

Supporting Information for World Wide Web Edition.

General Methods and Materials. Unless otherwise noted, all starting materials and solvents were obtained from commercial suppliers and used without further purification. All reactions involving air or moisture sensitive materials were carried out under argon atmosphere. Tetrahydrofuran (THF) and diethyl ether (Et₂O) were distilled just prior to use from sodium and benzophenone. Dichloromethane (CH₂Cl₂) was distilled from CaCl₂ and methanol from KOH. Bulb to bulb distillation was used for purification of volatile compounds. Column chromatography was performed on Merck silica gel 60 (35-70 mesh), and Merck neutral aluminium oxide 90 (70-230 mesh). Thin layer chromatography was carried out on Merck silica gel 60 F254 plates (0.2 mm, 20 x 20 cm). FT-IR spectra were recorded in chloroform solutions on a Michelson Bomem MB-120. ¹H NMR and ¹³C NMR spectra were recorded using a Varian Unity 300 instrument at 300 or 75 MHz for ¹H and ¹³C, respectively. Deuteriochloroform was used as solvent, and chemical shifts are expressed as ppm downfield from tetramethylsilane. The elemental analyses were performed with a Carlo Erba model 1106. Melting points were determined in a Koffler apparatus and are uncorrected. GC analyses were carried out with a flame ionization detector Fisons gas chromatograph (8000 series) equipped with a 30 m x 0.32 mm SPB-5 fused silica capillary column. Gas chromatography-coupled to mass spectrometry (GC-MS) was performed at 70 eV on a Fisons gas chromatograph (8000 series) coupled to a Fisons MD-800 mass selective detector. The system was equipped with a non-polar Hewlett Packard HP-1 capillary column (30 m x 0.20 mm I.D.) using the following temperature program: from 120°C to 180°C at 5°C/min and then to 260°C at 2°C/min after an initial delay of 2 min.

Synthesis of probes.

2,4-Dioxa-15-bromopentadecane and 2,4-Dioxa-14-bromotetradecane were prepared from the corresponding alcohols as reported in the literature (1). 2-Methyl-1,3-dithiane (3a) (2) and 2-ethyl-1,3-dithiane (3) were obtained as previously described, using BF₃-Et₂O.

2-Methyl-2-(12,14-dioxapentadecyl)-1,3-dithiane (4a). Compound **4a** was obtained in 85% yield from **2a** (1.54 g, 11.5 mmol) and 2,4-dioxa-15-bromopentadecane (2 g, 6.8 mmol) following the reported procedure.⁽³⁾ IR: 2970, 2852, 1463, 1147, 1110, 1045, 919, 721 cm⁻¹. ¹H RMN : δ 4.63 (s, 2H, C13'-H); 3.55 (t, $J = 6.5$ Hz; 2H; C11'-H); 3.34 (s, 3H; C15'-H); 2.86 (c; 4H, C4-H and C6-H); 1.93 (c, 4H, C5-H and C1'-H); 1.64 (c, 5H, C1''-H and C10'-H); 1.25 (broad, 16H, C2'-H to C9'-H). ¹³C RMN: δ 96.3 (C13'); 68.9 (C11'); 55.0 (C15'); 49.2 (C2); 41.6 (C1'); 29.7, 29.6, 29.5, 29.4, 29.3 (C2' to C9'); 27.7 (C4 and C6); 26.4, 26.2 (C1'' and C10'); 25.4 (C5).

2-Ethyl-2-(11,13-dioxatetradecyl)-1,3-dithiane. (4b). The same procedure was applied to 1.78 g (12 mmol) of **3b** to obtain 2.1 g (6 mmol, 84%) of pure dithiane **4b**. IR: 2925, 1716, 1458, 1152, 1108, 1037, 917, 718 cm⁻¹. ¹H RMN : δ 4.62 (s, 2H, C12'-H); 3.53 (t, $J = 6.5$ Hz, 2H, C10'-H); 3.33 (s, 3H, C14'-H); 2.84 (c, 4H, C4-H and C6-H); 1.92 and 1.86 (c, 4H, C1'-H and C5-H); 1.65 (c, 4H, C1''-H and C9'-H); 1.34 (broad, 14H, C2'-H to C8'-H); 1.04 (t, $J = 7.5$ Hz, 3H, C2''-H). ¹³C RMN: δ 95.8 (C12'); 67.5 (C10'); 53.9 (C14'); 48.2 (C2); 37.3 (C1'). 29.3, 29.2, 29.1, 29.0 (C2' to C8'); 25.8 (C1'' and C9'); 25.4 (C4 and C6); 25.2 (C5); 8.4 (C2'').

14,16-Dioxa-2-heptadecanone (5a). The procedure reported by Corey and Erickson⁽²⁾ was applied to **4a** (1 g, 2.9 mmol), using *N*-bromosuccinimide as reagent and 95% aqueous acetone as solvent, to obtain 0.7 g (2.8 mmol, 96 %) of pure **5a**. IR: 2927, 2854, 1718, 1465, 1359, 1151, 1110, 1045, 919, 721 cm⁻¹. ¹H RMN : δ 4.63 (s, 2H, C15); 3.54 (t, $J = 6.5$ Hz, 2H, C13-H); 3.33 (s, 3H, C17); 2.35 (t, $J = 7.5$ Hz, 2H, C3-H); 2.05 (s, 3H, C1-H); 1.57 (c, 4H, C4-H and C12-H); 1.24 (broad, 14H, C5-H to C11-H). ¹³C RMN: δ 209.1 (C2); 96.2 (C15); 67.6 (C13); 54.85 (C17); 43.6 (C3); 29.6, 29.5, 29.4, 29.3, 29.2, 29.1, 29.0 (C5 to C12); 26.0 (C1); 23.6 (C4).

14,16-Dioxa-3-heptadecanone (5b). The same procedure was applied to a 0.75 g (23 mmol) of **4b** to obtain 0.52 g (2 mmol, 93 %) of pure **5b**. IR: 2929, 2858, 1714, 1461,

1261, 1110, 1045, 919, 800 cm^{-1} . ^1H RMN : δ 4.63 (s, 2H, C15-H); 3.52 (t, $J = 6,5$ Hz, 2H, C13-H); 3.43 (s, 3H, C17-H); 2.52 (t, $J = 6,5$ Hz, 4H, C2-H and C4-H); 1.64 (broad, 4H, C5-H and C12-H); 1.34 (s, 12H, C6-H to C11-H); 1.05 (t, $J = 7.0$ Hz; 3H, C1-H). ^{13}C RMN: δ 212.0 (C3); 96.2 (C15); 67.7 (C13); 54.9 (C17); 42.2 (C4); 35.7 (C2); 29.6, 29.4, 29.3, 29.1, (C6 to C10 and C12); 26.0 (C11); 23.8 (C5); 7.7 (C1).

(2- ^2H)-14,16-dioxaheptadecan-2-ol (6a). A solution of 420 mg (1.6 mmol) of **5a**, and 139 mg of NaBD_4 (3.3 mmol) in 2 mL de MeOD was stirred at 25°C for 1 h. After this time, water was added and the product was extracted with CH_2Cl_2 . The organic layer was dried (Na_2SO_4) and the solvent was removed under vacuum to afford 392 mg (1.5 mmol, 94 %) of pure **6a**. IR: 3427, 2925, 2854, 1465, 1371, 1149, 1110, 1045, 919, 722 cm^{-1} . ^1H RMN : δ 4.65 (s, 2H, C15-H); 3.54 (t, $J = 6.5$ Hz, 2H, C13-H); 3.41 (s, 3H, C17-H); 1.75 (broad, 1H, -OH); 1.53 (c, 2H, C12-H); 1.21 (broad, 18H, C3-H to C11-H); 1.11 (s, 3H, C1-H). ^{13}C RMN: δ 96.2 (C15); 67.8 (C13); 67.5 (t, $J = 21.5$ Hz, C2); 54.9 (C17); 39.1(C3); 29.7, 29.6, 29.5, 29.4 (C5 to C10 and C12); 26.1 (C11); 25.7 (C1); 23.3 (C4).

(3- ^2H)-14,16-dioxaheptadecan-3-ol (6b). The same procedure was applied to 168 mg (0.7 mmol) de **5b** to obtain 148 mg (0.6 mmol, 87 %) of pure **6b**. IR: 3422, 2912, 2834, 1425, 1351, 1149, 1110, 1045, 919, 722 cm^{-1} . ^1H RMN : δ 4.64 (s, 2H, C15-H); 3.55 (t, $J = 6,5$ Hz, 2H, C13-H); 3.46 (s, 3H, C17-H); 1.77 (broad, 1H,-OH); 1.5 (c, 2H, C12-H); 1.34 and 1.26 (c, 18H, C2-H and C4-H to C11-H); 0.97 (t, $J = 7,5$ Hz, C1-H). ^{13}C RMN: δ 96.2 (C15); 67.8 (C13); 73.0 (t, $J = 21.5$ Hz, C3); 54.9 (C17); 36.7 (C4); 30.0 (C12); 29.6, 26.4, 29.2 (C2 and C6 to C10); 26.1 (C11); 25.5 (C5); 9.7 (C1).

(2- ^2H)-14,16-Dioxaheptadec-2-yl *p*-toluensulfonate (7a). A solution of 352 mg (1.3 mmol) of **6a**, 0.5 mL (9.5 mmol) of triethylamine and a catalytic amount of dimetilaminopyridine in 2 mL of CH_2Cl_2 was stirred at 25°C for 30 min and was added 382 mg (2 mmol) of tosyl chloride dissolved in CH_2Cl_2 (2 mL). The reaction mixture was

stirred for 2 days at 25°C, the crude was treated with 10% HCl and the product was extracted with CH₂Cl₂. The organic solution was dried (Na₂SO₄) and the solvent was removed to furnish 458 mg (1.1 mmol, 83%) of **7a**. IR: 2927, 2854, 1716, 1598, 1465, 1362, 1178, 1110, 1045, 910, 663, 557 cm⁻¹. ¹H RMN : δ 7.86 (d, *J* = 8.0 Hz, 2H, C2'-H and C6'-H); 7.34 (d, *J* = 8.0 Hz, 2H, C3'-H and C5'-H); 4.65 (s, 2H, C15-H); 3.54 (t, *J* = 6.5 Hz, 2H, C13-H); 3.43 (s, 3H, C17-H); 2.43 (s, 3H, C7'-H); 1.64 (m, 2H, C12-H); 1.35 (s, 18H, C3-H to C11-H); 1.24 (s, 3H, C1-H). ¹³C RMN: δ 144.1 and 134.6 (C1' and C4'); 129.5 and 127.6 (C2'-C3' and C5'-C6'); 96.2 (C15); 67.7 (C13); 54.7 (C17); 36.2 (C3); 29.7, 29.6, 29.5, 29.4 (C5 to C10 and C12); 26.0 (C11); 25.1 (C4); 21.1 (C7'); 20.5 (C1).

(3-²H)-14,16-Dioxaheptadec-3-yl *p*-toluensulfonate (**7b**). The same procedure was applied to 140 mg (0.5 mmol) of **6b**, to obtain 170 mg (0.4 mmol, 80 %) of pure **7b**. IR: 2927, 2854, 1712, 1643, 1463, 1359, 1178, 1110, 1043, 910, 813, 665, 555 cm⁻¹. ¹H RMN : δ 7.74 (d, *J* = 8.0 Hz, 2H, C2'-H and C6'-H); 7.25 (d, *J* = 8.0 Hz, 2H, C3'-H and C5'-H); 4.66 (s, 2H, C15-H); 3.46 (t, *J* = 6.5 Hz, 2H, C13-H); 3.35 (s, 3H, C17-H); 2.43 (s, 3H, C7'-H); 1.54 (m, 2H, C12-H); 1.24 and 1.14 (broad, 18H, C2-H and C4-H to C11-H); 0.86 (t, *J* = 6.5 Hz, 3H, C1-H). ¹³C RMN: δ 144.1 and 134.6 (C1' and C4'); 129.4 and 127.5 (C2', C3', C5' and C6'); 96.2 (C15); 85.0 (t, *J* = 21.5 Hz, C3); 67.7 (C13); 54.7 (C17); 33.3 (C4); 29.6, 29.4, 29.3, 29.1 (C6 to C10 and C12); 27.0 (C2); 26.0 (C11); 24.5 (C5); 21.5 (C7'); 9.0 (C1).

(12,12-²H₂)-Tridecan-1-ol (**8a**). Under argon atmosphere, 47 mg (1.2 mmol) of LiAlD₄ was treated with a solution of **7a** (252 mg, 0.6 mmol) in 2 mL of dry Et₂O. After 3 h at 25°C, the reaction mixture was treated with 10% HCl and the product was extracted with hexane. The organic layer was dried (Na₂SO₄) and the solvent was removed under vacuum to afford 135 mg of an oil that was treated with 6 mL of 10% HCl in methanol at 25°C for 18 h. After this time, the solvent was removed and the resulting residue was extracted with CH₂Cl₂. The organic layer was dried (Na₂SO₄) and the solvent was

evaporated to furnish a crude that was purified by silicagel column chromatography.

Elution with hexane/ethyl acetate (9:1) afforded 71 mg (0.4 mmol, 80 %) of pure **8a**. IR: 3380, 2921, 2852, 1458, 1056, 734 cm^{-1} . ^1H RMN : δ 3.63 (t, $J = 6.5$ Hz, 2H, C1-H); 1.76 (broad, 1H, OH); 1.65 (m, 2H, C2-H); 1.35 (broad, 18H, C3-H to C11-H); 0.97 (s, 3H, C13-H). ^{13}C RMN: δ 62.9 (C1); 32.7 (C2); 31.6 (C11); 29.6, 29.5, 29.3, 29.1 (C4 to C10); 25.5 (C3); 13.7 (C13). Anal. Calcd for $\text{C}_{13}\text{H}_{26}\text{D}_2\text{O}$: C, 77.22; H+D, 14.85. Found: C, 77.28; H+D, 14.81.

(11,11- $^2\text{H}_2$)-Tridecan-1-ol (**8b**). The same procedure was applied to 160 mg (0.4 mmol) of **7b** to obtain 30 mg (0.2 mmol, 49%) of **8b**. IR: 3300, 2923, 2854, 1463, 1056, 800, 722 cm^{-1} . ^1H RMN : δ 3.64 (t, $J = 6.5$ Hz, 2H, C1-H); 1.53 (m, 2H, C2-H); 1.35 (broad, 18H, C3-H to C10-H and C12-H); 0.94 (t, $J = 6.5$ Hz, 3H, C13-H). ^{13}C RMN: 63.1 (C1); 32.7 (C2); 29.6, 29.5, 29.3, 29.1 (C4 to C10); 25.5 (C3); 22.4 (C12); 14.1 (C13). Anal. Calcd for $\text{C}_{13}\text{H}_{26}\text{D}_2\text{O}$: C, 77.22; H+D, 14.85. Found: C, 77.26; H+D, 14.91.

(12,12- $^2\text{H}_2$)-Tridecanoic acid (**1a**). Jones oxidation of **8a** (51 mg, 0.3 mmol) afforded acid **1a**, which was purified by 10% H_2O - SiO_2 column chromatography eluting with CH_2Cl_2 to furnish 47 mg (0.2 mmol, 87 %) of **1a** as a white solid. m. p. 37-39°C. IR: 2921, 2852, 1712, 1465, 1288, 910, 734 cm^{-1} . ^1H RMN : δ 2.54 (t, $J = 5.0$ Hz, 2H, C2-H); 1.82 (m, 2H, C3-H); 1.42 (s, 16H, C4-H to C11-H); 1.0 (s, 3H, C13-H). ^{13}C RMN: δ 180.2 (C1); 34.1 (C2); 31.7 (C11); 29.6, 29.5, 29.4, 29.3, 29.2, 29.1 (C4 to C10); 24.7 (C3); 13.9 (C13). GC-MS (m/z , methyl ester): 74 (100 %), 87, 187, 199, 230 (M^+). Anal. Calcd for $\text{C}_{13}\text{H}_{24}\text{D}_2\text{O}_2$: C, 77.22; H+D, 12.96. Found: C, 77.24; H+D, 12.99. The deuterium contents of **1a** were determined by GC-MS analysis of the respective methyl ester and were found to be 90.0% $^2\text{H}_2$, 8.9% $^2\text{H}_1$ and 1.1% $^2\text{H}_0$.

(11,11- $^2\text{H}_2$)-Tridecanoic acid (**1b**). Jones oxidation of **8b** (28 mg, 0.1 mmol) afforded acid **1b**, which was purified by 10% H_2O - SiO_2 column chromatography eluting with CH_2Cl_2 to furnish 11 mg (0.05 mmol, 50 %) of **1b** as a white solid. m. p. 37-39°C. IR:

2954, 2920, 2852, 1704, 1411, 1292, 933, 723 cm^{-1} . ^1H RMN: δ 2.44 (t, $J= 5.0$ Hz, 2H, C2-H); 1.66 (m, 2H, C3-H); 1.32 (s, 16H, C4-H to C10-H and C12-H); 0.93 (s, 3H, C13-H). ^{13}C RMN: δ 180.2 (C1); 33.9 (C2); 29.6, 29.5, 29.4, 29.2, 29.1, 29.0 (C4 to C10); 24.7 (C3); 22.5 (C12); 13.9 (C13). GC-MS (m/z , methyl ester): 74 (100), 87, 143, 187, 199, 230 (M^+). Anal. Calcd for $\text{C}_{13}\text{H}_{24}\text{D}_2\text{O}_2$: C, 77.22; H+D, 12.96. Found: C, 77.23; H+D, 12.95.

The deuterium contents of **1b** were determined by GC-MS analysis of the respective methyl esters and were found to be 88.2% $^2\text{H}_2$, 8.7% $^2\text{H}_1$ and 3.1% $^2\text{H}_0$.

REFERENCES

1. Gras, J. L., Chang, Y. Y. K. W., Guerin, A. (1985) *Synthesis* 74-75.
2. Corey, E. J., Erickson, B. W. (1971) *J. Org. Chem.* 36, 3553-3560.
3. Seebach, D., Corey, E. J. (1975) *J. Org. Chem.* 40, 231-237.