3050, 2955, 2934, 2871, 2829, 2359, 2341, 2247, 1749, 1509, 1457, 1369, 1237, 1134, 1050, 957, 806, 781 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ = 0.55 (t, J = 7.3 Hz, 3 H), 0.58 (m, 1 H), 0.73 (m, 1 H), 0.86 (m, 2 H), 1.33 (m, 2 H), 1.78 (d, J = 2.0 Hz, 3 H), 2.02 (s, 3 H), 3.10 (s, 3 H), 5.31 (ddq, J = 7.1, 5.7, 2.0 Hz, 1 H), 7.45 (m, 3 H), 7.60 (dd, J = 7.3, 1.1 Hz, 1 H), 7.83 (m, 2 H), 8.42 (m, 1 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 3.6, 13.6, 21.5, 21.8, 26.3, 34.4, 50.9, 65.2, 76.4, 81.5, 81.6, 124.6, 125.4, 125.7, 125.9, 126.4, 128.6, 129.4, 131.5, 134.1, 134.9, 173.2 ppm. UV (EtOH): λ_{max} (ε) = 291.8 (4700), 281.2 (6800), 271.4 (5500), 224.2 (64700 $L\,mol^{-1}\,cm^{-1}$) nm. CD (EtOH): λ_{ext} ($\Delta\varepsilon$) = 292.0 (–1.2), 280.8 (–1.7), 270.6 (–1.4), 231.6 (+2.5), 212.8 (–11.6), 210.8 (–11.8 $L\,mol^{-1}\,cm^{-1}$) nm. $C_{22}H_{26}O_3$ (338.44): calcd. C 78.07, H 7.74; found C 77.91, H 7.93.

(*S*,3*S*)-(–)-1-Trimethylsilyl-1-dodecyn-3-ol MαNP Ester (23a): Yield 0.114 g, 49%; colorless syrup. $[\alpha]_D^{20}$ = –46.7 (c = 1.10, $CHCl_3$). IR (neat): $\tilde{\nu}_{max}$ = 3051, 2926, 2855, 2358, 2179, 1737, 1600, 1510, 1463, 1398, 1372, 1344, 1250, 1180, 1133, 1119, 1053, 954, 845, 805, 778, 761 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ = 0.05 (s, 9 H), 0.88 (t, J = 7.1 Hz, 3 H), 1.14 (m, 2 H), 1.17 (m, 6 H), 1.22 (m, 2 H), 1.27 (m, 2 H), 1.28 (m, 2 H), 1.62 (m, 2 H), 1.98 (s, 3 H), 3.20 (s, 3 H), 5.35 (dd, J = 7.3, 6.4 Hz, 1 H), 7.45 (m, 3 H), 7.65 (dd, J = 7.3, 0.9 Hz, 1 H), 7.83 (m, 2 H), 8.33 (m, 1 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 0.0, 14.1, 22.2, 22.6, 24.8, 29.2, 29.3, 29.4, 31.6, 31.9, 34.4, 51.3, 65.3, 81.9, 90.2, 102.1, 124.7, 125.1, 125.3, 125.5, 126.3, 128.7, 129.3, 131.0, 134.1, 135.5, 172.9 ppm. UV (EtOH): λ_{max} (ε) = 291.6 (4000), 281.2 (5800), 271.2 (4800), 223.8 (57000 $L\,mol^{-1}\,cm^{-1}$) nm. CD (EtOH): λ_{ext} ($\Delta\varepsilon$) = 281.6 (+0.6), 248.0 (–0.6), 244.4 (–0.5), 223.2 (–13.0), 221.0 (–12.6 $L\,mol^{-1}\,cm^{-1}$) nm. $C_{29}H_{42}O_3Si$ (466.73): calcd. C 74.63, H 9.07; found C 74.51, H 9.05.

(*S*,3*R*)-(–)-1-Trimethylsilyl-1-dodecyn-3-ol MαNP Ester (23b): Yield 0.118 g, 50%; colorless syrup. $[\alpha]_D^{20}$ = –3.27 (c = 1.08, $CHCl_3$). IR (neat): $\tilde{\nu}_{max}$ = 3053, 2955, 2926, 2855, 2363, 2341, 2178, 1754, 1600, 1510, 1464, 1368, 1250, 1133, 1120, 1051, 845, 804, 780, 760 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ = 0.13 (s, 9 H), 0.63 (m, 1 H), 0.74 (m, 1 H), 0.84 (m, 2 H), 0.89 (m, 2 H), 0.89 (t, J = 7.2 Hz, 3 H), 1.05 (tt, J = 7.3, 7.3 Hz, 2 H), 1.19 (m, 2 H), 1.22 (m, 2 H), 1.28 (tt, J = 7.2 Hz, 2 H), 1.36 (m, 2 H), 2.01 (s, 3 H), 3.10 (s, 3 H), 5.34 (dd, J = 7.3, 6.5 Hz, 1 H), 7.45 (m, 3 H), 7.60 (dd, J = 7.3, 1.1 Hz, 1 H), 7.83 (m, 2 H), 8.42 (m, 1 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 0.0, 14.1, 21.4, 22.7, 24.2, 28.6, 29.1, 29.2, 29.3, 31.9, 34.3, 51.0, 65.0, 81.5, 90.2, 102.4, 124.6, 125.3, 125.7, 125.9, 126.5, 128.6, 129.5, 131.5, 134.0, 134.7, 173.0 ppm. UV (EtOH): λ_{max} (ε) = 292.4 (4800), 281.4 (6700), 271.4 (5600), 224.2 (64000 $L\,mol^{-1}\,cm^{-1}$) nm. CD (EtOH): λ_{ext} ($\Delta\varepsilon$) = 291.0 (–1.3), 280.4 (–1.9), 271.0 (–1.5), 229.4 (+2.4), 212.2 (+13.2), 209.0 (–14.2 $L\,mol^{-1}\,cm^{-1}$) nm. $C_{29}H_{42}O_3Si$ (466.73): calcd. C 74.63, H 9.07; found C 74.60, H 9.00.

(*S*,9*S*)-(–)-10-Octadecyn-9-ol MαNP Ester (24a): Yield 0.894 g, 47%; colorless syrup. $[\alpha]_D^{22}$ = –42.6 (c = 1.03, $CHCl_3$). IR (neat): $\tilde{\nu}_{max}$ = 3050, 2927, 2856, 2362, 2342, 1735, 1460, 1245, 1133, 1119, 1053, 805, 778 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ = 0.88 (t, J = 7.1 Hz, 3 H), 0.88 (t, J = 7.1 Hz, 3 H), 1.1–1.35 (m, 16 H), 1.15 (m, 2 H), 1.19 (m, 2 H), 1.32 (m, 2 H), 1.60 (m, 2 H), 1.98 (s, 3 H), 2.00 (td, J = 7.1, 2.1 Hz, 2 H), 3.18 (s, 3 H), 5.34 (tt, J = 6.7, 2.1 Hz, 1 H), 7.45 (m, 3 H), 7.64 (dd, J = 7.3, 1.1 Hz, 1 H), 7.82 (m, 2 H), 8.36 (m, 1 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 14.1, 14.1, 18.5, 22.2, 22.6, 22.6, 24.9, 28.3, 28.7, 28.7, 28.9, 29.1, 29.3, 31.7, 31.8, 34.7, 51.3, 65.6, 81.8, 86.3, 124.7, 125.3, 125.3, 125.5, 126.1, 128.7, 129.3, 131.1, 134.1, 135.5, 173.0 ppm. UV

(EtOH): λ_{max} (ε) = 292.2 (3700), 281.4 (5300), 271.8 (4400), 224.4 (50000 L mol^{-1} cm^{-1}) nm. CD (EtOH): λ_{ext} ($\Delta\varepsilon$) = 285.2 (+0.4), 246.4 (–0.4), 234.4 (+0.3), 223.4 (–8.5), 222.4 (–8.4), 219.6 (–7.7 L mol^{-1} cm^{-1}) nm. $C_{32}H_{46}O_3$ (478.71): calcd. C 80.29, H 9.69; found C 80.18, H 9.59.

(*S*,9*R*)-(–)-10-Octadecyn-9-ol MαNP Ester (24b): Yield 0.853 g, 45%; colorless syrup. $[\alpha]_D^{22}$ = –6.1 (c = 1.08, $CHCl_3$). IR (neat): $\tilde{\nu}_{max}$ = 3051, 2927, 2856, 2359, 2337, 2243, 1752, 1600, 1510, 1465, 1369, 1346, 1237, 1134, 1053, 957, 805, 780, 723, 535 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 0.62 (m, 1 H), 0.75 (m, 1 H), 0.83 (m, 2 H), 0.88 (t, J = 7.3 Hz, 3 H), 0.88 (t, J = 7.1 Hz, 3 H), 1.06 (dddd, J = 7.2, 7.2, 7.2, 7.2 Hz, 2 H), 1.16 (dddd, J = 8.5, 7.2, 7.2, 7.1 Hz, 2 H), 1.34 (m, 2 H), 1.23–1.37 (m, 12 H), 1.44 (br. tt, J = 7.2, 7.2 Hz, 2 H), 2.00 (s, 3 H), 2.13 (td, J = 7.2, 2.0 Hz, 2 H), 3.10 (s, 3 H), 5.33 (ddt, J = 7.0, 5.6, 2.0 Hz, 1 H), 7.45 (m, 3 H), 7.59 (dd, J = 7.3, 1.1 Hz, 1 H), 7.82 (m, 2 H), 8.43 (m, 1 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 14.1, 14.1, 18.6, 21.4, 22.6, 22.6, 24.2, 28.4, 28.7, 28.7, 28.7, 29.1, 29.2, 31.7, 31.8, 34.7, 50.9, 65.2, 77.3, 81.4, 86.2, 124.6, 125.4, 125.6, 125.8, 126.4, 128.6, 129.4, 131.5, 134.0, 134.8, 173.1 ppm. UV (EtOH): λ_{max} (ε) = 292.2 (4400), 281.2 (6300), 271.4 (5200), 224.0 (60600 L mol^{-1} cm^{-1}) nm. CD (EtOH): λ_{ext} ($\Delta\varepsilon$) = 291.6 (–1.3), 280.6 (–1.9), 271.0 (–1.5), 232.0 (+1.8), 213.4 (–11.2), 210.2 (–12.4), 208.0 (–12.1), 205.0 (–11.4 L mol^{-1} cm^{-1}) nm. $C_{32}H_{46}O_3$ (478.71): calcd. C 80.29, H 9.69; found C 80.19, H 9.64.

(*S*,10*S*)-(–)-8-Nonacosyn-10-ol MαNP Ester (25a): Yield 0.105 g, 33%; colorless syrup. $[\alpha]_D^{30}$ = –33.1 (c = 1.03, $CHCl_3$). IR (neat): $\tilde{\nu}_{max}$ = 3054, 2925, 2854, 2359, 1736, 1509, 1466, 1371, 1246, 1180, 1119, 1053, 804, 777, 423 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 0.88 (t, J = 7.1 Hz, 3 H), 0.88 (t, J = 7.1 Hz, 3 H), 1.10–1.35 (m, 44 H), 1.32 (m, 2 H), 1.60 (m, 2 H), 1.98 (s, 3 H), 2.00 (td, J = 7.1, 2.1 Hz, 2 H), 3.18 (s, 3 H), 5.34 (tt, J = 6.7, 2.1 Hz, 1 H), 7.45 (m, 3 H), 7.64 (dd, J = 7.3, 1.1 Hz, 1 H), 7.82 (m, 2 H), 8.36 (m, 1 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 14.1, 14.1, 18.5, 22.2, 22.6, 22.7, 24.9, 28.3–29.7 (m), 31.7, 31.9, 34.7, 51.3, 65.6, 81.9, 86.3, 124.7, 125.3, 125.3, 125.5, 126.1, 128.7, 129.3, 131.1, 134.1, 135.6, 173.0 ppm. UV (EtOH): λ_{max} (ε) = 291.8 (2100), 281.6 (3100), 271.8 (2600), 224.4 (30000 L mol^{-1} cm^{-1}) nm. CD (EtOH): λ_{ext} ($\Delta\varepsilon$) = 282.6 (+0.2), 247.6 (–0.3), 235.2 (+0.1), 221.8 (–4.5), 218.8 (–4.7), 216.6 (–4.6 L mol^{-1} cm^{-1}) nm. $C_{43}H_{68}O_3$ (633.00): calcd. C 81.59, H 10.83; found C 81.54, H 10.91.

(*S*,10*R*)-(–)-8-Nonacosyn-10-ol MαNP Ester (25b): Yield 0.139 g, 44%; colorless syrup. $[\alpha]_D^{22}$ = –3.2 (c = 1.12, $CHCl_3$). IR (neat): $\tilde{\nu}_{max}$ = 3051, 2925, 2853, 1754, 1509, 1466, 1368, 1247, 1133, 803, 778 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 0.61 (m, 1 H), 0.74 (m, 1 H), 0.83 (m, 2 H), 0.88 (t, J = 7.1 Hz, 3 H), 0.88 (t, J = 7.1 Hz, 3 H), 0.89 (m, 2 H), 1.05 (tt, J = 7.3, 7.3 Hz, 2 H), 1.16 (m, 2 H), 1.20–1.40 (m, 36 H), 1.44 (tt, J = 7.3, 7.3 Hz, 2 H), 2.01 (s, 3 H), 2.13 (td, J = 7.1, 2.0 Hz, 2 H), 3.10 (s, 3 H), 5.33 (ddt, J = 7.1, 5.6, 2.0 Hz, 1 H), 7.45 (m, 3 H), 7.59 (dd, J = 7.2, 1.0 Hz, 1 H), 7.82 (m, 2 H), 8.43 (m, 1 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 14.1, 14.1, 18.6, 21.5, 22.6, 22.7, 24.2, 28.4–29.7 (m), 31.7, 31.9, 34.7, 50.9, 65.2, 77.3, 81.5, 86.2, 124.6, 125.4, 125.6, 125.8, 126.4, 128.6, 129.4, 131.33, 134.0, 134.9, 173.1 ppm. UV (EtOH): λ_{max} (ε) = 292.4 (2200), 281.6 (3200), 272.0 (2700), 224.4 (31300 L mol^{-1} cm^{-1}) nm. CD (EtOH): λ_{ext} ($\Delta\varepsilon$) = 291.6 (–0.5), 280.8 (–0.8), 228.2 (+1.3), 210.0 (–4.9), 207.6 (–4.9 L mol^{-1} cm^{-1}) nm. $C_{43}H_{68}O_3$ (633.00): calcd. C 81.59, H 10.83; found C 81.61, H 11.05.

(*S*,19*S*)-(–)-17-Octatriacontyn-19-ol MαNP Ester (26a): Yield 47%; colorless solid. $[\alpha]_D^{29}$ = –26.0 (c = 1.36, $CHCl_3$). IR (film): $\tilde{\nu}_{max}$ = 3053, 2924, 2853, 1736, 1510, 1466, 1371, 1245, 1180, 1120, 1054, 804, 777, 721 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 0.88 (t, J = 7.1 Hz, 3 H), 0.88 (t, J = 7.1 Hz, 3 H), 1.10–1.35 (m, 62 H), 1.59 (m, 2 H), 1.98 (s, 3 H), 1.98 (dtd, J = 16.7, 7.1, 2.0 Hz, 1 H), 2.02 (dtd, J = 16.7, 7.1, 2.0 Hz, 1 H), 3.19 (s, 3 H), 5.32 (tt, J = 6.7, 2.0 Hz, 1 H), 7.43–7.47 (m, 3 H), 7.64 (dd, J = 7.3, 1.2 Hz, 1 H), 7.80–7.84 (m, 2 H), 8.36 (m, 1 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 14.1, 14.1, 18.5, 22.2, 22.7, 22.7, 24.9, 28.4, 28.7, 28.9, 29.1, 29.4–29.7 (m), 31.9, 34.7, 51.3, 65.6, 81.9, 86.3, 124.7, 125.3, 125.3, 125.5, 126.1, 128.7, 129.3, 131.1, 134.1, 135.6, 173.0 ppm. UV (EtOH): λ_{max} (ε) = 293.6 (4900), 281.8 (7000), 271.8 (5800), 224.6 (68800 L mol^{-1} cm^{-1}) nm. CD (EtOH): λ_{ext} ($\Delta\varepsilon$) = 281.8 (+0.6), 234.0 (+0.5), 221.6 (–11.6 L mol^{-1} cm^{-1}) nm. $C_{52}H_{86}O_3$ (759.24): calcd. C 82.26, H 11.42; found C 82.29, H 11.66.

(*S*,19*R*)-(–)-17-Octatriacontyn-19-ol MαNP Ester (26b): Yield 49%; colorless needles from *i*PrOH. $[\alpha]_D^{29}$ = –2.7 (c = 10.89, $CHCl_3$). IR (film): $\tilde{\nu}_{max}$ = 3050, 2925, 2853, 1754, 1601, 1510, 1466, 1368, 1237, 1181, 1134, 1054, 804, 778, 721 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 0.63 (m, 1 H), 0.75 (m, 1 H), 0.88 (t, J = 7.1 Hz, 3 H), 0.88 (t, J = 7.1 Hz, 3 H), 0.80–0.94 (m, 4 H), 1.05 (tt, J = 7.2, 7.2 Hz, 2 H), 1.17 (m, 2 H), 1.19–1.39 (m, 52 H), 1.43 (tt, J = 7.2, 7.2 Hz, 2 H), 2.01 (s, 3 H), 2.13 (td, J = 7.2, 1.9 Hz, 2 H), 3.10 (s, 3 H), 5.33 (ddt, J = 7.0, 5.6, 1.9 Hz, 1 H), 7.42–7.47 (m, 3 H), 7.59 (dd, J = 7.2, 0.8 Hz, 1 H), 7.80–7.83 (m, 2 H), 8.42–8.44 (m, 1 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 14.1, 14.1, 18.6, 21.5, 22.6, 22.7, 24.2, 28.5, 28.7, 28.7, 29.1, 29.2, 29.4, 29.4, 29.5, 29.6–29.7 (m), 31.6, 31.9, 34.7, 50.9, 65.2, 77.3, 81.5, 86.2, 124.6, 125.4, 125.6, 125.8, 126.4, 128.6, 129.4, 131.5, 134.1, 134.9, 173.1 ppm. UV (EtOH): λ_{max} (ε) = 291.8 (5000), 281.8 (7300), 271.8 (6000), 224.6 (70400 L mol^{-1} cm^{-1}) nm. CD (EtOH): λ_{ext} ($\Delta\varepsilon$) = 291.6 (–1.5), 281.0 (–2.2), 271.0 (–1.7), 229.0 (+2.9), 208.0 (–14.7 L mol^{-1} cm^{-1}) nm. $C_{52}H_{86}O_3$ (759.24): calcd. C 82.26, H 11.42; found C 82.14, H 11.64.

Deprotection of the TMS Group of MαNP Esters 23a/23b and HPLC Separation: A THF solution of tetrabutylammonium fluoride (TBAF, 1.0 M, 0.439 mL, 0.439 mmol) was added to a solution of MαNP esters **23a**/**23b** (diastereomeric mixture, 0.171 g, 0.366 mmol) in THF (0.3 mL), and the mixture was stirred at room temperature overnight. The mixture was subjected to short-column chromatography on silica gel (hexane/EtOAc, 10:1) to give a mixture of diastereomeric esters which was further separated by HPLC on silica gel (Table 1) to give the first- and second-eluted esters **27a** and **27b**, respectively.

(*S*,3*S*)-(–)-1-Dodecyn-3-ol MαNP Ester (27a): Yield 0.0545 g, 38%; colorless syrup. $[\alpha]_D^{25}$ = –50.2 (c = 1.02, $CHCl_3$). IR (neat): $\tilde{\nu}_{max}$ = 3309, 3291, 3051, 2927, 2855, 2359, 2341, 1752, 1510, 1465, 1369, 1237, 1181, 1134, 1121, 1052, 991, 805, 780 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 0.88 (t, J = 7.1 Hz, 3 H), 1.15 (m, 8 H), 1.23 (m, 4 H), 1.28 (m, 2 H), 1.65 (m, 2 H), 1.99 (s, 3 H), 2.26 (d, J = 2.2 Hz, 1 H), 3.20 (s, 3 H), 5.34 (td, J = 6.7, 2.2 Hz, 1 H), 7.45 (m, 3 H), 7.65 (dd, J = 7.1, 1.1 Hz, 1 H), 7.83 (m, 2 H), 8.33 (m, 1 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 14.1, 22.2, 22.7, 24.7, 28.8, 29.2, 29.3, 29.4, 31.8, 34.2, 51.3, 64.8, 73.6, 80.5, 81.8, 124.7, 125.1, 125.3, 125.5, 126.3, 128.8, 129.4, 131.0, 134.1, 135.4, 173.0 ppm. UV (EtOH): λ_{max} (ε) = 291.4 (3400), 281.0 (5000), 271.4 (4100), 223.8 (49000 L mol^{-1} cm^{-1}) nm. CD (EtOH): λ_{ext} ($\Delta\varepsilon$) = 243.4 (–0.7), 241.8 (–0.6), 237.2 (–0.5), 222.4 (–4.9), 218.8 (–4.7 L mol^{-1} cm^{-1}) nm. $C_{26}H_{34}O_3$ (394.55): calcd. C 79.15, H 8.69; found C 79.41, H 8.83.

(*S*,3*R*)-(+)-1-Dodecyn-3-ol MαNP Ester (27b): Yield 0.0549 g, 38%; colorless syrup. $[\alpha]_D^{25}$ = +3.27 (c = 1.03, $CHCl_3$). IR (neat): $\tilde{\nu}_{max}$ = 3309, 3291, 3051, 2926, 2855, 2358, 2341, 1752, 1600, 1510, 1465, 1369, 1237, 1181, 1134, 1121, 1052, 991, 805, 780 cm^{-1}. ^{1}H NMR

(600 MHz, $CDCl_3$): δ = 0.58 (m, 1 H), 0.73 (m, 1 H), 0.77–0.92 (m, 4 H), 0.89 (t, J = 7.3 Hz, 3 H), 1.05 (tdd, J = 7.5, 7.5, 7.2 Hz, 2 H), 1.17 (m, 2 H), 1.21 (m, 2 H), 1.28 (tt, J = 7.2, 7.2 Hz, 2 H), 1.36 (m, 2 H), 2.02 (s, 3 H), 2.37 (d, J = 2.0 Hz, 1 H), 3.10 (s, 3 H), 5.34 (ddd, J = 7.1, 5.6, 2.0 Hz, 1 H), 7.46 (m, 3 H), 7.60 (dd, J = 7.3, 0.9 Hz, 1 H), 7.83 (m, 2 H), 8.41 (m, 1 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 14.1, 21.4, 22.7, 24.0, 28.6, 29.1, 29.2, 29.3, 31.8, 34.2, 50.9, 64.3, 73.5, 80.8, 81.4, 124.6, 125.2, 125.7, 125.9, 126.5, 128.6, 129.5, 131.5, 134.0, 134.6, 173.1 ppm. UV (EtOH): λ_{max} (ε) = 292.0 (4200), 281.4 (6000), 271.6 (5000), 224.2 (58000 L mol^{-1} cm^{-1}) nm. CD (EtOH): λ_{ext} ($\Delta\varepsilon$) = 292.0 (–1.0), 281.0 (–1.4), 270.4 (–1.1), 230.0 (+3.3), 213.8 (–11.3), 212.0 (–11.1 L mol^{-1} cm^{-1}) nm. $C_{26}H_{34}O_3$ (394.55): calcd. C 79.15, H 8.69; found C 78.85, H 8.61.

Recovery of Enantiopure Acetylene Alcohols 5–8: For example, KOH (0.343 g, 6.11 mmol) was added to a solution of MαNP ester (*S*,9*S*)-(–)-**24a** (0.450 g, 0.94 mmol) in EtOH (3.1 mL), and the mixture was stirred at room temperature overnight. After addition of aqueous saturated $NaHCO_3$, the mixture was extracted several times with diethyl ether. The combined organic layers were washed with brine, dried with anhydrous $MgSO_4$, and the solvents evaporated to dryness to yield crude alcohol **6**, which was purified by HPLC on silica gel (hexane/EtOAc, 20:1).

(*S*)-(–)-10-Octadecyn-9-ol (6): Yield 0.253 g, 99%; colorless oil. $[\alpha]_D^{24}$ = –8.0 (σ = 0.30, ρ = 0.858, neat); $[\alpha]_D^{23}$ = –6.4 (c = 6.07, cyclohexane). IR and ^{1}H and ^{13}C NMR spectroscopic data agree with those of racemic alcohol (±)-**6**.

(*S*)-(–)-8-Nonacosyn-10-ol (7): Yield 0.210 g, 99%; colorless solid. $[\alpha]_D^{26}$ = –3.8 (σ = 0.03, c = 10.13, cyclohexane). IR and ^{1}H and ^{13}C NMR spectroscopic data agree with those of racemic alcohol (±)-**7**. $C_{29}H_{56}O$ (420.76): calcd. C 82.78, H 13.42; found C 82.09, H 13.49.

(*S*)-(–)-17-Octatriacontyn-19-ol (8): Yield 0.164 g, 91%; colorless solid. $[\alpha]_D^{28}$ = –2.4 (σ = 0.07, c = 3.13, cyclohexane). $[\alpha]_D^{49}$ = –2.6 (σ = 0.14, c = 7.23, cyclohexane). IR and ^{1}H and ^{13}C NMR spectroscopic data agree with those of racemic alcohol (±)-**6**. $C_{38}H_{74}O$ (546.99): calcd. C 83.44, H 13.64; found C 83.08, H 13.91.

(*R*)-(+)-1-Dodecyn-3-ol (5): Yield 83%; colorless oil. $[\alpha]_D^{21}$ = +3.0 (c = 1.13, $CHCl_3$). IR (neat): $\tilde{\nu}_{max}$ = 3354, 3312, 2927, 2856, 1467, 1017 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88 (t, J = 7.0 Hz, 3 H), 1.20–1.35 (m, 12 H), 1.40–1.50 (m, 2 H), 1.74–1.75 (m, 2 H), 1.82 (d, J = 5.6 Hz, 1 H), 2.46 (d, J = 2.2 Hz, 1 H), 4.37 (td, J = 6.3, 2.2 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 22.6, 25.0, 29.2, 29.3, 29.5, 29.5, 31.8, 37.6, 62.3, 72.8, 85.0 ppm. HRMS: calcd. for $C_{12}H_{22}O$ 182.1671; found 182.1627.

(*R*)-(+)-8-Nonacosyn-10-ol (7): Yield 0.188 g, 89%; colorless solid. $[\alpha]_D^{26}$ = +3.5 (c = 8.75, cyclohexane). IR and ^{1}H and ^{13}C NMR spectroscopic data agree with those of racemic alcohol (±)-**7**. $C_{29}H_{56}O$ (420.76): calcd. C 82.78, H 13.42; found C 82.30, H 13.43.

Supporting Information (see also the footnote on the first page of this article): Figure S1. ^{1}H NMR spectra of MαNP esters.

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