Synthesis of Dideuterated and Enantiomers of Monodeuterated Tridecanoic Acids at C-9 and C-10 Positions

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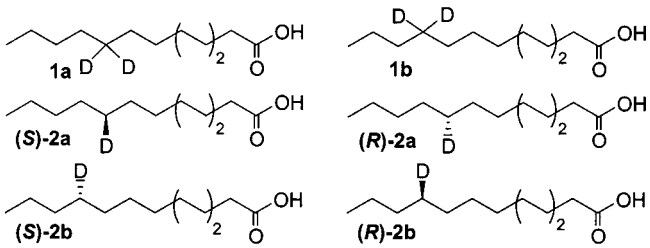
We report a route for the preparation of mono and dideuterated tridecanoic acids: (*R*)-[9-$^2H_1$]-, (*S*)-[9-$^2H_1$]-, (*R*)-[10-$^2H_1$]-, (*S*)-[10-$^2H_1$]-, [9,9-$^2H_2$]-, and [10,10-$^2H_2$]-tridecanoic acids required as probes for biochemical studies on desaturases. The key intermediates in the synthesis of all these probes are ketones **9**, which give rise to the corresponding alcohols **10** and **13** by reduction with $LiAlD_4$ and $LiAlH_4$, respectively. Derivatization of nondeuterated racemic alcohols **13** with (*S*)-(+)-9-anthranylmethoxyacetic acid ((*S*)-(+)-9-AMA) and chromatographic resolution of both diastereoisomers allowed us to determine the absolute configuration of the stereogenic centers by ^1H NMR using an adaptation of the model proposed by Riguera and co-workers which was validated with alcohols of known absolute configuration. Both enantiomeric alcohols (*R*)- and (*S*)-**13** were recovered by reduction of each diastereomeric ester with $LiAlH_4$. Mesylation of alcohols **10** and **13** followed by nucleophilic substitution by $LiAlD_4$ generated the saturated methoxymethyl derivatives **12** and **16**, respectively. Final deprotection and Jones oxidation of the resulting alcohols afforded the above deuterated tridecanoic acids.

Introduction

Biosynthesis of unsaturated fatty acids in living organisms occurs by the direct introduction of double bonds into a saturated precursor in an outstanding reaction that is catalyzed by specific desaturases.[1] In addition to the enzymes that transform saturated fatty acids, other desaturases that use unsaturated substrates to give dienes do also occur in nature. The most ubiquitous monoene desaturase is Δ^{12} oleoyl CoA desaturase, which convert oleic acid into linoleic acid, a methylene-interrupted dienoic fatty acid, and for which several mechanistic studies have been reported.[2−4] No mechanistic investigations have been conducted, however, on other monoene desaturases that give rise to conjugated dienoic fatty acids.[5−10] To gain insight into general desaturase enzyme catalysis, research on the latter enzymes is also desirable. Our ongoing interest in the mechanism of desaturase enzymes has led us to undertake a mechanistic study on a Δ^9 monoene desaturase that produces (*Z*,*E*)-9,11-tetradecadienoic acid from (*E*)-11-tetradecenoic acid using the moth *Spodoptera littoralis* as biological model.[9] This particular Δ^9 monoene desaturase is specially interesting because it catalyzes the formation of a conjugated dienoic fatty acid, but it does not desaturate tetradecanoic acid.[9] Therefore, comparing the reaction features of this (*Z*)-9 desaturase with those reported for the general (*Z*)-9 stearoylCoA desaturase was appealing. To perform these investigations, we first undertook the synthesis of selected deuterated fatty acids to be used as probes. Although tetradecanoic acid is the natural precursor of the (*Z9*,*E11*)-9,11-tetradecadionate, in a previous paper we reported that tridecanoic acid is also a suitable substrate.[11]

In this paper, we describe the preparation of dideuterated tridecanoic acids at C-9 and C-10 (**1a,b**), useful to investigate the site of initial oxidation in the desaturation reaction (cryptoregiochemistry), and the synthesis of the enantiomerically pure monodeuterated probes (*R*)- and (*S*)- at C-9 and C-10 (**2a,b**) to be used in the stereospecificity studies. Determination of the absolute configuration of key intermediates, enantiomerically pure alcohols **13a**,**b** by ^1H NMR studies on the corresponding diastereomeric esters of (*S*)-(+)-9-anthranylmethoxyacetic acid ((*S*)-(+)-9-AMA) is also described.



Results and Discussion

Preparation of Deuterated Tridecanoic Acids. Double deuterated products **1** were prepared following

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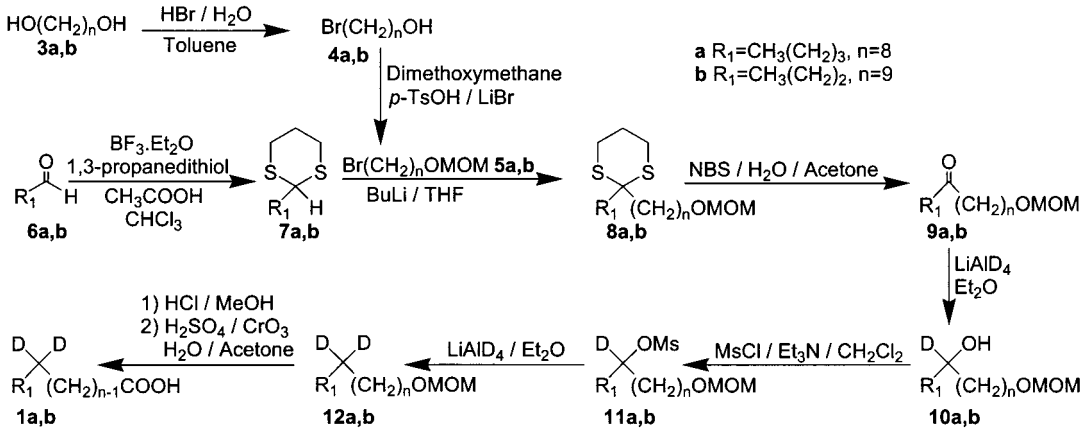
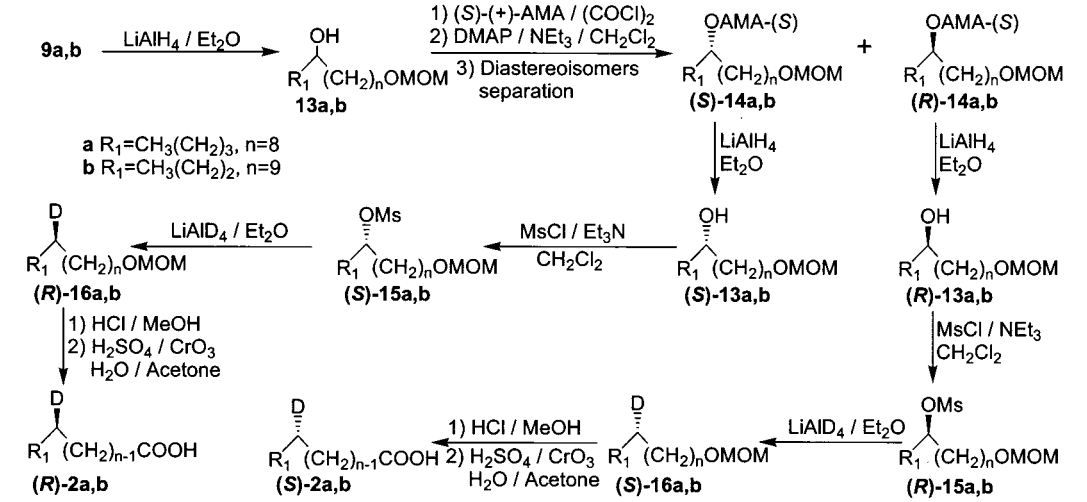
Scheme 1



Scheme 2



the reactions depicted in Scheme 1. Thus, properly functionalized dithianes **8** were obtained by coupling reaction of bromoalkylderivatives **5** with the anion of dithiane **7**, generated by reaction with BuLi. Dithiane **8** cleavage with NBS afforded ketone **9** and deuterated alcohol **10** could be obtained by reduction of **9** with $LiAlD_4$. Mesylation of the hydroxyl group and nucleophilic substitution with $LiAlD_4$ produced dideuterated compound **12**. Protective group cleavage in acidic media and final Jones oxidation of the resulting alcohol gave the corresponding *gem*-dideuterated tridecanoic acids **1**.

As shown in Scheme 2, enantiomerically pure deuterated tridecanoic acids **2** were prepared from ketones **9**. Reduction of these ketones with $LiAlH_4$ afforded alcohols **13**, which were submitted to kinetic enantiomeric resolution with different lipases (*Candida cylindracea*, *Chromobacterium viscosum*, triacylglycerol lipase, LPS, CAL), through the acetate formation with vinyl acetate.[12] Although CAL and LPS showed conversions of around 50%, we did not get good enantiomeric excesses probably because both substituents of the ketone were sterically too similar for enzymatic differentiation. As an alternative, we investigated a way to separate both enantiomers of alcohols **13** and later to determine the corresponding absolute configurations. For this purpose, we decided to explore the alcohol derivatization with different known chiral acids such as α-methoxy-α-trifluoromethylphenylacetic acid (MTPA)[13] or α-methoxy-α-(9-anthryl)-acetic acid (9-AMA)[14] that have been recently proposed to determine the absolute configuration by ^{1}H NMR. Thus, we decided to use this strategy for synthesizing both stereoisomers of each one of the corresponding monodeuterated tridecanoic acids **2**.

Initial reversed-phase-HPLC separation trials with the diastereomeric Mosher esters resulting from (*R*)-MTPA were unsuccessful. Resolution was slightly improved by using (*S*)-(+)-acetoxyphenylacetic acid ((*S*)-(+)-APA) as a derivatizing agent, but in this case, the unambiguous assignment of most of the ^{1}H NMR chemical shifts was not possible. For this reason, we decided to use a stronger shielding derivatizing agent, such as 9-anthranylmethoxyacetic acid (9-AMA).[14]

Synthesis of (*S*)-(+)-9-AMA esters **14** was accomplished by reaction of carbinols **13** with the freshly prepared acid chloride of (*S*)-(+)-9-anthranylmethoxyacetic acid. In this case, the two resulting diastereomers (*R*)- and (*S*)-**14a,b** were well separated by HPLC (direct and reversed phase) and appreciable chemical shift changes were observed in the ^{1}H NMR spectra corresponding to each diastereomer that allowed, as described below, the unequivocal deter-

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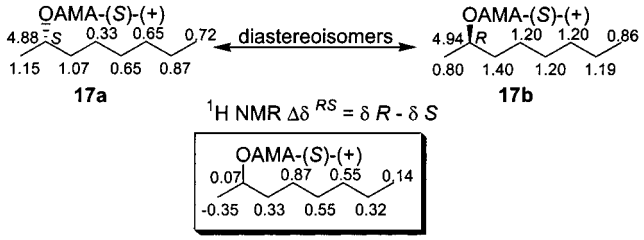

Figure 1. ^{1}H NMR chemical shifts (in ppm) and differences ($\Delta\delta^{RS}$) for all positions of both (*S*)-(+)-AMA esters of (*S*)-(+)- and (*R*)-(−)-2-octanol skeleton.

mination of the absolute configuration of the stereogenic centers present in the tridecanoic acid skeleton.

Determination of Absolute Configuration of Intermediate Alcohols 13. Seco et al.[15] have reported that it is possible to determine the absolute configuration of one enantiomer of secondary alcohols from the ^{1}H NMR chemical shifts differences between both diastereoisomeric esters of (*R*)- and (*S*)-9-anthranylmethoxyacetic acids. Such differences are originated by the anisotropy effect of the aromatic ring in a preferred conformation. However, we were interested in the absolute configuration determination of both enantiomers of **13a**,**b** by using only one chiral acid ((*S*)-(+)-9-AMA). In this context, (*S*)-(+)-9-AMA esters **14** are long-chain molecules with a high conformational mobility that could lead to erratic chemical shift differences between both diastereoisomers, thus precluding the application of the Riguera's model. For this reason, we decided to test our modified method by using the (*S*)-(+)-9-AMA esters of (*S*)-(+)- (**17a**) and (*R*)-(−)-2-octanol (**17b**). Since these alcohols were commercially available and its absolute configuration was already known, they would offer a clear validation of the applied model.

For this purpose, ^{1}H, ^{13}C, DQFCOSY, and XH-CORFE NMR spectra for both (*S*)-(+)-9-AMA diastereomeric esters **17** were recorded. As shown in Figure 1, $\Delta\delta^{RS} = \delta R - \delta S$ calculations from the ^{1}H NMR chemical shifts of the corresponding diastereoisomeric esters of 2-octanol gave the opposite sign at each site of the substituted ester function and in the proper position for the corresponding absolute configuration determination in the model proposed by Seco et al.[14] Consequently, these results validate that application of the modified Riguera's procedure would allow the assignment of the absolute configuration to both enantiomeric alcohols **13**.

Thus, spectra for (*S*)-(+)-9-AMA diastereomeric esters **14** were recorded and the chemical shifts for most of the hydrogen atoms of each diastereomer were assigned. As depicted in Figure 2, arrangement of $\Delta\delta$ differences for **14** diastereomeric pairs allowed us to determine the absolute configuration of each one of the alcohol stereogenic centers. For both studied cases, those products with HPLC shorter retention times showed (*S*)-configuration ((*S*)-**14a**,**b**), whereas those compounds with longer retention time showed (*R*)-configuration ((*R*)-**14a**,**b**).

Once we had determined the absolute configuration, reduction of the diastereomeric esters with $LiAlH_4$ regenerated the enantiomerically pure alcohols without racemization. Mesylation of (*R*)- and (*S*)-**13** in the presence of Et_3N and further treatment of the mesylates with

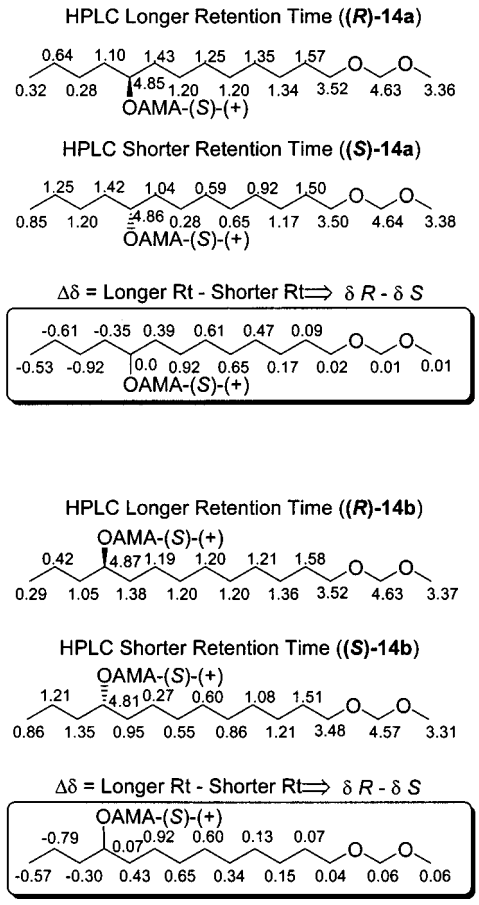

Figure 2. ^{1}H NMR chemical shifts (in ppm) and differences ($\Delta\delta^{RS}$) for both (*S*)-(+)-AMA diasteromeric esters **14a** and **14b**.

$LiAlD_4$ (inversion of configuration) gave each enantiomerically pure monodeuterated products **16**. The final acids were obtained as showed above for the double deuterated tridecanoic acids (Scheme 2).

Conclusions

Preparation of tridecanoic acids mono- and dideuterated at C-9 and C-10 is described. The pure enantiomers of the monodeuterated acids were obtained from HPLC purified (*S*)-(+)-9-AMA diastereoisomers **14** which were also used to determine the absolute configuration at the stereogenic centers of the tridecanoic acid skeleton by ^{1}H NMR spectroscopy. This novel adaptation of the previously reported Riguera's model is another example of absolute configuration determination in acyclic compounds with high conformational mobility.

Experimental Section

General Methods. The HPLC analysis and semipreparative separations were performed by using Spherisorb ODS-2 (5 μm) columns (10 × 0.6 cm and 15 × 1 cm, respectively) and eluting with MeOH−H_2O mixtures. All ^{1}H NMR spectra were acquired at 300 MHz, and ^{13}C NMR spectra, at 75 MHz in freshly neutralized $CDCl_3$ solutions, and chemical shifts are given in ppm using as internal standards $Si(CH_3)_4$ for ^{1}H, and $CDCl_3$ for ^{13}C. The standard ^{1}H DQFCOSY and XH-CORFE spectra for the determination of the absolute configuration of (*S*)-(+)-9-AMA esters were recorded at 25 °C using the same concentration for both diastereomeric pairs as described

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elsewhere.[16] Gas chromatography coupled to mass spectrometry (GC/MS) analysis was performed by electron impact (EI) setting the source at 20 eV, using a nonpolar HP-1 capillary column (30 m × 0.20 mm i.d.).

All IR spectra were run in CCl_4 solutions. Elemental analyses were obtained in the Microanalysis Service of IIQAB-CSIC and they were conventional combustion analyses without discrimination between hydrogen and deuterium contents.

$LiAlD_4$ (Deuterium content 98%) was obtained from Aldrich Chemical Co. The final deuterium contents of the labeled substrates were determined by GC−MS analysis of their respective methyl esters and were found to be as follows: **1a**, 89.0% $^2H_2$, 8.7% $^2H_1$ and 1.1% $^2H_0$; **1b**, 88.2.% $^2H_2$, 8.7% $^2H_1$ and 3.1% $^2H_0$; (*R*)-**2a**, 92.0% $^2H_1$ and 6.7% $^2H_0$; (*S*)-**2a**, acid: 93.2% $^2H_1$ and 5.9% $^2H_0$; (*R*)-**2b**, 92.0% $^2H_1$ and 7.7% $^2H_0$; (*S*)-**2b**, 92.2% $^2H_1$ and 6.7% $^2H_0$. Unless otherwise stated, organic solutions obtained from workup of crude reaction mixtures were dried over $MgSO_4$. The purification procedures were carried out by flash chromatography on silica gel (230−400 mesh) and products were mostly obtained as oils unless otherwise specified. Visualization of UV-inactive materials was accomplished by soaking the TLC plates in an ethanolic solution of anisaldehyde and sulfuric acid (v/v/v, 96:2:2). Optical rotations were determined at 25° in $CHCl_3$ solution at the specified concentration (g/100 mL). Enantiomeric and diasteromeric excesses (ee and de) values were calculated by HPLC or NMR analysis of the corresponding (*S*)-(+)-9-AMA or MTPA diastereomeric esters.

Preparation of 1,3-Dithianes 7. General Procedure. To a refluxing mixture of 12 mL of BF_3·Et_2O, 24 mL of acetic acid and 40 mL of $CHCl_3$ in a dry three-necked round-bottom flask was added dropwise a 100 mL $CHCl_3$ solution containing 40 mmol of the appropriate aldehyde and 6.5 g (60 mmol) of 1,3-propanedithiol. Reflux was continued for 16 h; the reaction mixture was cooled at room temperature and washed sequentially with a 10% aqueous KOH solution and with a saturated aqueous NaCl solution; and the organic layer was dried, filtered, and concentrated at reduced pressure. The residue was purified by flash chromatography on silica gel using a gradient of 0−10% MTBE (methyl *tert*-butyl ether) in hexane to give the expected dithianes in 90−95% yields.

2-Butyl-1,3-dithiane (7a). This compound was obtained from valeraldehyde in 95% yield (6.67 g): ^{1}H NMR δ 4.05 (t, J = 7 Hz, 1H), 2.98−2.76 (m, 4H), 2.13 (m, 1H), 1.86 (m, 1H), 1.75 (q, J = 7 Hz, 2H), 1.49 (m, 2H), 1.33 (m, 2H), 0.91 (t, J = 7 Hz, 3H); ^{13}C NMR δ 47.7, 35.2, 30.5, 28.8, 26.1, 22.3, 13.8.

2-Propyl-1,3-dithiane (7b). This compound was obtained from butyraldehyde in 90% yield (5.82 g). ^{1}H NMR δ 4.06 (t, J = 7 Hz, 1H), 2.98−2.76 (m, 4H), 2.12 (m, 1H), 1.86 (m, 1H), 1.73 (q, J = 7 Hz, 2H), 1.53 (m, 2H), 0.94 (t, J = 7 Hz, 3H); ^{13}C NMR δ 47.3, 37.5, 30.5, 26.1, 19.9, 13.7.

Preparation of Bromo Alcohols 4. General Procedure. The procedure reported by Camps et al.[17] was used with minor modifications. To a solution of diol (10 mmol) in 25 mL of toluene cooled at 0 °C was added 14 mL of HBr (47%, 80 mmol), and then the mixture was refluxed in the dark for 5 h (GC monitoring). The reaction was allowed to cool at room temperature, and 25 mL of brine was added. The mixture was extracted with hexane, dried, filtered, and concentrated at reduced pressure. The residue was purified by flash chromatography on silica gel using hexane/MTBE 5:1 to afford the expected product.

8-Bromo-1-octanol (4a). This compound was obtained in 85% yield (1.77 g): ^{1}H NMR δ 3.64 (t, J = 6.5 Hz, 2H), 3.41 (t, J = 7 Hz, 2H), 1.86 (q, J = 7 Hz, 2H), 1.57 (m, 2H), 1.50−1.24 (8H); ^{13}C NMR δ 62.8, 33.9, 32.7, 32.6, 29.1, 28.6, 28.0, 25.6.

9-Bromo-1-nonanol (4b). This compound was obtained in 90% yield (2.01 g): ^{1}H NMR δ 3.64 (t, J = 6.5 Hz, 2H), 3.41 (t, J = 7 Hz, 2H), 1.86 (q, J = 7 Hz, 2H), 1.57 (m, 2H), 1.50−1.24 (10H); ^{13}C NMR δ 96.4, 67.8, 55.1, 34.0, 32.8, 29.7, 29.2, 28.7, 28.1, 25.6.

Preparation of Derivatives 5. General Procedure. These compounds were prepared using the procedure reported by Gras et al.[18] To a stirred solution of the bromo alcohol **4** (15 mmol) in 60 mL of dimethoxymethane were added LiBr (435 mg, 5 mmol) and *p*-toluenesulfonic acid (190 mg, 1 mmol) at room temperature. Stirring was continued overnight. Brine was added (50 mL), and the reaction mixture was extracted with hexane, dried, and concentrated at reduced pressure to give an oil that was purified by flash chromatography on silica gel using hexane/MTBE 85:15 to afford the expected product in 95−98% yields.

1-Bromo-9,11-dioxadodecane (5a). This compound was obtained in 96% yield (3.64 g): ^{1}H NMR δ 4.62 (s, 2H), 3.52 (t, J = 6.5 Hz, 2H), 3.41 (t, J = 7 Hz, 2H), 3.36 (s, 3H), 1.86 (q, J = 7 Hz, 2H), 1.59 (m, 2H), 1.52−1.24 (8H); ^{13}C NMR δ 96.4, 67.8, 55.1, 34.0, 32.8, 29.7, 29.2, 28.7, 28.1, 26.1.

1-Bromo-10,12-dioxatridecane (5b). This compound was obtained in 98% yield (3.92 g): ^{1}H NMR δ 4.62 (s, 2H), 3.52 (t, J = 6.5 Hz, 2H), 3.41 (t, J = 7 Hz, 2H), 3.36 (s, 3H), 1.86 (q, J = 7 Hz, 2H), 1.59 (m, 2H), 1.52−1.22 (10H); ^{13}C NMR 96.4, 67.8, 55.1, 34.0, 32.8, 29.7, 29.3, 29.3, 28.7, 28.1, 26.1.

Synthesis of Dithianes 8. General Procedure. These products were obtained using the procedure reported by Seebach and Corey.[19] To a solution of the dithiane **7** (10 mmol) in 15 mL of dry THF and kept at −20 °C was added 12 mmol of an hexane BuLi solution (7.5 mL, 1.6 M). The pale colored reaction mixture was stirred for 30 min, cooled at −78 °C, and kept for 10 min, and then product **5** (8 mmol) was added dropwise and stirring was continued at −78 °C for 2 h. The resulting solution was allowed to warm to room temperature and the solvent was then evaporated. The residue was suspended in 50 mL of H_2O, extracted with CH_2Cl_2, dried, and concentrated to dryness. The residue was purified by flash chromatography on silica gel using a gradient of 0−10% MTBE in hexane to give the pure dithianes **8**.

2-Butyl-2-(9,11-dioxadodecyl)-1,3-dithiane (8a). This compound was obtained in 80% yield (2.22 g): IR 2935, 2860, 1465, 1150, 1110, 1050, 920 cm^{-1}; ^{1}H NMR δ 4.62 (s, 2H), 3.52 (t, J = 6.5 Hz, 2H), 3.36 (s, 3H), 2.80 (m, 4H), 2.02−1.90 (m, 2H), 1.90−1.80 (4H), 1.66−1.52 (3H), 1.48−1.23 (13H), 0.93 (t, J = 7 Hz, 3H); ^{13}C NMR δ 96.3, 67.8, 55.0, 53.3, 38.1, 37.8, 29.7, 29.7, 29.4, 29.3, 26.2, 26.1, 25.9, 25.5, 23.9, 22.9, 14.0; MS *m*/*z* (relative intensity) 348 (M^+, 22), 175 (100). Anal. Calcd for $C_{18}H_{36}O_2S_2$: C, 62.01; H, 10.40; S, 18.39. Found: C, 62.13; H, 10.37; S, 18.26.

2-Propyl-2-(10,12-dioxatridecyl)-1,3-dithiane (8b). This compound was obtained in 74% yield (2.06 g): IR 2935, 2855, 1465, 1150, 1110, 1050, 920 cm^{-1}; ^{1}H NMR δ 4.62 (s, 2H), 3.52 (t, J = 6.5 Hz, 2H), 3.36 (s, 3H), 2.80 (m, 4H), 1.95 (m, 2H), 1.92−1.78 (4H), 1.66−1.54 (3H), 1.54−1.22 (13H), 0.94 (t, J = 7 Hz, 3H); ^{13}C NMR 96.3, 67.7, 54.9, 53.2, 40.4, 38.1, 29.7, 29.6, 29.4, 29.3, 29.3, 26.1, 25.9, 25.5, 23.9, 17.4, 14.2; MS *m*/*z* (relative intensity) 348 (M^+, 22), 161 (100). Anal. Calcd for $C_{18}H_{36}O_2S_2$: C, 62.01; H, 10.40; S, 18.39. Found: C, 62.13; H, 10.38; S, 18.16.

Synthesis of Ketones 9. General Procedure. To a solution of NBS (10.9 g, 60 mmol) in 95 mL of acetone and 5 mL of H_2O kept at −30 °C was added dropwise 3.5 g of dithiane **8** (10 mmol) dissolved in 100 mL of the same solvent mixture. Stirring was continued for 5 min, and a 10% $Na_2S_2O_3$ water solution was added until the orange color of the solution disappeared. Solvent was concentrated, extracted with CH_2Cl_2, dried, and concentrated to dryness. The residue was purified by flash chromatography on silica gel using a gradient of 0−10% MTBE in hexane to give 2.46 g (96% yield) of the pure ketones.

14,16-Dioxa-5-heptadecanone (9a): IR 1715 cm^{-1}; ^{1}H NMR δ 4.62 (s, 2H), 3.51 (t, J = 6.5 Hz, 2H), 3.36 (s, 3H), 2.39

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(t, J = 7 Hz, 4H), 1.66−1.46 (6H), 1.40−1.18 (10H), 0.90 (t, J = 7 Hz, 3H); ^{13}C NMR 211.5, 96.3, 67.8, 55.0, 42.7, 42.5, 29.7, 29.3, 29.2, 29.1, 26.1, 25.9, 23.8, 22.3, 13.8; MS m/z (relative intensity) 227 (M^+-31, 30), 85 (100). Anal. Calcd for $C_{15}H_{30}O_3$: C, 69.72; H, 11.70. Found: C, 69.67; H, 11.69.

14,16-Dioxa-4-heptadecanone (9b): IR 1715 cm^{-1}; ^{1}H NMR δ 4.62 (s, 2H), 3.51 (t, J = 6.5 Hz, 2H), 3.36 (s, 3H), 2.38 (t, J = 7 Hz, 2H), 2.37 (t, J = 7 Hz, 2H), 1.68−1.45 (6H), 1.43−1.18 (10H), 0.91 (t, J = 7 Hz, 3H); ^{13}C NMR 211.5, 96.3, 67.8, 55.0, 44.7, 42.8, 29.7, 29.4, 29.3, 29.3, 29.2, 26.2, 23.8, 17.3, 13.7; MS m/z (relative intensity) 227 (M^+ − 31, 35), 71 (100). Anal. Calcd for $C_{15}H_{30}O_3$: C, 69.72; H, 11.70. Found: C, 69.77; H, 11.68.

Preparation of Alcohols 13 by Reduction of Ketones. A solution of the corresponding ketone **9** in Et_2O, maintained under argon and at room temperature, was treated with 5 molar equiv of $LiAlH_4$, and the mixture was stirred until the reaction was completed (TLC monitoring). After the usual workup, the residue obtained was purified by flash chromatography on silica gel using hexane/MTBE 80:20 to give the corresponding pure alcohols **13** in 98% yields.

14,16-Dioxa-5-heptadecanol (13a). This alcohol was isolated (254 mg, 98%) starting from 260 mg of ketone **9a**: IR 3505 cm^{-1}; ^{1}H NMR δ 4.62 (s, 2H), 3.58 (bs, 1H), 3.52 (t, J = 6.5 Hz, 2H), 3.36 (s, 3H), 1.59 (m, 2H), 1.52−1.22 (19H), 0.91 (t, J = 7 Hz, 3H); ^{13}C NMR δ 96.4, 72.0, 67.8, 55.1, 37.5, 37.2, 29.7, 29.6, 29.5, 29.4, 27.8, 26.2, 25.6, 22.8, 14.1; MS m/z (relative intensity) 211 (M^+ − 49, 18), 171 (100). Anal. Calcd for $C_{15}H_{32}O_3$: C, 69.18; H, 12.39. Found: C, 69.16; H, 12.48.

14,16-Dioxa-4-heptadecanol (13b). This alcohol was isolated (250 mg, 98%) starting from 256 mg of ketone **9b**: IR 3505 cm^{-1}; ^{1}H NMR δ 4.62 (s, 2H), 3.58 (bs, 1H), 3.52 (t, J = 6.5 Hz, 2H), 3.36 (s, 3H), 1.59 (m, 2H), 1.52−1.22 (19H), 0.93 (t, J = 6.5 Hz, 3H); ^{13}C NMR δ 96.4, 71.7, 67.8, 55.1, 39.7, 37.5, 29.7, 29.7, 29.5, 29.5, 29.4, 26.2, 25.6, 18.8, 14.1; MS m/z (relative intensity) 211 (M^+-49, 11), 185 (75). Anal. Calcd for $C_{15}H_{32}O_3$: C, 69.18; H, 12.39. Found: C, 68.99; H, 12.35.

Preparation of Deuterated Alcohols 10a and 10b. The same procedure described above was followed using $LiAlD_4$.

[5-^{2}H]-14,16-Dioxa-5-heptadecanol (10a). This alcohol was isolated (126 mg, 97%) starting from 130 mg of ketone **9a**: IR 3630 cm^{-1}; ^{1}H NMR δ 4.62 (s, 2H), 3.52 (t, J = 6.5 Hz, 2H), 3.36 (s, 3H), 1.59 (m, 2H), 1.52−1.22 (19H), 0.91 (t, J = 7 Hz, 3H) ^{13}C NMR δ 96.3, 71.4 (t, J = 21.5 Hz), 67.8, 55.0, 37.3, 37.0, 29.7, 29.6, 29.5, 29.3, 27.8, 26.1, 25.5, 22.7, 14.0; MS m/z (relative intensity) 212 (M^+ − 49, 5), 172 (55), 82 (100). Anal. Calcd for $C_{15}H_{31}{}^2HO_3$: C, 68.92; H, 12.34. Found: C, 68.80; H, 12.33.

[4-^{2}*H*]-14,16-Dioxa-4-heptadecanol (10b). This alcohol was isolated (97 mg, 97%) starting from 100 mg of ketone **9b**: IR 3630 cm^{-1}; ^{1}H NMR δ 4.62 (s, 2H), 3.52 (t, J = 6.5 Hz, 2H), 3.36 (s, 3H), 1.59 (m, 2H), 1.52−1.22 (19H), 0.93 (t, J = 6.5 Hz, 3H); ^{13}C NMR δ 96.3, 71.1 (t, J = 21.5 Hz), 67.8, 55.0, 39.5, 37.3, 29.7, 29.7, 29.6, 29.5, 29.4, 26.1, 25.5, 18.7, 14.1; MS m/z (relative intensity) 212 (M^+ − 49, 7), 186 (40), 82 (100). Anal. Calcd for $C_{15}H_{31}{}^2HO_3$: C, 68.92; H, 12.34. Found: C, 68.99; H, 12.30.

Acid Chloride and 9-AMA Esters Preparation. General Procedure. The procedure of Ward and Rhee[20] was used with minor modifications. Oxalyl chloride (5 mmol) was added to a mixture of (*S*)-(+)-AMAA (0.5 mmol) and DMF (0.05 mmol) in hexane at room temperature. After 2 days, the solvent was evaporated to dryness at reduced pressure. This residue was dissolved in 5 mL of CH_2Cl_2 and added to a solution of racemic alcohol **13** (105 mg, 0.40 mmol), Et_3N (175 μL, 1.2 mmol), and DMAP (12 mg, 0.1 mmol) in 10 mL of CH_2Cl_2. After 15 min TLC monitoring revealed a complete conversion, the solution was washed with H_2O (2 × 5 mL), dried and concentrated to a residue which was purified by flash chromatography on silica gel using a gradient of 0−10% MTBE in hexane to give the expected diastereomeric (*S*)-(+)-AMA esters **14** and **17** (85−90% yields).

(20) Ward, D. E.; Rhee, C. K. *Tetrahedron Lett.* **1991**, *42*, 7165−7166.

(*S*)-(+)-2-Octyl-(*S*)-(+)-α-*O*-methyl-α-(9-anthryl)acetate (17a). This ester was isolated as a waxy solid (32 mg, 85%) starting from 13 mg of (*S*)-(+)-2-octanol: IR 1745 cm^{-1}; ^{1}H NMR δ 8.58 (d, J = 9 Hz, 2H), 8.47 (s, 1H), 8.01 (m, 2H), 7.60−7.40 (4H), 6.24 (s, 1H), 4.88 (sext, J = 6.5 Hz, 1H), 3.43 (s, 3H), 1.15 (d, J = 6 Hz, 2H), 1.12−1.02 (m, 2H), 0.98−0.78 (m, 2H), 0.72 (t, J = 6.5 Hz, 3H), 0.72−0.54 (4H), 0.38−0.24 (m, 2H); ^{13}C NMR δ 171.1, 131.4, 130.6, 129.1, 129.0, 127.7, 126.3, 124.9, 124.5, 77.2, 72.1, 57.4, 55.1, 35.4, 31.3, 28.4, 24.1, 22.3, 20.0, 14.0; MS m/z (relative intensity) 378 (M^+, 12), 221 (100); $[\alpha]_D$ = +140 (c 1.0, 96% de).

(*R*)-(−)-2-Octyl-(*S*)-(+)-α-*O*-methyl-α-(9-anthryl)acetate (17b). This ester was isolated as a waxy solid (23 mg, 84%) starting from 10 mg of (*R*)-(−)-2-octanol: IR 1745 cm^{-1}; ^{1}H NMR δ 8.56 (d, J = 9 Hz, 2H), 8.48 (s, 1H), 8.02 (m, 2H), 7.60−7.42 (4H), 6.24 (s, 1H), 4.94 (m, 1H), 3.40(s, 3H), 1.58−1.04 (10H), 0.86 (t, J = 7 Hz, 3H), 0.80 (d, J = 6.5 Hz, 2H); ^{13}C NMR δ 171.1, 131.4, 130.5, 129.1, 129.1, 127.6, 126.3, 124.9, 124.5, 77.3, 72.5, 57.5, 35.5, 31.6, 29.0, 25.2, 22.5, 19.4, 14; MS m/z (relative intensity) 378 (M^+, 10), 221 (100); $[\alpha]_D$ = +102 (c 0.7, 96% de).

Starting from alcohol **13a** (130 mg, 0.5 mmol) and **13b** (120 mg, 0.46 mmol)**,** 229 mg (90% yield), and 208 mg (89% yield) of the expected mixture of diastereoisomers **14a** and **14b** were isolated, respectively. These (*S*)-(+)-AMA diastereomeric mixtures were separated by semipreparative reversed-phase HPLC using an isocratic flow rate (MeOH/H_2O, 75:25) of 4 mL/min to afford, after flash chromatography on silica gel of the collected compound, (*S*)-**14a** (94 mg) and (*R*)-**14a** (88 mg); (*S*)-**14b** (89 mg) and (*R*)-**14b** (83 mg).

(*S*)-14,16-Dioxa-5-heptadecyl-(*S*)-(+)-α-methoxy-α-(9-anthryl)acetate ((*S*)-14a) (shorter t_R in HPLC separation, 42.5 min): IR 1745 cm^{-1}; ^{1}H NMR δ 8.58 (d, J = 9 Hz, 2H), 8.47 (s, 1H), 8.01 (m, 2H), 7.60−7.40 (4H), 6.26 (s, 1H), 4.86 (m, 1H), 4.64 (s, 2H), 3.49 (t, J = 6.5 Hz, 2H), 3.42 (s, 3H), 3.38 (s, 3H), 1.50 (m, 2H), 1.42 (m, 2H), 1.32−1.10 (6H), 1.04 (m, 2H), 0.92 (m, 2H), 0.85 (t, J = 7 Hz, 3H), 0.72−0.52 (4H), 0.29 (m, 2H); ^{13}C NMR δ 171.1, 131.4, 130.6, 129.0, 129.0, 127.7, 126.3, 124.9, 124.6, 96.4, 77.2, 75.4, 67.9, 57.4, 55.1, 33.6, 33.4, 29.7, 29.1, 29.0, 28.9, 27.5, 26.1, 24.0, 22.5, 14.0; MS m/z (relative intensity) 508 (M^+, 10), 221 (100); $[\alpha]_D$ = +95 (c 1.0, 96% de). Anal. Calcd for $C_{32}H_{44}O_5$: C, 75.54; H, 8.72. Found: C, 75.55; H, 8.80.

(*R*)-14,16-Dioxa-5-heptadecyl-(*S*)-(+)-α-methoxy-α-(9-anthryl)acetate ((*R*)-14a) (longer t_R in HPLC separation, 47.3 min): IR 1745 cm^{-1}; ^{1}H NMR δ 8.58 (d, J = 9 Hz, 2H), 8.47 (s, 1H), 8.01 (m, 2H), 7.60−7.40 (4H), 6.26 (s, 1H), 4.85 (m, 1H), 4.63 (s, 2H), 3.52 (t, J = 6.5 Hz, 2H), 3.43 (s, 3H), 3.37 (s, 3H), 1.59 (m, 2H), 1.52−1.12 (12H), 1.04 (m, 2H), 0.64 (m, 2H), 0.32 (t, J = 7 Hz, 3H), 0.29 (m, 2H); ^{13}C NMR δ 171.1, 131.4, 130.6, 129.0, 129.0, 127.7, 126.3, 124.9, 124.6, 96.4, 77.2, 75.4, 67.8, 57.4, 55.1, 33.8, 33.1, 29.7, 29.4, 29.4, 29.3, 26.2, 26.2, 25.3, 22.0, 13.4; MS m/z (relative intensity) 508 (M^+, 10), 221 (100); $[\alpha]_D$ = +72 (c 1.0, 97% de). Anal. Calcd for $C_{32}H_{44}O_5$: C, 75.54; H, 8.72. Found: C, 75.55; H, 8.80.

(*S*)-14,16-Dioxa-4-heptadecanyl-(*S*)-(+)-α-methoxy-α-(9-anthryl)acetate ((*S*)-14b) (shorter t_R in HPLC separation, 40.7 min): IR 1745 cm^{-1}; ^{1}H NMR δ 8.58 (d, J = 9 Hz, 2H), 8.47 (s, 1H), 8.01 (m, 2H), 7.60−7.40 (4H), 6.25 (s, 1H), 4.88 (m, 1H), 4.64 (s, 2H), 3.52 (t, J = 6.5 Hz, 2H), 3.42 (s, 3H), 3.38 (s, 3H), 1.51 (m, 2H), 1.46−0.9 (8H), 0.92 (m, 2H), 0.87 (t, J = 7 Hz, 3H), 0.60 (4H), 0.27 (m, 2H); ^{13}C NMR δ 171.1, 131.4, 130.5, 129.0, 129.0, 127.6, 126.3, 124.9, 124.5, 96.3, 77.1, 75.1, 67.8, 57.3, 55.0, 36.0, 33.4, 29.7, 29.3, 29.2, 28.9, 28.9, 26.1, 24.0, 18.5, 13.9; MS m/z (relative intensity) 508 (M^+, 10), 221 (100); $[\alpha]_D$ = +95 (c 1.0, 95% ee). Anal. Calcd for $C_{32}H_{44}O_5$: C, 75.54; H, 8.72. Found: C, 75.55; H, 8.80.

(*R*)-14,16-Dioxa-4-heptadecanyl-(*S*)-(+)-α-methoxy-α-(9-anthryl)acetate ((*R*)-14b) (longer t_R in HPLC separation, 44.8 min): IR 1745 cm^{-1}; ^{1}H NMR δ 8.57 (d, J = 9 Hz, 2H), 8.47 (s, 1H), 8.01 (m, 2H), 7.58−7.42 (4H), 6.25 (s, 1H), 4.87 (m, 1H), 4.63 (s, 2H), 3.52 (t, J = 6.5 Hz, 2H), 3.43 (s, 3H), 3.37 (s, 3H), 1.60 (m, 2H), 1.50−1.12 (12H), 1.05 (m, 2H), 0.60−0.20 (6H), 0.29 (t, J = 6.5 Hz, 3H); ^{13}C NMR δ 171.1, 131.4, 130.6, 129.0, 129.0, 127.7, 126.3, 124.9, 124.5, 96.4, 77.2, 75.3,

67.8, 57.4, 55.1, 35.4, 33.8, 29.7, 29.4, 29.4, 26.2, 25.3, 17.3, 13.3; MS *m/z* (relative intensity) 508 (M^+, 10), 221 (100); $[\alpha]_D = +72$ (*c* 1.0, 95% de). Anal. Calcd for $C_{32}H_{44}O_5$: C, 75.54; H, 8.72. Found: C, 75.55; H, 8.80.

Preparation of Alcohols (*S*)- and (*R*)-13 by Reduction of (*S*)-(+)-AMA Esters. A solution of the corresponding (*S*)-(+)-AMA ester **14** in Et_2O, maintained under argon and at room temperature was treated with 5 molar equiv of $LiAlH_4$, and the mixture was stirred until the reaction was completed (TLC monitoring). After the usual work up, the residue obtained was purified by flash chromatography on silica gel using hexane/MTBE 85:15 to give the corresponding pure alcohols.

(*S*)-14,16-Dioxa-5-heptadecanol ((*S*)-13a). This alcohol was isolated (22 mg, 97%) starting from 45 mg of (*S*)-**14a**: $[\alpha]_D = +1.3$ (*c* 1.0, 96% ee).

(*R*)-14,16-Dioxa-5-heptadecanol ((*R*)-13a). This alcohol was isolated (21 mg, 97%) starting from 43 mg of (*R*)-**14a**: $[\alpha]_D = -1.4$ (*c* 1.0, 97% ee).

(*S*)-14,16-Dioxa-4-heptadecanol ((*S*)-13b). This alcohol was isolated (21 mg, 97%) starting from 43 mg of (*S*)-**14b**: $[\alpha]_D = +0.9$ (*c* 1.0, 95% ee).

(*R*)-14,16-Dioxa-4-heptadecanol ((*R*)-13b). This alcohol was isolated (20 mg, 98%) starting from 40 mg of (*R*)-**14b**: $[\alpha]_D = -0.9$ (*c* 1.0, 95% ee).

Preparation of Mesyl Esters 11 and 15. General Procedure. These products were prepared by the procedure described by Abad et al.[16] A solution of alcohol (26 mg, 0.1 mmol) and Et_3N (45 μL, 0.3 mmol) in 5 mL of CH_2Cl_2 was treated with CH_3SO_3Cl (11 μL, 0.14 mmol), and the mixture was stirred under argon for 2 h at room temperature (TLC monitoring). The reaction mixture was washed with H_2O (2 × 2 mL), dried, concentrated and purified by flash chromatography on silica gel using hexane/MTBE 85:15 to give the expected pure products.

[5-^{2}*H*]-14,16-Dioxa-5-heptadecyl Methanesulfonate (11a). This compound (64 mg, 95%) was obtained from 52 mg (0.2 mmol) of alcohol **10a**: IR 1360, 1340, 1180, 910 cm^{-1}; ^{1}H NMR δ 4.62 (s, 2H), 3.52 (t, $J = 6.5$ Hz, 2H), 3.36 (s, 3H), 3.00 (s, 3H), 1.69 (4H), 1.59 (m, 2H), 1.52−1.22 (15H), 0.92 (t, $J = 7$ Hz, 3H); ^{13}C NMR δ 96.3, 83.8 (t, $J = 22.5$ Hz), 67.7, 55.0, 38.6, 34.2, 33.9, 29.6, 29.3, 29.2, 26.9, 26.1, 24.8, 22.4, 13.8.

[4-^{2}*H*]-14,16-Dioxa-4-heptadecyl Methanesulfonate (11b). This compound (62 mg, 94%) was obtained from 52 mg (0.2 mmol) of alcohol **10b**: IR 1350, 1340, 1180, 910 cm^{-1}; ^{1}H NMR δ 4.62 (s, 2H), 3.52 (t, $J = 6.5$ Hz, 2H), 3.36 (s, 3H), 3.00 (s, 3H), 1.69 (4H), 1.59 (m, 2H), 1.52−1.22 (15H), 0.95 (t, $J = 7$ Hz, 3H); ^{13}C NMR δ 96.3, 83.6 (t, $J = 22.5$ Hz), 67.7, 55.0, 38.6, 36.3, 34.3, 29.6, 29.4, 29.3, 26.1, 24.8, 18.2, 13.8.

14,16-Dioxa-5-heptadecyl Methanesulfonate (15a): IR 1360, 1340, 1175, 905 cm^{-1}; ^{1}H NMR δ 4.70 (quint, $J = 6.5$ Hz, 1H), 4.62 (s, 2H), 3.52 (t, $J = 6.5$ Hz, 2H), 3.36 (s, 3H), 3.00 (s, 3H), 1.69 (4H), 1.59 (m, 2H), 1.52−1.22 (15H), 0.92 (t, $J = 7$ Hz, 3H); ^{13}C NMR δ 96.3, 84.3, 67.8, 55.1, 38.7, 34.2, 34.1, 29.7, 29.4, 29.3, 27.1, 26.1, 24.9, 22.4, 13.9. **(*S*)-14,16-Dioxa-5-heptadecyl methanesulfonate ((*S*)-15a)**. This compound (32 mg, 95%) was obtained from 26 mg (0.1 mmol) of alcohol (*S*)-**13a**: $[\alpha]_D = -0.7$ (*c* 1.0, 96% ee), **(*R*)-14,16-Dioxa-5-heptadecyl methanesulfonate ((*R*)-15a)**. This compound (30 mg, 91%) was obtained from 26 mg (0.1 mmol) of alcohol (*R*)-**13a**: $[\alpha]_D = +0.7$ (*c* 1.0, 97% ee).

14,16-Dioxa-4-heptadecyl methanesulfonate (15b): IR 1365, 1340, 1175, 910 cm^{-1}; ^{1}H NMR δ 4.71 (quint, $J = 6.5$ Hz, 1H), 4.62 (s, 2H), 3.52 (t, $J = 6.5$ Hz, 2H), 3.36 (s, 3H), 3.00 (s, 3H), 1.69 (4H), 1.59 (m, 2H), 1.52−1.22 (15H), 0.95 (t, $J = 7$ Hz, 3H); ^{13}C NMR δ 96.3, 84.0, 67.7, 55.0, 38.6, 36.5, 34.4, 29.6, 29.4, 29.3, 26.1, 24.8, 18.2, 13.8. **(*S*)-14,16-Dioxa-4-heptadecyl methanesulfonate ((*S*)-15b).** This compound (31 mg, 95%) was obtained from 26 mg (0.1 mmol) of alcohol (*S*)-**13b**: $[\alpha]_D = -3.2$ (*c* 1.0, 95% ee), **(*R*)-14,16-Dioxa-4-heptadecyl methanesulfonate ((*R*)-15b)**. This compound (30 mg, 94%) was obtained from 26 mg (0.1 mmol) of alcohol (*R*)-**13b**: $[\alpha]_D = +3.2$ (*c* 1.0, 95% ee).

Reaction of Mesylates 11 and 15 with $LiAlD_4$. General Procedure. The mesyl derivative was dissolved in Et_2O (4 mL) and treated with $LiAlD_4$ (8 molar equiv.) for 16 h at 20 °C (TLC monitoring). H_2O was added dropwise to the crude reaction mixture and the resulting white precipitate was filtered through Celite and concentrated to give a residue that, after purification by flash chromatography on silica gel using a gradient of 0−10% MTBE in hexane, afforded the corresponding pure deuterated products.

[13,13-$^2H_2$]-2,4-Dioxaheptadecane (12a). This compound (22 mg, 90%) was obtained from 34 mg (0.1 mmol) of **11a**: ^{1}H NMR δ 4.62 (s, 2H), 3.52 (t, $J = 6.5$ Hz, 2H), 3.36 (s, 3H), 1.59 (m, 2H), 1.42−1.20 (18H), 0.88 (t, $J = 6.5$ Hz, 3H); ^{13}C NMR δ 96.3, 67.8, 55.0, 31.8, 29.7, 29.6, 29.5, 29.4, 29.1, 28.8 (quint, $J = 19$ Hz), 26.2, 22.7, 14.1; MS *m/z* (relative intensity) 245 ($M^+ - 1$, 5), 213 (20), 182 (30), 98 (100). Anal. Calcd for $C_{15}H_{30}{}^2H_2O_2$: C, 73.17; H, 13.00. Found: C, 73.15; H, 13.04.

[14,14-$^2H_2$]-2,4-Dioxaheptadecane (12b). This compound (21 mg, 86%) was obtained from 34 mg (0.1 mmol) of **11b**: ^{1}H NMR δ 4.62 (s, 2H), 3.52 (t, $J = 6.5$ Hz, 2H), 3.36 (s, 3H), 1.59 (m, 2H), 1.42−1.18 (18H), 0.88 (t, $J = 7$ Hz, 3H); ^{13}C NMR δ 96.3, 67.8, 55.0, 31.7, 29.7, 29.6, 29.6, 29.4, 28.5 (quint, $J = 19$ Hz), 26.2, 22.6, 14.1; MS *m/z* (relative intensity) 245 ($M^+ - 1$, 5), 213 (12), 182 (15), 82 (100). Anal. Calcd for $C_{15}H_{30}{}^2H_2O_2$: C, 73.17; H, 13.00. Found: C, 73.25; H, 12.99.

[13-^{2}*H*]-2,4-Dioxaheptadecane (16a). Compounds **(*R*)-[13-^{2}*H*]-2,4-dioxaheptadecane (**(*R*)-**16a)** (11 mg, 89%) and **(*S*)-[13-^{2}*H*]-2,4-dioxaheptadecane (**(*S*)-**16a)** (10 mg, 87%) were obtained from 17 mg of (*S*)-**15a** and 16 mg of (*R*)-**15a**, respectively: ^{1}H NMR δ 4.62 (s, 2H), 3.52 (t, $J = 6.5$ Hz, 2H), 3.36 (s, 3H), 1.59 (m, 2H), 1.42−1.18 (18H), 0.88 (t, $J = 6.5$ Hz, 3H); ^{13}C NMR δ 96.4, 67.9, 55.0, 31.9, 29.7, 29.6, 29.6, 29.4, 29.2, 29.2 (t, $J = 19$ Hz), 26.2, 22.7, 14.1; MS *m/z* (relative intensity) 244 ($M^+ - 1$, 2), 212 (15), 181 (25), 97 (100). Anal. Calcd for $C_{15}H_{31}{}^2HO_2$: C, 73.47; H, 13.06. Found: C, 73.25; H, 13.16.

[14-^{2}*H*]-2,4-Dioxaheptadecane (16b). Compounds **(*R*)-[14-^{2}*H*]-2,4-dioxaheptadecane (**(*R*)-**16b)** (10 mg, 92%) and **(*S*)-[14-^{2}*H*]-2,4-dioxaheptadecane (**(*S*)-**16b)** (11 mg, 89%) were obtained from 15 mg of (*S*)-**15b** and 17 mg of (*R*)-**15b**, respectively: ^{1}H NMR δ 4.62 (s, 2H), 3.52 (t, $J = 6.5$ Hz, 2H), 3.36 (s, 3H), 1.60 (m, 2H), 1.42−1.18 (18H), 0.88 (t, $J = 7$ Hz, 3H); ^{13}C NMR δ 96.4, 67.9, 55.0, 31.8, 29.7, 29.6, 29.6, 29.5, 29.4, 28.9 (t, $J = 19$ Hz), 26.2, 22.6, 14.1; MS *m/z* (relative intensity) 244 ($M^+ - 1$, 2), 212 (12), 181 (18), 97 (96), 82 (100). Anal. Calcd for $C_{15}H_{31}{}^2HO_2$: C, 73.47; H, 13.06. Found: C, 73.45; H, 13.03.

Carboxylic Acids Preparation. General Procedure. Products **12** and the proper enantiomers of **16** were deprotected to the corresponding alcohols by treatment with a MeOH/HCl solution (0.5 M) for 16 h at room temperature. Solvent was evaporated and the crude was treated with 2 mL of water, extracted with CH_2Cl_2, dried, and concentrated to a residue which was dissolved in a solution of 4 mL of acetone and 350 μL of H_2SO_4 at −5 °C and then 350 mg of CrO_3 dissolved in 700 μL of water was added dropwise. The reaction mixture was stirred at −10 °C for 1 h and then allowed to warm to room temperature and stirred overnight. At this time, the reaction mixture was concentrated and 2 mL of HCl (1 M) was added, extracted with CH_2Cl_2, dried, and concentrated to a residue that was purified by flash chromatography on silica gel using hexane/MTBE 85:15 to give the corresponding acid as a solid.

[10,10-$^2H_2$]-Tridecanoic Acid (1a). This product (12 mg, 70%) was isolated from 20 mg of **12a**: mp 40−41 °C; IR 1710 cm^{-1}; ^{1}H NMR δ 2.35 (t, $J = 7.5$ Hz, 2H), 1.63 (quint, $J = 7.5$ Hz, 2H), 1.42−1.16 (16H), 0.88 (t, $J = 6.5$ Hz, 3H); ^{13}C NMR δ 180.4, 34.1, 31.9, 29.5, 29.4, 29.2, 29.1, 29.0, 28.8 (quint, $J = 19$ Hz), 24.7, 22.7, 14.1. Anal. Calcd for $C_{13}H_{25}{}^2H_2O_2$: C, 72.18; H, 12.11. Found: C, 72.22; H, 12.03.

[11,11-$^2H_2$]-Tridecanoic Acid (1b). This product (11 mg, 67%) was isolated from 19 mg of **12b**: mp 40−41 °C; IR 1710 cm^{-1}; ^{1}H NMR δ 2.35 (t, $J = 7.5$ Hz, 2H), 1.63 (quint, $J = 7.5$ Hz, 2H), 1.40−1.18 (16H), 0.88 (t, $J = 6.5$ Hz, 3H); ^{13}C NMR δ 180.5, 34.1, 31.7, 29.6, 29.4, 29.2, 29.0, 28.5 (quint, $J = 19$ Hz) 24.7, 22.6, 14.1. Anal. Calcd for $C_{13}H_{25}{}^2H_2O_2$: C, 72.18; H, 12.11. Found: C, 72.05; H, 12.01.

[10-^{2}*H*]-Tridecanoic Acid (2a). Compounds **(*S*)-[10-^{2}*H*]-tridecanoic acid ((*S*)-2a)** (6.7 mg, 69%) and **(*R*)-[10-^{2}*H*]-tridecanoic acid ((*R*)-2a)** (5.9 mg, 67%) were obtained from 11 mg of (*S*)-**16a** and 10 mg of (*R*)-**16a**, respectively: mp 39−41 °C; IR 1710 cm^{-1}; ^{1}H NMR δ 2.35 (t, J = 7.5 Hz, 2H), 1.63 (quint, J = 7.5 Hz, 2H), 1.42−1.16 (16H), 0.88 (t, J = 6.5 Hz, 3H); ^{13}C NMR δ 179.7, 34.0, 31.9, 29.5, 29.5, 29.4, 29.2, 29.0, 28.9, 29.2 (t, J = 19 Hz), 24.7, 22.7, 14.1. Anal. Calcd for $C_{13}H_{25}{}^2HO_2$: C, 72.51; H, 12.17. Found: C, 72.56; H, 12.09.

[11-^{2}H]-Tridecanoic Acid (2b). Compounds **(*S*)-[11-^{2}*H*]-Tridecanoic acid ((*S*)-2b)** (6.5 mg, 67%) and **(*R*)-[11-^{2}*H*]-Tridecanoic acid ((*R*)-2b)** (5.8 mg, 66%) were obtained from 11 mg of (*S*)-**16b** and 10 mg of (*R*)-**16b**: mp 40−41 °C; IR 1710 cm^{-1}; ^{1}H NMR δ 2.35 (t, J = 7.5 Hz, 2H), 1.63 (quint, J = 7.5 Hz, 2H), 1.40−1.18 (16H), 0.88 (t, J = 6.5 Hz, 3H); ^{13}C NMR δ 179.6, 33.9, 31.8, 29.6, 29.6, 29.5, 29.4, 29.2, 29.0, 28.9 (quint, J = 19 Hz), 24.7, 22.7, 14.1. Anal. Calcd for $C_{13}H_{25}{}^2HO_2$: C, 72.51; H, 12.17. Found: C, 72.35; H, 12.10.

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Supporting Information Available: ^{1}H and ^{13}C NMR and DEPT spectra for compounds **1, 2**, **8**−**17** and additional DQFCOSY and HETCOR for compounds **14** and **17**. This material is available free of charge via the Internet at http://pubs.acs.org.

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