DOI: 10.1002/ejoc.200800325

Solution-Phase Synthesis of First-Generation Tetraester Dendritic Branches Involving Microwave and/or Ultrasonic Irradiation

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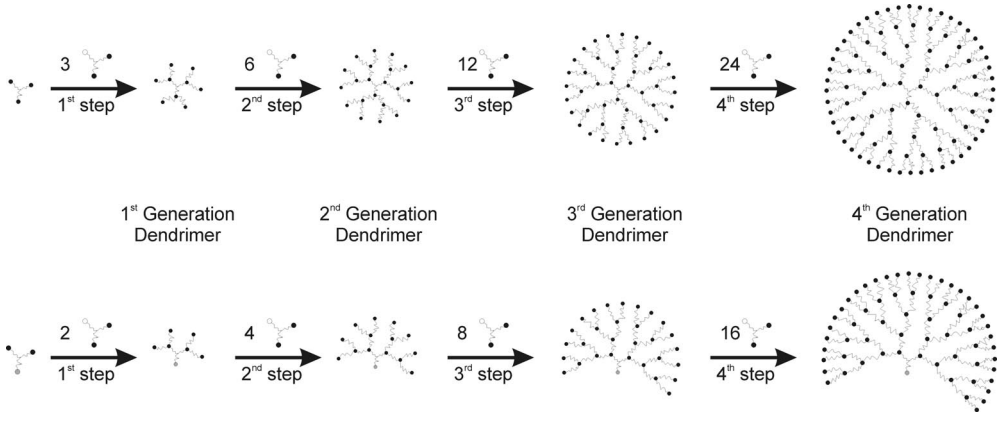
Keywords: Dendrimers / Nucleophilic substitution / Microwave / Ultrasound

Trifunctionalized aromatic cores were selectively protected to obtain precursors for bidirectional dendritic unit growth through stepwise divergent syntheses. The synthesis of first-generation dendrimer building blocks was performed by nucleophilic substitution of bromomethyl-substituted aromatic cores with diethyl malonate anions in the presence of carbonate in halogen-free solvents. The screening of the reaction parameters revealed the optimum conditions for small- and larger-scale synthesis: these require microwave or ultrasonic irradiation to achieve yields around 70 % in reaction times as short as 15 min. As a result of the heterogeneity of the reaction mixtures, efficient stirring was important to suppress by-product formation.

Introduction

Dendrimers are of particular interest in numerous applications as diverse as stabilizing agents in suspensions,[1,2] metal complexation,[1–4] encapsulation of small-to-medium-sized organic molecules,[5,6] and delivery of pharmaceutically active compounds.[7–9] Rather recently, dendrimers have also been used to increase the loading capacity of a resin and/or to increase the distance of the reaction sites and core of the resin.[10,11] The synthesis of dendrimers can follow two alternative principle routes: a divergent or a convergent approach[12] (Scheme 1). In the case of the more-common divergent route,[13] the synthesis starts from the dendrimer core, which has multiple functional sites. From this core, the dendrimer grows through stepwise reactions with molecules with two types of functional groups: one type reacts with functional sites on the core or on the lower generation dendrimer, whereas the other type is intended for the continuation of the dendrimer growth. From the



Scheme 1. Dendrimer growth from a trifunctional precursor: The upper part of this scheme shows the dendrimer growth from all three reaction sites. The lower part of this scheme describes the dendrimer growth from only two of the formerly three reaction sites (e.g., after selective protection of one of the reaction sites).

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stepwise growth it becomes apparent that long reaction times are required to complete each step of the synthesis, in particular for the higher-generation dendrimers. Hence, acceleration of the syntheses involved in dendrimer preparation is a key prerequisite to make any future application profitable.

Results and Discussion

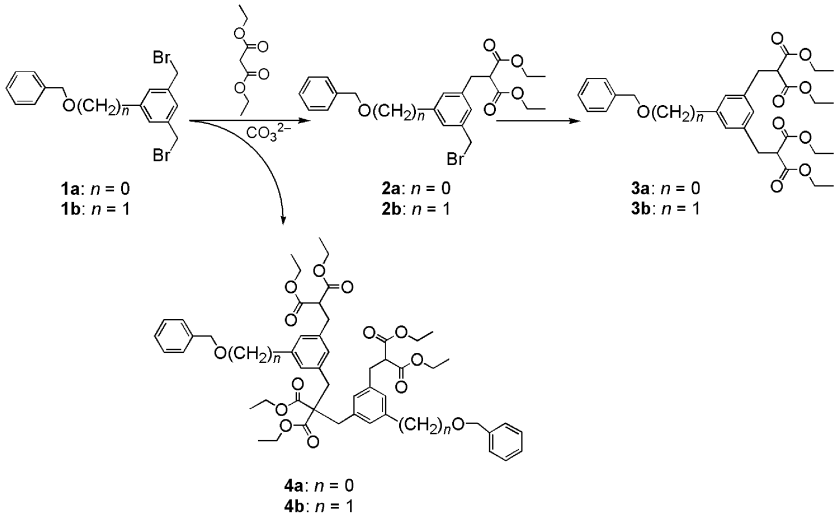
Current studies in our group focus in particular on the solution-phase synthesis of dendrimers that can be attached to resins. Depending on the linkage of the dendrimer on the resin, these modified resins offer two advantages: temporarily attached dendrimers allow solid-phase dendrimer growth by, for example, click-chemistry techniques,[14] whereas permanently attached ones multiply the loading capacity of the resin and make it an interesting candidate for solid-phase synthesis in general.[10,11] For the synthesis of these dendrimers, 1,3,5-trisubstituted benzenes have been modified in such a way that they carry one benzyl-protected hydroxy or hydroxymethyl group and two bromomethyl groups (Scheme 2).[15,16]

For nucleophilic substitution of both bromine atoms, these precursors were treated with diethyl malonate anions to yield first-generation dendritic units. According to literature reports, this reaction can be performed in acetonitrile with an excess amount of potassium carbonate as base for the in situ generation of diethyl malonate anions,[17] thus excluding the formation of gases like hydrogen, which would be formed with, for example, sodium hydride as base.[18] Consequently, this reaction can be conveniently performed in closed vessels at elevated temperatures (>82 °C) by employing so-called high-energy techniques, that is, microwave and ultrasonic irradiation, which could result in significant acceleration of the reaction time. Special attention was given to finding the right balance between reaction speed and yield optimization. Improvement in the yields and product purity by volumetric and quasigradient-free heating by microwave irradiation was recently shown for the synthesis of linear polymers from living polymerizations and dendrimer synthesis.[19–23] A similarly efficient and uniform heat distribution was expected from an ultrasound probe.[24]

The synthesis of tetraesters **3a** and **3b** from **1a** and **1b**[15,16] (Scheme 2) in acetonitrile was investigated under microwave irradiation on a small scale (0.2 mmol) in an initial temperature screening starting from 100 °C (Table 1). A maximum yield of tetraester **3a** (72%) was obtained at 120 °C within 1 h of reaction time. Shorter reaction times, concomitant with higher temperatures, favor decomposition of the reactants (140 °C: 20–30 min, 57%). The yield is also lower at temperatures less than 120 °C (100 °C: 90–120 min, 63%), which indicates that at higher temperatures side reactions are less accelerated. The yields of tetraester **3b** were generally lower than those of its homologue **3a**, with a maximum yield of **3b** of 57% at 120 °C within 20–30 min of reaction time. Because at 140 °C the yield was 56% and the reaction time was shorter (6–8 min), this temperature was chosen for future experiments. Less acceleration at elevated temperatures was observed for the reaction of **1a**

Table 1. Temperature dependence of reaction times and yields for the conversion of **1a** and **1b** (0.2 mmol scale) into tetraesters **3a** and **3b** in acetonitrile (1 mL) by using potassium carbonate (4.5 equiv.) under microwave irradiation.

T [°C]	**1a** → **3a**		**1b** → **3b**	
	t [min]	Yield [%]	*t* [min]	Yield [%]
100	90–120	63	90–120	51
120	45–60	72	20–30	57
140	20–30	57	6–8	56



Scheme 2. Scheme for the reactions of **1a**,**b** to yield tetraesters **3a**,**b** by mixed bromo-/diesters **2a**,**b**. The structure of the most prominent byproduct hexaester **4a**, which is observed in particular during scale-up by utilizing ultrasound, contains mono- and disubstituted malonates in a 2:1 ratio. Compounds **2b** and **4b** were not isolated; comparison of the TLCs of the reactions **1a**,**b** → **3a**,**b**, however, suggests analogous byproduct formation.

(Table 1), and only the reaction of **1b** seems to follow the "rule of thumb" derived from the Arrhenius equation saying that a temperature increase of 10 K (20 K) should decrease the reaction time by a factor of 2 (4).

$$k = Z\,e^{-\frac{E_A}{RT}} \Leftrightarrow E_A = R\frac{T_1 T_2}{T_2 - T_1}\ln\frac{k_1}{k_2}$$

From the data obtained (Table 1), only intervals of the activation energies can be calculated. The reaction of **1b** covers the range of 78–96 kJ mol^{-1}, whereas that of **1a** spans a range of 35–57 kJ mol^{-1}. This difference in activation energy is assumed to originate from the presence or absence of a methylene group between the aromatic ring and the oxygen atom (Scheme 2), which disables or enables the involvement of the oxygen atom in resonance (de)stabilization of the overall rate-determining step.

Scale Up under Microwave Irradiation

Scale up is preferentially performed in batch mode, as the solid potassium carbonate forms a stable suspension in acetonitrile only when vigorously agitated. The standard closed-vessel system (CEM Discover) can handle a maximum volume of 50 mL; in open-vessel ("reflux") conditions, the maximum volume is limited to 100 mL. Consequently, the set up described in this publication allows a maximum starting amount of 14 mmol or around 5 g of **1a**,**b**.

For future linkage to a resin, the phenolic core was favored over the benzylic one, and hence, scale up was focused on **1a**. The first scale-up experiments were performed on a 1.0-mmol scale at 120 °C. "Standard" closed-vessel hardware was used: a tube-shaped vial with conical bottom (inner dimensions: height × diameter = 86 mm × 12.5 mm) and a regular-shaped stirring bar (length × diameter = 10 mm × 2 m). Stirring of the heterogeneous suspension was inefficient, resulting in an increased reaction time from expected 30–60 min to 90–120 min and a decreased yield from the expected 72 to 32% (Table 2, Entries 1 and 2).

Further proof of inefficient stirring was exhibited by the most prominent byproduct **4a**, which was recovered in 14% yield. The structure of this symmetrical molecule was proven by a 2D *g*HMBC NMR spectroscopic experiment, which revealed the medium-range interaction of the protons (3.154 ppm) and carbon atoms (δ =39.0 ppm) in direct proximity to the quaternary carbon atom (δ =59.9 ppm; Figure 1). Byproduct **4a** contains two mono- and one disubstituted diethyl malonate. Deprotonation of the diethyl

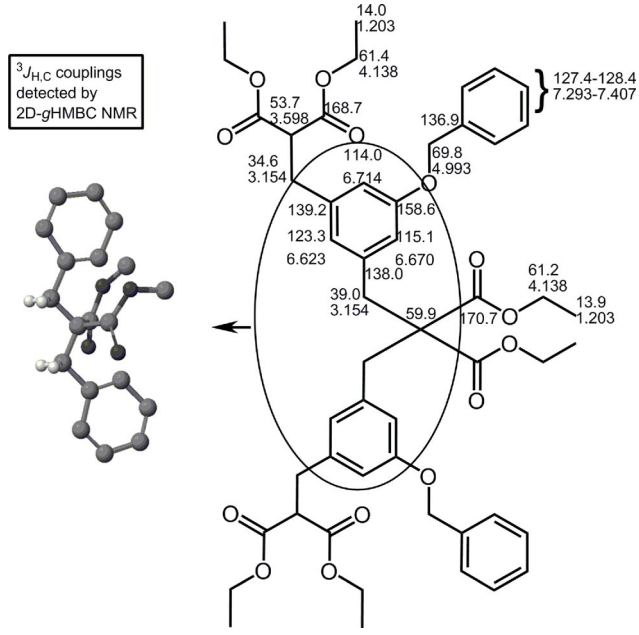


Figure 1. Allocation of NMR signals for compound **4a**, verified by a 2D *g*HMBC NMR experiment. In particular, the $^3J_{H,C}$ couplings at {^{1}H; ^{13}C} = {3.154; 39.0} was beneficial for the structure determination. In the left half of this scheme, the corresponding part of the molecule (energy minimization by HyperChem) is shown for elucidation.

Table 2. Scale up of the synthesis of tetraester **3a** from **1a** under various conditions. Unless indicated otherwise, all reactions were performed at 120 °C with 5.0 mL of solvent per 1.0 mmol of **1a** and a molar ratio of **1a**:malonate:carbonate, 1:4:5.[a]

	n [**1a**] [mmol]	System	Remarks	Time [min]	Yield [%]
1	0.2	MeCN/K_2CO_3	MW, closed vessel, small stirring bar	45–60	72
2	1.0	MeCN/K_2CO_3	MW, closed vessel, small stirring bar	90–120	32
3	0.8	MeCN/K_2CO_3	MW, closed vessel, large stirring bar	90–120	55
4	0.2	DMF/Cs_2CO_3	MW, closed vessel, small stirring bar	<15	65
5	1.0	DMF/Cs_2CO_3	MW, closed vessel, small stirring bar	20–30	25
6	0.2	DMF/Cs_2CO_3	CH, closed vessel, small stirring bar	<15	54
7	1.5	DMF/Cs_2CO_3	CH, reaction at 60 °C, round flask, large stirring bar	90–120	71
8	0.2	Cs_2CO_3	MW, solvent free, closed vessel, small stirring bar	10–13	54
9	1.5	DMF/Cs_2CO_3	MW, open flask, large egg-shaped stirring bar	<30	67
10	1.5	DMF/Cs_2CO_3	MW, open flask, large egg-shaped stirring bar, dropwise addition[b]	<30	64
11	1.5	DMF/Cs_2CO_3	1. US at room temp. 2. MW, open flask, large egg-shaped stirring bar	1. 30 2. <15	66
12	1.5	DMF/Cs_2CO_3	US at 102 °C, open flask[c]	<13	62

[a] MW: microwave irradiation; CH: conventional heating (oil bath); US: ultrasound. [b] A solution of **1a** (1.5 mmol) in DMF (7.5 mL) was added dropwise to a suspension of diethyl malonate (6.0 mmol) and cesium carbonate (7.5 mmol) in DMF (7.5 mL) over 20 min. Heating was continued for 10 min. [c] The addition of DMF (15 mL) was required because of the geometry of the flask/overhead probe.

malonate by undissolved potassium carbonate occurs after absorption of diethyl malonate onto the solid surface. After complete reaction of deprotonated diethyl malonate with compound **1a**, the product/intermediate should desorb from the solid surface. As a consequence of inefficient stirring, extended residence times of **2a** and **3a** on the surface of solid cesium carbonate can favor second deprotonation. The importance of efficient stirring was recently shown in a literature report on the existence or absence of nonthermal microwave effects.[25]

Because efficient stirring could not be achieved in a closed vessel by using MeCN/K_2CO_3, we changed to DMF/Cs_2CO_3 owing to the partial solubility of Cs_2CO_3 in DMF. In addition, operation in DMF offers the major advantage over MeCN that at 120 °C, syntheses are not restricted to closed-vessel conditions. Comparison of conventional heating at 120 °C with microwave-assisted heating (Table 2) indicated higher yields with the latter, which is assumed to originate from a more uniform heat distribution in the case of microwave-assisted heating. It is worth mentioning that solvent-free conditions also failed to give good yields of **3a** (Table 2, Entry 8): obviously the solid carbonate, which acts as primary absorber, did not provide uniform heat distribution.

Performance of the reaction on a 1.5-mmol scale in DMF gave product **3a** in 67% yield, which is very close to the maximum yield of 72% obtained on a 0.2-mmol scale (Table 2, Entry 9) and is the best yield achieved on a larger scale. The yield of **3a** could not be further increased by dropwise addition of **1a** to a hot suspension of diethyl malonate and cesium carbonate in DMF (Table 2, Entry 10).

Scale Up Involving Ultrasonic Irradiation

The influence of ultrasound on the scale up of this reaction was also investigated. Application of ultrasonic irradiation (through an ultrasonic bath) to the reaction mixture in DMF/cesium carbonate at room temperature for 30 min perhaps decreased the size of the cesium carbonate particles and hence increased the surface available for reaction. The suspension itself, however, was not stable and agitation was required for dispersion of the solid cesium carbonate. The reaction itself (Table 2, Entry 11) was performed under microwave irradiation at 120 °C. Product **3a** was obtained in 66% yield, showing no improvement relative to the plain microwave experiment (Table 2, Entry 9). Remarkably, in both experiments involving ultrasonic irradiation (see below), byproduct **4a** was also formed in large quantities of more than 10%. On the basis of our previous hypothesis, the formation of byproduct **4a** is assumed to originate from prolonged absorption times of intermediate **2a** and product **3a** on the solid surface of the carbonate, which in the ultrasonic experiments probably relates to the increased surface area of cesium carbonate.

The synthesis of tetraester **3a** was also performed exclusively by utilizing a self-heating overhead ultrasound probe. After an exposure time of 10 min, the final temperature of the reaction mixture was 102 °C. The reaction was complete, and dendritic building block **3a** was recovered in 62% yield (Table 2, Entry 12).

Conclusions

The syntheses of first-generation dendritic tetraesters **3a**,**b** from bromo bifunctional precursors **1a**,**b** were performed by nucleophilic substitution with diethyl malonate anions in heterogeneous media, either in MeCN/K_2CO_3 or in DMF/Cs_2CO_3 at elevated temperatures. The comparably high temperature of 120 °C was optimum for that system in terms of maximum yield and short reaction times, as revealed by precedent temperature screening. Extended residence times of intermediates **2a**,**b** and/or products **3a**,**b** on the solid surface of carbonate favored the formation of byproducts like **4a**,**b**, and therefore, efficient stirring was necessary. Larger-scale syntheses were performed exclusively in open vessels by using the DMF/Cs_2CO_3 system. Best yields of 72 and 58% of **3a**,**b**, respectively, were obtained with the aid of microwave irradiation with reaction times as low as 15 min. The use of conventional heating or ultrasonic irradiation, in contrast, lowered the yield at identical temperatures and proved the superiority of microwave heating over those two alternatives. This superiority is due to the (quasi)-gradient-free heating that obviously was maintained despite the large amounts of solid carbonate present. The solid carbonate is the best absorbing material of all reactants in the reaction mixture, and in this context, it is worth emphasizing again that thorough stirring was the key strategy for successful synthesis. It also provided even distribution of the solid carbonate, and hence, averaged the absorbance of microwave irradiation and subsequent generation of heat throughout the reaction mixture. Future experiments will aim at the solid-phase synthesis of the first-generation dendritic tetraesters **3a**,**b** from resin-bound starting material **1a**,**b**. Because of steric hindrance of the resin-bound reactants at the surface of solid carbonate, this strategy will favor the nucleophilic substitution involving dissolved carbonate. Hence, the formation of byproducts of type **4a**,**b** will not be favored.

Experimental Section

General: Acetonitrile and *N*,*N*-dimethylformamide were stored over molecular sieves (3 Å) under an atmosphere of argon. Cesium carbonate and potassium carbonate were oven dried. Silica-gel plates (Merck F254) were used for thin layer chromatography. Chromatographic purification was performed with silica gel (200–400 mesh). NMR spectra were recorded with a Bruker AC 300 spectrometer operating at 300 MHz for ^1H and 75.43 MHz for ^{13}C. All NMR spectra were recorded in $CDCl_3$; ^1H and ^{13}C NMR spectra are reported in units of δ relative to internal $CHCl_3$ at 7.26 and 77.0 ppm, respectively. ^{13}C NMR spectra were proton-noise decoupled. Infrared spectra of neat samples were recorded with a Bruker Tensor27 FTIR spectrometer equipped with a single reflection diamond crystal (PIKE Technologies). Mass spectra were recorded with a Finnigan Mat TSQ7000 mass spectrometer. Analyses indi-

cated by the symbols of the elements were carried out by the microanalytical section of the Institute of Organic and Pharmaceutical Chemistry of the National Hellenic Research Foundation. Microwave-assisted reactions were performed in a CEM Discover microwave apparatus (f = 2.45 GHz, P_{max} = 300 W), either in closed-vessel or in open-vessel operation mode. The internal temperature of the reaction mixture was measured with an IR pyrometer, the calibration of which was verified for all experimental set ups (Figure 2). Reactions under microwave irradiation in closed-vessel mode were performed in vials specially designed for operation in the microwave apparatus. In general, the glassware was heated to 140 °C, cooled down in a desiccator and filled with argon prior to addition of chemicals and solvents. Ultrasonic irradiation was applied either with a probe (titanium alloy, length 254 mm, diameter 13 mm) controlled by a 650-W, 20-kHz ultrasonic processor (Sonics and Materials) or through an ultrasonic bath (LSB2 by Falc, f = 40 kHz, P_{max} = 150 W). Reference experiments with conventional heating were performed in preheated oil baths.

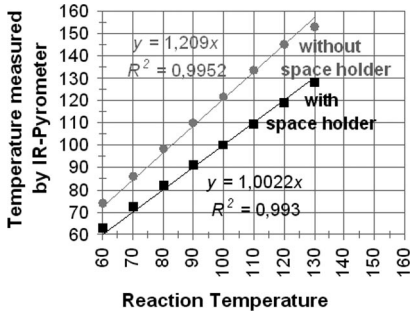


Figure 2. Open-vessel operation in the CEM discover microwave apparatus: Correlation between the temperatures inside the reaction mixture and the temperatures measured by the IR pyrometer. On the basis of its calibration, the distance between the pyrometer and the surface of the vial must be kept constant. The space holder (standard accessory) ensures the proper distance: deviations from this distance lead to large differences between real and measured temperatures.

General Procedure for the Synthesis of Tetraesters 3a and 3b: Compound **1a** or **1b** (76.8 or 74.0 mg, 0.2 mmol), diethyl malonate (128.1 mg, 0.8 mmol), potassium or cesium carbonate (138.2 or 325.8 mg, 1.0 mmol), and the solvent (acetonitrile or DMF, 1.0 mL) were placed in a vial. Subsequently, the reaction mixture was stirred, and argon was bubbled through the solution for 10 min. The vessel was then heated at the targeted temperature for the indicated time (Tables 1 and 2). After completion of the reaction, distilled water was added, and the product was extracted from the mixture with diethyl ether. The organic layer was dried (Na_2SO_4), the solvent was evaporated in vacuo, and the crude product was purified by flash column chromatography [gradient petroleum ether (40–60 °C)/ethyl acetate, 95:5 to 90:10 to 80:20, or petroleum ether (40–60 °C)/ethyl acetate, 85:15). All scale-up experiments were performed by maintaining the ratio of the three reactants and solvents as indicated above, with the exception of the experiments involving the dropwise addition of **1a** and the overhead ultrasonifier, where twice the amount of solvent was used (15 mL of DMF for 1.5 mmol of **1a**).

Diethyl 2-(3-Benzyloxy-5-bromomethylbenzyl)malonate (2a): R_f = 0.52 [petroleum ether (40–60 °C)/ethyl acetate, 4:1]. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.22 (t, J = 7.2, 6 Hz, CH_3), 3.19 (d, J = 7.8 Hz, 2 H, $ArCH_2C$), 3.63 [t, J = 7.8 Hz, 1 H, $CH(CO_2Et)$], 4.10–4.21 (m, 4 H, OCH_2C), 4.51 (s, 2 H, CH_2Br), 5.04 (s, 2 H, OCH_2Ar), 6.80 (s, 1 H, CH_3R_3), 6.84 (s, 1 H, CH_3R_3), 6.88 (s, 1 H, CH_3R_3), 7.31–7.44 (m, 5 H, C_6H_5R) ppm. ^{13}C NMR (75.43 MHz, $CDCl_3$, 25 °C): δ = 14.0, 34.5, 46.1, 53.6, 61.5, 70.0, 113.3, 115.5, 121.6, 127.5, 128.0, 128.6, 136.6, 139.0, 140.0, 159.1, 168.7 ppm. IR: $\tilde{\nu}$ = 1729 [s, δ_{asym}(C–O)], 1595 [w, δ(C=C)], 1296 [ms, δ(C–O–C)], 1263 [m, $\delta(CH_2Br)$], 1224 [ms, δ_{sym}(C–O)], 1030 [ms, δ(=C–H)] cm^{-1}. MS (ESI): m/z (%) = 448.5 (25.1) $[M]^+$, 450.5 (12.1) $[M + 2]^+$.

Tetraethyl 2,2′-[5-Benzyloxy-1,3-phenylene]bis(methylene)dimalonate (3a): R_f = 0.33 [petroleum ether (40–60 °C)/ethyl acetate, 4:1]. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.21 (t, J = 7.2 Hz, 12 H, CH_3), 3.14 (d, J = 7.8 Hz, 4 H, $ArCH_2C$), 3.59 [t, J = 7.8 Hz, 2 H, $CH(CO_2Et)$], 4.08–4.22 (m, 8 H, OCH_2C), 5.04 (s, 2 H, OCH_2Ar), 6.65 (s, 1 H, CH_3R_3), 6.69 (s, 2 H, CH_3R_3), 7.30–7.41 (m, 5 H, C_6H_5R) ppm. ^{13}C NMR (75.43 MHz, $CDCl_3$, 25 °C): δ = 14.0, 34.6, 53.7, 61.4, 69.8, 113.7, 121.9, 127.4, 127.9, 128.5, 136.8, 139.6, 159.0, 168.7 ppm. IR: $\tilde{\nu}$ = 1729 [s, δ_{asym}(C–O)], 1595 [w, δ (C=C)], 1274 [ms, δ(C–O–C)], 1224 (ms, δ_{sym}(C–O)], 1031 [ms, δ(=C–H)] cm^{-1}. MS (ESI): m/z (%) = 551.7 (100) $[M + Na]^+$. $C_{29}H_{36}O_9$ (528.60): calcd. C 65.89, H 6.86; found C 66.10, H 6.95.

Tetraethyl 2,2′-[5-Benzyloxymethyl-1,3-phenylene]bis(methylene)dimalonate (3b): R_f = 0.34 [petroleum ether (40–60 °C)/ethyl acetate, 4:1]. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.20 (t, J = 7.2 Hz, 12 H, CH_3), 3.17 (d, J = 7.8 Hz, 4 H, $ArCH_2C$), 3.60 [t, J = 7.8 Hz, 2 H, $CH(CO_2Et)$], 4.12–4.18 (m, 8 H, OCH_2C), 4.46 (s, 2 H, OCH_2), 4.52 (s, 2 H, OCH_2), 6.98 (s, 1 H, CH_3R_3), 7.06, (s, 2 H, CH_3R_3), 7.28–7.36 (m, 5 H, CH_5R) ppm. ^{13}C NMR (75.43 MHz, $CDCl_3$, 25 °C): δ = 14.0, 34.5, 53.8, 61.4, 71.9, 72.2, 126.7, 127.6, 127.8, 128.4, 128.9, 138.1, 138.3, 138.7, 168.7 ppm. IR: $\tilde{\nu}$ = 1729 [s, δ_{asym}(C–O)], 1606 [w, δ(C=C)], 1266 [ms, δ_{sym}(C–O)], 1095 [ms, δ(C–O–C)], 1031 [ms, δ(=C–H)] cm^{-1}. MS (ESI): m/z (%) = 565.6 (100) $[M + Na]^+$. $C_{30}H_{38}O_9$ (542.63): calcd. C 66.40, H 7.06; found C 66.69, H 6.98.

Tetraethyl 2,2′-{5,5′-[2,2-Bis(ethoxycarbonyl)propane-1,3-diyl]bis[3-(benzyloxy)-5,1-phenylene]}bis(methylene)dimalonate (4a): R_f = 0.26 [petroleum ether (40–60 °C)/ethyl acetate, 4:1]. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.14–1.23 (m, 18 H), 3.13 (s, 4 H), 3.14 (d, J = 7.8 Hz, 4 H), 3.60 (t, J = 7.8 Hz, 2 H), 4.05–4.22 (m, 12 H), 5.00 (s, 4 H), 6.62 (s, 2 H), 6.67 (s, 2 H), 6.71 (s, 2 H), 7.29–7.41 (m, 10 H) ppm; for an allocation of signals, see Figure 2. ^{13}C NMR (75.43 MHz, $CDCl_3$, 25 °C): δ = 13.9, 14.0, 34.7, 39.0, 53.7, 59.9, 61.2, 61.4, 69.8, 114.0, 115.1, 123.3, 127.4, 127.8, 128.5, 136.9, 138.0, 139.2, 158.7, 168.7, 170.7 ppm. gHMBC NMR {^{1}H; ^{13}C}: δ = {1.20; 61.2, 61.4}, {3.15; 39.0, 53.7, 59.9, 114.0, 115.1, 123.3, 138.0, 139.2, 168.7, 170.7}, {3.60; 34.6, 139.2, 168.7}, {4.14; 13.9, 14.0, 168.7, 170.7}, {5.00; 127.4, 127.8, 136.9, 158.7}, {6.62; 34.7, 39.0, 114.0, 115.1}, {6.67; 39.0, 114.0, 123.3, 158.7}, {6.71; 34.7, 115.1, 123.3, 158.7}, {7.29–7.41; 69.8, 127.4, 127.8, 128.5, 136.9} ppm. MS (ESI): m/z (%) = 920.2 (6.3) $[M + Na]^+$. $C_{51}H_{60}O_{14}$ (897.04): calcd. C 68.29, H 6.74; found C 67.97, H 6.80.

Acknowledgments

Financial support from the European Commission Marie-Curie Transfer of Knowledge Programme (MTKD-CT-2004-014399) "SOPHOLIDES" is gratefully acknowledged.

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Received: March 27, 2008
Published Online: July 21, 2008

