Synthesis of Homo- and Heteroprotected Furcated Units for Modular Chemistry

Adi Dahan and Moshe Portnoy*

School of Chemistry, Raymond and Beverly Sackler Faculty of Exact Sciences, Tel-Aviv University, Tel-Aviv 69978, Israel

portnoy@post.tau.ac.il

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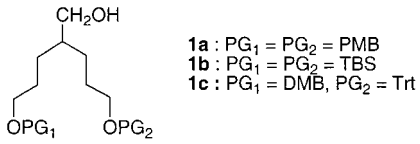
Furcated modular units of type AB_2 or ABB′ are possible monomers for the construction of branched oligomers. One of the leading routes to dendrimer synthesis is based on such building blocks.[1] Moreover, such furcated units are used as branching-inducing templates in solid-phase synthesis.[2]

Numerous units of type AB_2 are readily available (commercially or via well-established procedures).[1b] However, specific requirements, in numerous cases, dictate the design of novel dendrimer structures and, consequently, the development of suitable building blocks for modular chemistry. Recently, our attention has been focused on flexible dendrimers, which are based on ether linkage. Surprisingly, we could not find a concise procedure for the preparation of flexible, aliphatic, partially protected polyols. Herein, we report the synthesis of units **1**, which are suitable for the construction of ether-linked dendrimers through a divergent strategy.[3]

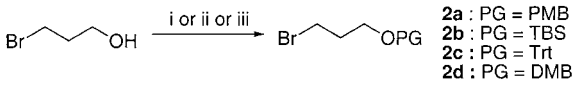


The synthetic strategy was based on malonic ester synthesis[4] using readily available bromopropanols **2**, protected under mildly basic or acidic conditions (Scheme 1). Numerous attempts to perform alkylation of diethyl malonate with **2a** or **2b** in alcoholic solvents failed. Finally, a successful dialkylation was accomplished in THF using NaH as a base and Bu_4NI as a promoter (Scheme 2). Remarkably, with only 15% excess of **2** employed, solely the dialkylation products were formed, accompanied by negligible traces of monoalkylated products.

The remaining steps of the malonic ester synthesis, i.e., hydrolysis and decarboxylation, worked perfectly well with the PMB protecting group, leading to carboxylic acid **4a** (Scheme 3). However, the hydrolysis was not compatible with the TBDMS ethers. Accordingly, the two steps were successfully replaced by a single decarbethoxylation step.[5] Optimization of this process for compounds **3** demonstrated that the best results were achieved with 3 equiv of dry LiCl in rigorously dried DMSO containing 1 equiv of H_2O. While the optimized yield of this step is not very high, most of the unreacted starting material can be recovered and recycled, leading to good overall conversion to monoesters **5a** and **5b** (Scheme 3).

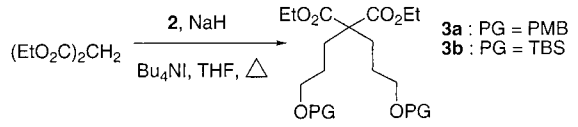
Synthesis of the target compounds **1a** and **1b** was accomplished by the reaction of esters **5a**,**b** or acid **4a** with a 1 M solution of $LiAlH_4$ in THF at 0 °C. Preparation of the heteroprotected unit **1c** was based on stepwise alkylation of diethyl malonate with **2d** and **2c**, in that order (Scheme 4). We were able to easily perform monoalkylation with both bromides when an excess of malonate was used. However, the reverse course of substitutions caused severe separation problems after the

Scheme 1

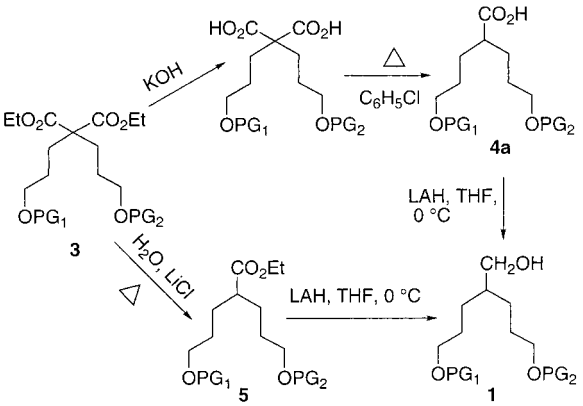


i) **2a**, **2d**: O-(4-methoxybenzyl)- or O-(3,4-dimethoxybenzyl)-trichloroacetimidate,CSA, DCM, cyclohexane
ii) **2b**: TBSCl, imidazol, DMF, 0°C
iii) **2c**: TrtCl, TEA, DMAP, DMF

Scheme 2

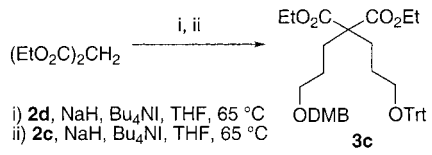


Scheme 3



1a, **3a**, **4a**, **5a** : $PG_{1,2}$ = PMB
1b, **3b**, **5b** : $PG_{1,2}$ = TBS
1c, **3c**, **5c** : PG_1 = DMB, PG_2 = Trt

Scheme 4



i) **2d**, NaH, Bu_4NI, THF, 65 °C
ii) **2c**, NaH, Bu_4NI, THF, 65 °C

* To whom correspondence should be addressed. Fax: +972-3-640-9293.

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second alkylation. The diester product, **3c**, was subjected to the decarbethoxylation and reduction leading to **1c** (Scheme 3). The lower yield of **1c** is explained by the diminished stability of the trityl protecting group under decarbethoxylation conditions. The chosen DMB and trityl protecting groups can be independently removed, enabling selective functionalization of each arm.[6]

In conclusion, we developed a fast route to branching homo- and heteroprotected units **1** with a range of protecting groups. These previously unknown units can now be used in modular chemistry.

Experimental Section

General. All reactions were conducted under an atmosphere of nitrogen in oven-dried glassware with magnetic stirring. THF, ether, and hexanes were dried over, and distilled from, sodium metal with benzophenone as the indicator. Dichloromethane (DCM) and DMSO were dried over, and distilled from, CaH_2. NaH (60% suspension in oil) was washed with dry hexanes and dried in vacuo before use. ^{1}H NMR (200 MHz) and ^{13}C NMR (50 MHz) spectra were recorded in $CDCl_3$ using TMS (^{1}H, 0 ppm), residual $CHCl_3$ (^{1}H, 7.26 ppm), or solvent (^{13}C, 77.16 ppm) as internal standard. The IR spectra were measured in $CHCl_3$ using a FTIR. The Elemental Analysis Laboratory of the Hebrew University of Jerusalem performed the elemental analysis. Column chromatography was performed using silica gel 60 (particle size 0.04−0.063 mm).

1-Bromo-3-*tert*-butyldimethylsilyloxypropane (2b). The compound **2b** was prepared according to the literature procedure.[7] Bp 85−90 °C (12 Torr). ^{1}H NMR (200 MHz, $CDCl_3$): δ 3.73 (t, J = 5.7 Hz, 2H), 3.63 (t, J = 6.4 Hz, 2H), 1.93 (quin, J = 6.0 Hz, 2H), 0.67 (s, 9H), 0.40 (s, 6H).

General Procedure for the Protection of 3-Bromo-1-propanol with Benzylic Protecting Groups (2a, 2d). A solution of the appropriate benzyl alcohol (37.6 mmol, 1.5 equiv) in dry ether (35 mL) was slowly added to a suspension of sodium hydride (0.15 g, 60%, 3.8 mmol, 0.15 equiv) in dry ether (40 mL) at room temperature. The reaction mixture was stirred for 30 min and then cooled to 0 °C. Trichloroacetonitrile (3.8 mL, 37.6 mmol, 1.5 equiv) was added, and the reaction mixture was allowed to warm slowly to room temperature over 4 h. After evaporation of the solvent, the residue was dissolved in petroleum ether (50 mL) containing methanol (0.16 mL). The suspension was filtered through Celite, and the filtrate was concentrated into a yellow oil. The crude imidate was dissolved in cyclohexane (60 mL), and a solution of 3-bromo-1-propanol (4.9 g, 2.3 mL, 25 mmol, 1 equiv) in 30 mL of methylene chloride was added. The resulting solution was cooled to 0 °C and treated with a catalytic amount of 10-camphorsulfonic acid. The reaction mixture was warmed to room temperature and stirred for 12 h, while a white precipitate was formed. The solution was filtered through Celite, and the solids were washed with 1:2 methylene chloride/cyclohexane (2 x 25 mL). The filtrate was washed with saturated aqueous sodium bicarbonate (50 mL), dried over magnesium sulfate, and concentrated. The residue was purified by flash chromatography (EtOAc/hexanes) to give the pure product (**2a**, **2d**) as a colorless oil.

2a:[8] 60% yield. ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.23 (d, J = 8.5 Hz, 2H), 6.85 (d, J = 8.5 Hz, 2H), 4.39 (s, 2H), 3.74 (s, 3H), 3.54 (t, J = 5.8 Hz, 2H), 3.49 (t, J = 5.8 Hz, 2H), 2.06 (quin, J = 6.1 Hz, 2H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 159.2, 130.4, 129.3, 113.6, 72.7, 67.4, 5.2, 32.9, 30.7.

2d: 66% yield. ^{1}H NMR (200 MHz, $CDCl_3$): δ 6.88 (s, 1H), 6.86 (m, 2H), 4.45 (s, 2H), 3.89 (s, 3H), 3.87 (s, 3H), 3.58 (t, J = 5.8 Hz, 2H), 3.55 (t, J = 5.8 Hz, 2H), 2.12 (quin, J = 6.1 Hz, 2H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 148.8, 148.3, 130.6, 119.8, 110.8, 72.5, 67.0, 55.5, 55.4, 32.5, 30.3. HRMS (CI): found (m/z), 289.0439/291.0419; calcd for $C_{12}H_{18}BrO_3$ (M + 1), 289.0433/291.0376.

1-Bromo-3-triphenylmethyloxypropane (2c). Trityl bromide (9.69 g, 30 mmol, 1.0 equiv), triethylamine (7.5 mL, 53.8 mmol, 1.8 equiv), and DMAP (291 mg, 1.5 mmol) were added to a solution of 3-bromo-1-propanol (4.12 g, 2.71 mL, 30 mmol, 1.0 equiv) in dry DMF (50 mL) at room temperature. The reaction mixture was stirred for 12 h. Ice-cold water (300 mL) was added to the pink cloudy solution, and the resulting mixture was extracted with DCM (4 × 100 mL). The combined organic layer was washed with an aqueous ammonium chloride solution (2 × 100 mL) and dried over sodium sulfate. After evaporation of the solvent, the colorless solid was recrystallized from ethanol to give 6.6 g (85%) of pure **2c**. Mp = 77 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.44 (m, 6H), 7.5 (m, 9H), 3.55 (t, J = 6.8 Hz, 2H), 3.20 (t, J = 5.7 Hz, 2H), 2.10 (quin, J = 6.4 Hz, 2H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 144.3, 128.8, 127.9, 127.1, 86.8, 61.4, 39.0, 33.7, 30.8. Anal. Calcd for $C_{22}H_{21}BrO$: C, 69.30; H, 5.55. Found: C, 69.59; H, 5.57.

General Procedure for the Dialkylation of Ethyl Malonate (3a, 3b). Diethyl malonate (0.527 g, 0.5 mL, 3.3 mmol, 1.0 equiv) was slowly added to a suspension of NaH (0.36 g, 9 mmol, 2.7 equiv) in dry THF (15 mL) cooled to 0 °C. The mixture was stirred until the hydrogen evolution had ceased and the solution was homogeneous (1 h at 0 °C and 2 h at room temperature). The resultant reaction mixture was cooled to 0 °C, and tetrabutylammonium iodide (2.6 g, 7 mmol, 2.1 equiv) was added. Alkyl bromide **2** (7.7 mmol, 2.3 equiv) was added, and the reaction mixture was refluxed for 48 h. An aqueous ammonium chloride solution (10 mL) was added, and the resulting mixture was extracted with EtOAc (3 × 50 mL). The combined organic extracts were washed with water (2 × 50 mL) and dried over magnesium sulfate. After evaporation of the solvent, the residue was chromatographed on a silica gel column (EtOAc/hexanes) to give the pure product (**3a**, **3b**) as a colorless oil.

3a: 64% yield. ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.24 (d, J = 8.5 Hz, 4H), 6.85 (d, J = 8.5 Hz, 4H), 4.40 (s, 4H), 4.14 (q, J = 7.0 Hz, 4H), 3.79 (s, 6H), 3.41 (t, J = 6.5 Hz, 4H), 1.95 (m, 4H), 1.49 (m, 4H), 1.25 (t, J = 7.0 Hz, 6H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 171.6, 159.1, 130.5, 129.1, 113.7, 77.8, 72.46, 69.9, 61.0, 57.0, 55.2, 29.1, 24.4, 14.1. IR (chloroform) (cm^{-1}): ν 1723. Anal. Calcd for $C_{21}H_{31}O_7$: C, 67.42; H, 7.80. Found: C, 67.31; H, 7.81.

3b: 68% yield. ^{1}H NMR (200 MHz, $CDCl_3$): δ 4.17 (q, J = 6.9 Hz, 4H), 3.58 (t, J = 6.2 Hz, 4H), 1.9 (m, 4H), 1.4 (m, 4H), 1.32 (t, J = 6.9 Hz, 6H), 0.86 (s, 18H), 0.23 (s, 12H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 169.5, 62.8, 60.7, 56.7, 28.5, 27.2, 25.7, 18.1, 13.9, −5.4. IR (chloroform) (cm^{-1}): ν 1733. Anal. Calcd for $C_{25}H_{52}O_6Si_2$: C, 59.48; H, 10.38. Found: C, 59.78; H, 10.47.

2-(3-(3,4-Dimethoxybenzyloxy)-1-propyl) Malonate, Diethyl Ester. For this monoalkylation, the dialkylation procedure (vide supra) was adapted using appropriate amounts of the reagents: diethyl malonate (5.98 g, 5.68 mL, 37.5 mmol, 2.5 equiv), NaH (0.6 g, 15 mmol, 1 equiv), THF (40 mL), Bu_4NI (5.54 g, 15 mmol, 1 equiv), **2d** (4.29 g, 15 mmol, 1 equiv). Chromatography on a silica gel column (EtOAc/hexanes 1:10 to 1:2) gave the pure product as a colorless oil; 66% yield. ^{1}H NMR (200 MHz, $CDCl_3$): δ 6.81 (s, 1H), 6.77 (m, 2H), 4.34 (s, 2H), 4.08 (q, J = 7.1 Hz, 4H), 3.81 (s, 3H), 3.78 (s, 3H), 3.39 (t, J = 6.4 Hz, 2H), 3.28 (t, J = 7.6 Hz, 1H), 1.9 (m, 2H), 1.58 (m, 2H), 1.17 (t, J = 7.1 Hz, 6H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 169.3, 149.2, 148.6, 131.2, 120.2, 111.2, 72.7, 69.4, 61.2, 56.0, 55.9, 51.8, 27.4, 25.7, 14.0. IR (chloroform) (cm^{-1}): ν 1726. HRMS (CI): found (m/z), 368.1837; calcd for $C_{19}H_{28}O_7$ (M), 368.1835.

2-(3-(3,4-Dimethoxybenzyloxy)-1-propyl)-2-(3-triphenylmethyloxy-1-propyl) Malonate, Diethyl Ester (3c). For this alkylation, the dialkylation procedure (vide supra) was adapted using appropriate amounts of the reagents: monoalkylated malonate (3.5 g, 9.5 mmol, 1 equiv), NaH (0.57 g, 14.25 mmol, 1.5 equiv), THF (15 mL), KI (2.36 g, 14.25 mmol, 1.5 equiv), **2c** (3.72 g, 14.25 mmol, 1.5 equiv). Chromatography on a silica gel column (EtOAc/hexanes 1:10 to 1:2) gave the pure product **3c** as a colorless oil; 47% yield. ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.43 (m, 6H), 7.32 (m, 9H), 6.87 (s, 1H), 6.82 (m, 2H), 4.42 (s, 2H), 4.14 (q, J = 7.2 Hz, 4H), 3.86 (s, 3H), 3.85 (s, 3H), 3.44 (t, J = 6.4 Hz, 2H), 3.04 (t, J = 6.4 Hz, 2H), 1.94 (m, 4H), 1.49 (m, 4H), 1.22 (t, J = 7.1 Hz, 6H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 171.7, 149.3, 148.8, 144.5, 131.4, 128.8, 127.8, 127.0, 120.2, 111.3, 86.6, 72.8, 70.1, 63.7, 61.2, 57.3, 56.1, 56.0, 51.8, 29.4, 29.3, 25.0, 24.6,

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14.2. IR (chloroform) (cm^{-1}): ν 1723. Anal. Calcd for $C_{41}H_{48}O_8$: C, 73.63; H, 7.23. Found: C, 73.93; H, 7.34.

2,2-Bis[3-(4-methoxybenzyloxy)-1-propyl]malonic Acid. Compound **3a** (456 mg, 0.88 mmol) was dissolved in 9.26 mL of ethanol/water (70:30, v/v) containing 2.3 g of KOH. The two-phase mixture was stirred at 80 °C for 8 h, cooled to 0 °C, and acidified with 20% H_2SO_4 (18.5 mL). Water (20 mL) was then added, and the mixture was extracted with EtOAc (2 × 30 mL). The extract was washed with water (2 × 20 mL) and brine (2 × 10 mL) and then dried over magnesium sulfate. The dried extract was concentrated under reduced pressure, and the yellow solid residue was used without further purification (261 mg, 65%). ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.24 (d, J = 8.5 Hz, 4H), 6.88 (d, J = 8.5 Hz, 4H), 4.43 (s, 4H), 3.78 (s, 6H), 3.44 (t, J = 6.5 Hz, 4H), 1.93 (m, 4H), 1.24 (m, 4H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 177.1, 159.4, 129.7, 114.0, 72.7, 69.7, 55.4, 33.8, 25.6.

5-(4-Methoxybenzyloxy)-2-[3-(4-methoxybenzyloxy)-1-propyl]pentanoic Acid (4a). A sample of 2,2-bis[3-(4-methoxybenzyloxy)-1-propyl]malonic acid (56.5 mg) was placed in a small dry flask with a minimal volume of 1,2-dichlorobenzene and heated to 150 °C for 40 min. Evolution of CO_2 was visible during the first 30 min of heating. The solvent was then removed under reduced pressure, and the residue was purified by column chromatography (silica gel; $CHCl_3$, followed by $CHCl_3$/2% acetic acid), yielding **4a** as a yellow oil (43.2 mg, 85%). ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.24 (d, J = 8.5 Hz, 4H), 6.88 (d, J = 8.5 Hz, 4H), 4.41 (s, 4H), 3.79 (s, 6H), 3.43 (m, 4H), 2.3 (m, 1H), 1.62 (m, 8H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 181.5, 159.3, 130.6, 129.5, 113.9, 72.7, 69.8, 55.4, 45.0, 29.0, 27.5. HRMS (CI): found (m/z), 295.1531; calcd for $C_{16}H_{23}O_5$ (M − PMB), 295.1545.

Reduction of 5-(4-Methoxybenzyloxy)-2-[3-(4-methoxybenzyloxy)-1-propyl]pentanoic Acid (1a). A solution of **4a** (43 mg, 0.1 mmol, 1 equiv) in dry ether (2 mL) was dropwise added to a suspension of $LiAlH_4$ (16 mg, 0.42 mmol, 4.2 equiv) in dry ether (10 mL) at room temperature. The mixture was stirred overnight. After the mixture was cooled, water was added cautiously followed by a 10% solution of sulfuric acid until neutral pH was reached. The contents of the flask were washed with brine followed by a saturated aqueous solution of $NaHCO_3$ and dried over magnesium sulfate. The residue was evaporated and chromatographed on a silica gel column (EtOAc/hexanes 1:2) to give the pure product **1a** as a colorless oil; 30% yield. ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.24 (d, J = 8.6 Hz, 4H), 6.86 (d, J = 8.6 Hz, 4H), 4.40 (s, 4H), 3.77 (s, 6H), 3.54 (d, J = 4.8 Hz, 2H), 3.43 (t, J = 6.5 Hz, 4H), 1.53 (m, 4H), 1.53 (m, 1H), 1.38 (m, 4H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 159.2, 130.7, 129.2, 113.9, 72.6, 70.5, 65.2, 55.3, 40.2, 27.5, 27.0. IR (chloroform) (cm^{-1}): ν 3628, 3445. HRMS (CI): found (m/z), 281.1769; calcd for $C_{16}H_{25}O_4$ (M − PMB), 281.1753.

General Procedure for the Decarbethoxylation (5a, 5b, 5c). The proper diester (0.99 mmol, 1 equiv) was added to a solution of water (0.018 mL, 0.99 mmol, 1 equiv) and LiCl (126 mg, 2.97 mmol, 3 equiv) in dry DMSO (10 mL) at room temperature. The mixture was stirred for 3 days in a wax bath at 140 °C. Ice-cold water (30 mL) was added to the brown cloudy solution, and the resulting mixture was extracted with hexanes (4 × 50 mL) and dried over sodium sulfate. After evaporation of the solvent, the residue was chromatographed on a silica gel column (EtOAc/hexanes) to give the pure product (**5**) as a colorless oil.

5a: 38% yield (47% brsm).[9] ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.24 (d, J = 6.6 Hz, 4H), 6.86 (d, J = 6.6 Hz, 4H), 4.40 (s, 4H), 4.13 (q, J = 6.9 Hz, 2H), 3.79 (s, 6H), 3.41 (m, 4H), 2.34 (m, 1H), 1.50 (m, 8H), 1.24 (t, J = 6.9 Hz, 3H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 176.2, 159.4, 130.9, 129.3, 114.0, 72.7, 69.9, 60.2, 55.4, 45.3, 29.2, 27.7, 14.5. IR (chloroform) (cm^{-1}): ν 1722. HRMS (CI): found (m/z), 323.1878; calcd for $C_{18}H_{27}O_5$ (M − PMB), 323.1858.

5b: 55% yield (75% brsm).[9] ^{1}H NMR (200 MHz, $CDCl_3$): δ 4.13 (q, J = 6.9 Hz, 4H), 3.58 (t, J = 6.2 Hz, 4H), 2.34 (m, 1H), 1.50 (m, 8H), 1.24 (t, J = 6.9 Hz, 6H), 0.86 (s, 18H), 0.31 (s, 12H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 176.0, 63.0, 60.2, 45.2, 30.6, 28.8, 26.0, 18.4, 14.4, −5.1. IR (neat) (cm^{-1}): ν 1735. Anal. Calcd for $C_{22}H_{48}O_4Si_2$: C, 61.05; H, 11.18. Found: C, 61.33; H, 11.37.

5c: 13% yield (37% brsm).[9] ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.40 (m, 6H), 7.20 (m, 9H), 6.83 (m, 3H), 4.41 (s, 2H), 4.11 (q, J = 7.1 Hz, 2H), 3.40 (m, 4H), 2.32 (m, 1H), 1.60 (m, 8H), 1.23 (t, J = 7.1 Hz, 3H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 176.1, 148.7, 144.5, 131.3, 128.7, 128.4, 127.8, 126.9, 120.2, 111.2, 86.5, 72.8, 69.9, 63.4, 60.1, 56.0, 55.9, 45.6, 45.3, 29.3, 29.0, 27.9, 27.6, 14.4. IR (chloroform) (cm^{-1}): ν 1722. Anal. Calcd for $C_{38}H_{44}O_6$: C, 76.48; H, 7.43. Found: C, 76.70; H, 7.03.

General Procedure for Ester Reduction (1a, 1b, 1c). A solution of the monoester **5** (0.462 mmol, 1 equiv) in dry THF (5 mL) was dropwise added to a suspension of $LiAlH_4$ (0.36 mL, 0.36 mmol, 0.75 equiv, 1 M in THF) in dry THF (20 mL) at 0 °C. When TLC analysis indicated complete consumption of the starting material (2 h), the solution was quenched using the Fieser method (50 μL of H_2O, 50 μL of 15% NaOH, 150 μL of H_2O).[10] The solution was allowed to warm to room temperature and filtered through a 1 cm pad of Celite, and the Celite pad was washed with hot EtOAc (200 mL). The combined filtrates were concentrated, and the residue was chromatographed on a silica gel column (EtOAc/hexanes) to give the pure product (**1**) as a colorless oil.

1a: 83% yield.

1b: 88% yield. ^{1}H NMR (200 MHz, $CDCl_3$): δ 3.57 (t, J = 6.0 Hz, 4H), 3.50 (d, J = 5.2 Hz, 2H), 2.33 (s, 1H), 1.47 (m, 2H), 1.47 (m, 1H), 1.34 (m, 4H), 0.86 (s, 18H), 0.18 (s, 12H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 65.6, 63.6, 40.1, 30.0, 27.1, 26.1, 18.4, −5.1. IR (neat) (cm^{-1}): ν 3356. Anal. Calcd for $C_{20}H_{46}O_3Si_2$: C, 61.48; H, 11.87. Found: C, 61.69; H, 11.56.

1c: 80% yield. ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.40 (m, 6H), 7.20 (m, 9H), 6.83 (m, 3H), 4.42 (s, 4H), 3.86 (s, 6H), 3.52 (m, 2H), 3.43 (t, J = 6.5 Hz, 2H), 3.05 (t, J = 6.5 Hz, 2H), 1.53 (m, 4H), 1.53 (m, 1H), 1.38 (m, 4H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 149.3, 148.8, 144.6, 131.3, 128.8, 127.8, 127.0, 120.3, 111.3, 86.6, 73.0, 70.6, 65.5, 64.0, 63.3, 56.0, 40.3, 27.5, 27.0. IR (chloroform) (cm^{-1}): ν 3750, 3445. Anal. Calcd for $C_{36}H_{42}O_5$: C, 76.48; H, 7.43. Found: C, 76.64; H, 7.56.

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Supporting Information Available: ^{1}H NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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(9) To maximize the yield of **5**, the reaction should be terminated before the starting material **3** is fully consumed. Thus, part of **3** is recovered upon purification and brsm (i.e., based on recovered starting material) yields are included.

(10) Fieser, L. F.; Fieser, M. *Reagents of Organic Synthesis*; Wiley: New York, 1967; Vol. 1, p 584.