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PAPER

Vanillin and *o*-vanillin oligomers as models for dendrimer disassembly†‡

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Linear analogs have been synthesized to model disassembling dendrimers. These linear analogs provide a facile synthesis to molecules that can be used to test new trigger groups and cleavage vectors. Vanillin and *o*-vanillin were used as the monomer units of these analogs and two trigger groups, allyl and *o*-nitrobenzyl, were chosen to test the disassembly process. Allyl triggered analogs **1a–d** and **3a–d** and *o*-nitrobenzyl triggered analogs **2a–c** and **4a–c** showed good to excellent disassembly as followed by the evolution of *p*-nitrophenoxide reporter ion by UV-Visible spectroscopy. The rate and yield of disassembly was shown to depend on experimental conditions as well as length of the cleavage vector.

Introduction

We have reported a class of dendritic compounds that can disassemble linearly or geometrically upon application of the appropriate triggering stimulus.[1–6] The potential of these materials lies in using disassembly to tracelessly remove the dendritic components of a system, along with their contributions to said system, such as increased solubility, energy harvesting, or insulating capabilities, and in the nature of dendrimers as covalent assemblages of active species, and using the chemistry of disassembly to release these species into a system.[1] Indeed, both dendritic[7] and polymeric[8–11] disassembling systems, also termed "self-immolative," have been used to engineer controlled and precise degradation as a function inherent to systems for drug loading and release,[12–14] detectors,[15] signal amplifiers,[3,16–18] and degradable nanoparticles[11] or capsules.[19,20]

Compound **A**, an example of a linearly disassembling dendrimer, consists of a trigger group, cleavage vector, and reporter subunit (Fig. 1a). Removal of the trigger group initiates an electronic cascade cleavage through a 1,6-elimination mechanism[21–24] that ultimately liberates the reporter *p*-nitrophenoxide ion. The construction of compounds such as **A** involved the selective O-alkylation of 3,4-dihydroxybenzoate derivatives at several points throughout the synthesis.[2] Due to the near-statistical nature of the alkylation, these steps were low-yielding and resulted in undesireable consumption of advanced dendritic intermediates.

Since the dendritic nature of compounds such as **A** is in the side chains appended to the cleavage vector and is not critical to the disassembly process, we reasoned that linear *non-dendritic analogs of compound* **A** would be easier to prepare and would allow a more rapid evaluation of design parameters such as trigger groups and cleavage pathways. Hence, we sought a more accessible system that would allow rapid entry into compounds that maintained the essence of the disassembly system—a trigger group, cleavage vector, and reporter group—to further study the scope of the disassembly process. Consider compounds **1a–d**, whereby the dendritic framework has been removed from **A** by replacing the side chains with methyl groups, yet the same disassembly components of compound **A** remain. The simpler sidechain should facilitate a much more rapid and higher yielding synthesis of disassembling compounds, relative to compounds similar to **A**, allowing for rapid evaluation of design parameters.

We herein report the use of this simplified approach to disassembling compounds to study different trigger groups and disassembling pathways in model compounds **1–4**, a family of linear analogs of previously prepared disassembling dendrimers.[2] Compounds **1a–d** and **2a–c** contain the *para* cleavage, or 1,6-elimination pathway but differ in the trigger group, either allyl or the photolabile *o*-nitrobenzyl group shown. Compounds **3a–d** and **4a–c** contain the *ortho* cleavage, or 1,4-elimination pathway with the same two triggers. All compounds contained the PNP reporter to assay the disassembly process under the appropriate triggering conditions.

Results and discussion

Synthesis of disassembling oligomers

We adapted the synthetic scheme for linear disassembling dendrimers[2,5] but using vanillin (**5**) as the homologation unit to prepare compounds **1a–d** and **2a–c**. The synthesis of these vanillin-based oligomers was completed in an iterative fashion (Scheme 1). Vanillin (**5**) was treated with K_2CO_3 in the

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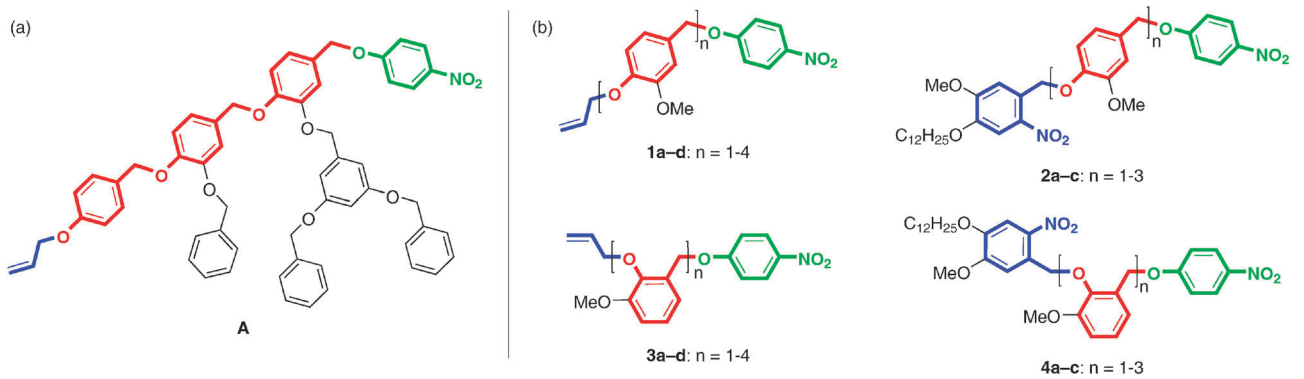
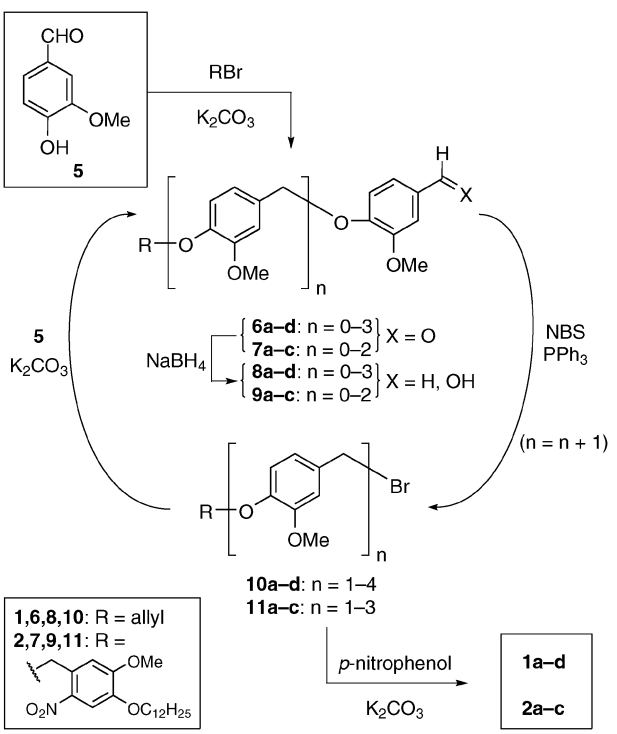


Fig. 1 (a) A second generation linearly disassembling dendrimer. Blue indicates trigger, red indicates cleavage vector, and green indicates reporter moieties. (b) Non-dendritic disassembling oligomers prepared in this study.

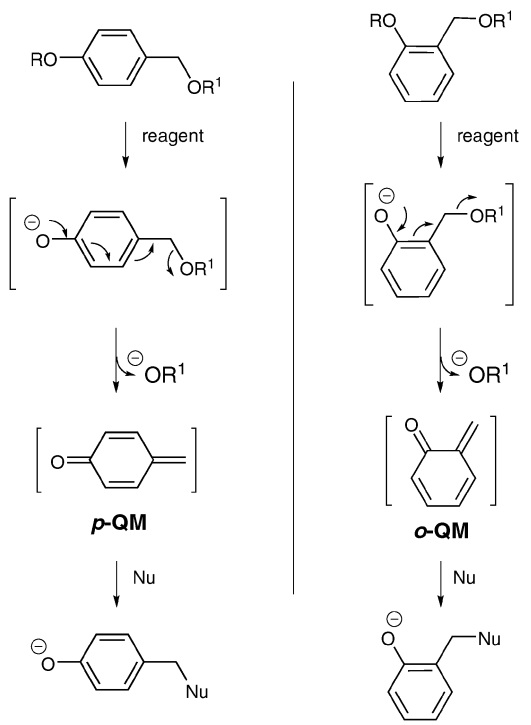
presence of allyl bromide in DMF to afford protected vanillin **6a**. Reduction of aldehyde **6a** with sodium borohydride in THF yielded benzyl alcohol **8a**, which was subsequently brominated to afford **10a**. Treatment of vanillin with bromide **10a** in the presence of K_2CO_3 and 18-crown-6 in refluxing acetone yielded dimer **6b** which was in turn reduced and brominated to yield **8b** and **10b**, respectively. Using the same sequence of steps, trimeric and tetrameric bromide analogs **10c** and **10d** were synthesized. Finally, the reporter group *p*-nitrophenoxide, the same used in our previous studies,[2–5] was affixed to the terminus of the oligmomers under Williamson etherification conditions to provide **1a–d**, zeroth, first, second, and third generation linearly disassembling oligomers.

Phototriggered disassembling oligomers **2a–c** were prepared in a parallel sequence that began with alkylation of vanillin (**5**) with 4-dodecyloxy-5-methoxy-2-nitrobenzyl bromide to install the photolabile trigger. The same sequence of reduction, bromination, and homologation steps provided, *via* intermediates **7a–c**, **9a–c** and **11a–c**, and after installation of the *p*-nitrophenoxide reporter group, zeroth, first, and second generation linearly disassembling oligomers **2a–c**.

Our previously reported linearly disassembling dendrons underwent 1,6-elimination during the cleavage process *via* *p*-quinone methode (***p*-QM**) intermediates (Scheme 2, left).[2,5] The analogous 1,4-elimination proceeding through *o*-quinone methide (***o*-QM**) is an electronically equivalent cleavage pathway that is present is our geometrically disassembling systems,[3,4,6] (Scheme 2, right). Both the 1,4- and 1,6-elimination mechanism have been basic mechanisms of protecting group removal in synthesis, release of enzyme-activated inhibitors, and unmasking of prodrugs.[24–27] The linear oligomer systems presented herein allow the direct study of the 1,4-elimination mechanism in a



Scheme 1 Synthesis of Vanillin-Based Oligomers with Allyl and *o*-Nitrobenzyl Trigger Groups



Scheme 2 (left) Mechanism of linear disassembly by the 1,6-elimination (*para*) pathway, and (right) the 1,4-elimination (*ortho*) pathway.

simplified disassembly system by employing *o*-vanillin (**12**), rather than vanillin (**5**), as the fundamental building block.

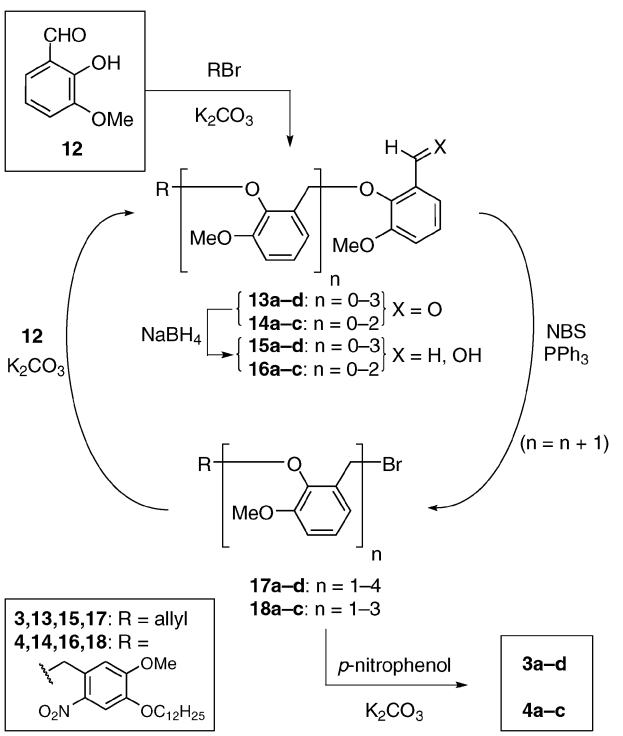
Accordingly, a synthetic sequence identical to that used for the preparation of vanillin-based oligomers **1a–d** and **2a–c** was used for the preparation of *o*-vanillin-based oligomers **3a–d** and **4a–c** but using *o*-vanillin (**12**) as the homologation unit (Scheme 3). Specifically, zeroth through third generation, allyl triggered, linearly disassembling oligomers **3a–d** were prepared *via* aldehydes **13a–d**, alcohols **15a–d**, and bromides **17a–d** in the iterative fashion illustrated.

Phototriggered disassembling oligomers **4a–c** were prepared in a parallel sequence to that of oligomers **2a–c**. Alkylation of *o*-vanillin (**12**) with 4-dodecyloxy-5-methoxy-2-nitrobenzyl bromide to install the photolabile trigger was followed by the same sequence of reduction, bromination, and homologation steps to provide, *via* intermediates **14a–c**, **16a–c** and **18a–c**, zeroth, first, and second generation linearly disassembling oligomers **4a–c**.

All oligomers (**1a–d**, **2a–c**, **3a–d**, and **4a–c**) were thermally stable (acetone, 55 °C, 12 h; solid state, rt, 3 months) and were readily characterized by ^{1}H and ^{13}C NMR, mass spectrometry, and elemental analysis.

Disassembly studies

Study of the disassembly of these compounds provided several advances in our understanding of dendrimer disassembly: (1) disassembly along the *ortho* cleavage pathway proceeded as efficiently as the *para* cleavage pathway, if not more so; (2) addition of MeOH to the disassembly conditions and switching the palladium source to $PdCl_2(PPh_3)_2$ for the allyl trigger dramatically decreased the incubation time for onset of disassembly from minutes to seconds; (3) rate of complete disassembly under these improved conditions was dependent on the cleavage pathway length, with the initial rate approximately proportional to 1/n where n is the number of benzyl groups in the pathway.



Scheme 3 Synthesis of *o*-Vanillin-Based Oligomers with Allyl and *o*-Nitrobenzyl Trigger Groups

Disassembly of allyl triggered oligomers. Vanillin oligomers **1a–d** with allyl triggers were subjected to allyl deprotection conditions.[2,5] Disassembly was initiated by reductive deprotection of the phenyl allyl ether trigger with catalytic $Pd(PPh_3)_4$ and $NaBH_4$ in DMF (Method A). For each disassembly, separate DMF solutions of **1a–d** were treated with mixtures of $NaBH_4$ and $Pd(PPh_3)_4$ in DMF. The reactions were monitored at regular intervals by UV-Vis. The disassembly was followed by the evolution of an absorption band at 431 nm which corresponds to *p*-nitrophenoxide anion in DMF. Each reaction solution was prepared at a concentration of substrate such that complete degradation would yield an absorbance of 1.00 at 431 nm (Fig. 2). Clean disassembly is noted by the evolution of an isosbestic point at 362 nm in each reaction (Fig. 2 inset). Upon evaluation of the absorbance at 431 nm, it was seen that compounds **1a–c** underwent disassembly to >90% completion, while **1d** underwent disassembly to 73% completion, all after an initial incubation period (*vide infra*). *O*-Vanillin-based oligomers **3a–3d** underwent disassembly to >90% completion in all cases, again after an initial incubation period.

The disassembly of the oligomers appeared to proceed *via* the same mechanism as previously described.[2,5] The initial step in the disassembly was the removal of the allyloxy trigger group and formation of phenoxide anion (Scheme 2) that cleaved to form a *p*-quinone methide (***p*-QM**) in the case of **1a–d** and an *o*-quinone methide (***o*-QM**) in the case of **3a–d**. The molar equivalents of quinone methide produced was equal to the number of monomer units in the respective oligomer. Quinone methides were not isolated but were trapped by the presence of hydride to form 2-methoxy-4-methylphenol in the case of **1a–d** and 2-methoxy-6-methylphenol in the case of **3a–d**, the presence of which were verified by NMR and MS.

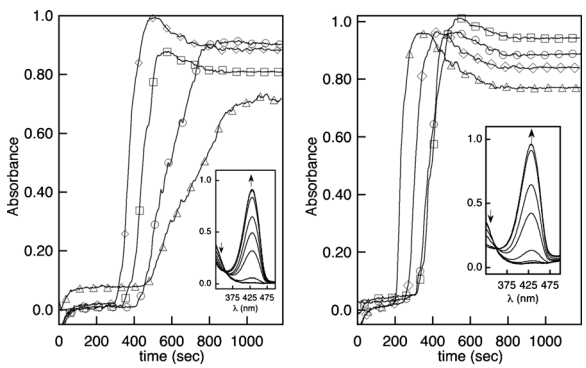


Fig. 2 Disassembly of allyl triggered compounds by Method A conditions ($Pd(PPh_3)_4/NaBH_4$/DMF) as monitored by the evolution of *p*-nitrophenoxide anion at 431 nm over time (symbols every 20 data points). (left) Disassembly of **1a** (○), **1b** (□), **1c** (◇), and **1d** (△). (right) Disassembly of **3a** (○), **3b** (□), **3c** (◇), and **3d** (△). Insets are the UV-Vis spectra recorded during the disassembly of (left) **1a** at t = 295, 369, 442, 516, 590, 664, 737, 811, 848 s and (right) **3a** at t = 184, 221, 258, 295, 332, 369, 405, 442, 516, 553 s.

Upon close examination of each time course plot (Fig. 2) three unusual features were evident. First, disassembly was observed in all cases following the aforementioned initial incubation period. During the incubation period, each system showed a decrease in the absorbance resulting from $Pd(PPh_3)_4$ at 280 nm, as observed in our previous disassembly systems,[2,3] indicating an evolution of the metal species necessary for catalyst activation. The rapid disassembly of the oligomers following the incubation period, indicated by the decrease in the absorbance of the starting material band at 325 nm coincident with the increase in absorbance of the nitrophenoxide band at 431 nm, led us to conclude that the rate-limiting step was the removal of the allyl triggering group.

Second, a slow decrease in absorbance at 431 nm was observed after the initial rise in *p*-nitrophenoxide concentration. This is consistent with protonation of the *p*-nitrophenoxide anion by adventitious protons in the system to give *p*-nitrophenol which has an absorbance maximum at 285 nm. Addition of excess base (K_2CO_3) after completion of disassembly resulted in the restoration of the previous maximum absorbance at 431 nm, supporting this hypothesis.

Third, the apparent rate of disassembly observed in Fig. 2 did not correlate with the length of the oligomers. For example, while the longest vanillin-based oligomer **1d** exhibited the slowest rate of appearance of *p*-nitrophenoxide ion, the shortest vanillin-based oligomer **1a** exhibited the next slowest rate of appearance of *p*-nitrophenoxide ion, rather than the fastest rate as would be expected. While this might suggest a dual mechanism situation as observed by Lee in a similar self-immolative system,[28] this is an unlikely scenario in the case of *para*-linked oligomers because of geometric constraints. The rate of disassembly of the *o*-vanillin oligomers **3a–d** was relatively constant with respect to oligomer length in contrast.

During the course of the current work, we developed modified allyl deprotection conditions (Method B) in an attempt to eliminate the incubation period observed above. We found that by switching the palladium source to $PdCl_2(PPh_3)_2$ and adding MeOH to the reaction mixture, disassembly took place after an initial incubation period of mere seconds following catalyst addition, and we applied these conditions to the compounds reported here as well as others with similar disassembly properties prepared in our laboratories.[5] Smooth disassembly of compounds **1a–d** and **3a–d** was observed in the UV-Vis by the same rapid increase in the absorption of *p*-nitrophenoxide ion (421 nm under these conditions), and this entire spectral evolution of the disassembly process took place within 200 s under the newly modified disassembly conditions (Fig. 3). The final absorbance values observed at 421 nm indicated complete disassembly (*i.e.*, disassembly proceeding to the focal point) of **1a–1d** in 97%, 96%, 95% and 83% yields, respectively. For *o*-vanillin-based compounds **3a–3d**, disassembly yields were 100%, 99%, 83%, and 54%, although this last number is based on the maximum absorbance value obtained at 421 nm for compound **3d** before an as of yet unexplained decrease in absorbance was observed. This decrease was not related to the protonation of *p*-nitrophenoxide ion as observed for the Method A disassembly conditions. Addition of K_2CO_3 did not affect the absorbance at 421 nm. The reason for this decrease is the subject of ongoing investigations.

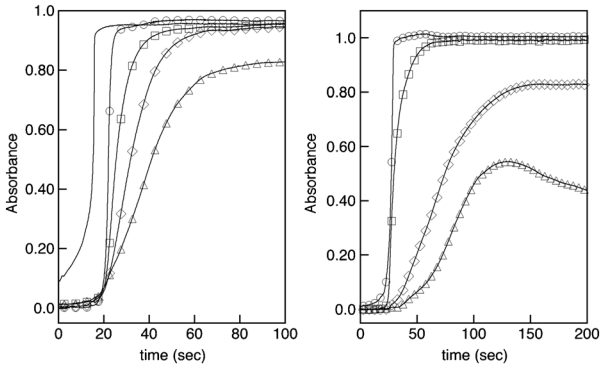


Fig. 3 Disassembly of allyl triggered compounds by Method B conditions ($PdCl_2(PPh_3)_2/NaBH_4$/MeOH/DMF) as monitored by the evolution of *p*-nitrophenoxide anion at 421 nm over time (symbols every 50 data points). (left) Disassembly of *p*-allyloxynitrobenzene (no symbol), **1a** (○), **1b** (□), **1c** (◇), and **1d** (△). (right) Disassembly of **3a** (○), **3b** (□), **3c** (◇), and **3d** (△).

There are two clear benefits to the modified disassembly conditions. First, these conditions are optimal for rapid disassembly. Dissasembly experiments with the previous conditions proceeded to completion within 10 min including a 3–4 min incubation period, whereas disassembly with the modified conditions were completely disassembled within 200 s requiring an incubation period of roughly 20 s. Second, they are sensitive to the generation of dendrimer being disassembled, in that the rate of complete disassembly (release of *p*-nitrophenoxide) under these conditions is dependent on the cleavage pathway length, with the initial rate approximately proportional to 1/n where n is the number of benzyl groups in the pathway.[28] Perhaps not unrelated to this is the clearly more rapid rates of disassembly observed for oligomers **1a–1d** that proceed through a 1,6-elimination pathway relative to the rates of oligomers **3a–3d** that proceed through a 1,4-elimination pathway. This is consistent with previous observations of similarly isolated 1,4- and 1,6-elimination systems.[29,30] Work is currently underway in our laboratory on the kinetics of disassembly and will be reported in due course.

Disassembly of *o*-Nitrobenzyl Triggered Oligomers. Oligomers **2a–c** and **4a–c** that contain the *o*-nitrobenzyl trigger were photolyzed at 314 nm in separate DMF solutions containing the same concentration of $NaBH_4$ as used in the disassembly of allyl trigger oligomers. The $NaBH_4$ was included to cleanly trap the intermediate quinone methide species.[4] The reactions were monitored at regular intervals by UV-Vis following the evolution of absorption band at 431 nm. As with previous experiments, each reaction solution was prepared in a manner so that complete degradation would yield an absorption band of 1.00 at 431 nm. Clean disassembly was noted for photolabile triggered oligomers by the evolution of an isosbestic point at 341 nm during the first 20 min in each reaction (Fig. 4 inset). The corresponding time course plots for each compound indicated that vanillin oligomers **2a** underwent disassembly to 60% completion, **2b** underwent disassembly to 69% completion, and **2c** underwent disassembly to 60% completion. *O*-Vanillin oligomers **4a–c** underwent disassembly in 97%, 89%, and 81% yields, respectively. As was seen in the disassembly of allyl triggered oligomers **1a–d** and **3a–d**, a decrease in absorption at 431 nm

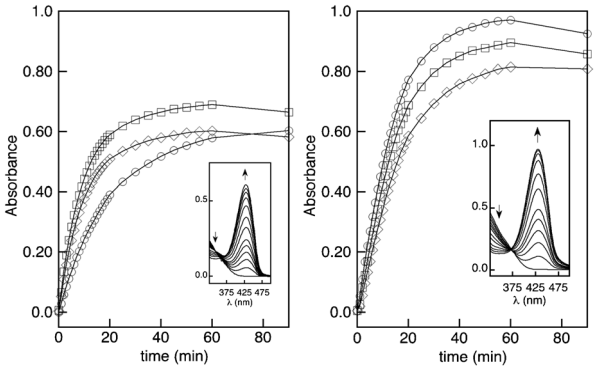
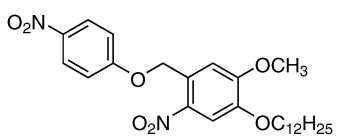


Fig. 4 Disassembly of photolytic triggered compounds as monitored by the evolution of *p*-nitrophenoxide anion at 431 nm over time. (left) Disassembly of **2a** (○), **2b** (□), and **2c** (◇). (right) Disassembly of **4a** (○), **4b** (□), and **4c** (◇). Insets are UV-Vis spectra recorded during the photolytic degradation of **2a** (left) and **4a** (right) in DMF with $NaBH_4$ at t = 0, 2, 4, 6, 8, 10, 15, 20, 30, 40, 50, 60, 90 min.

was observed after an initial maximum was attained. This again was due to protonation of the *p*-nitrophenoxide anion (*vide supra*), which resulted in a decrease in absorbance at 431 nm.

Of note is the higher yields of disassembly observed for the *o*-vanillin oligomers **4a–c** (81–97%) relative to vanillin oligomers **2a–c** (60–69%). We have previously reported the yield of photocleavage of compound **19**, the photolabile trigger directly attached to the *p*-nitrophenoxide reporter, to take place under the same conditions in 80% yield, indicating that non-quantitative reporter ion liberation can arise from the photochemical deprotection process of the *o*-nitrobenzyl trigger rather than from the subsequent disassembly. However, this does not sufficiently explain the high yields for disassembly of **4a–c** which exceed 80%. A change in mechanism for disassembly is not likely. The ^{1}H NMR of the disassembly reactions verified the course of the disassembly process. The photolytic disassembly of oligomers **2a–c** and **4a–c** was monitored by ^{1}H NMR (not shown) by following the disappearance of the benzyl protons (5.50–5.00 ppm) of the oligomers and the concomitant appearance of the methyl protons (2.20–2.10 ppm) of 4-methyl-2-methoxyphenoxide and 6-methyl-2-methoxyphenoxide indicating disassembly according to the mechanism of Scheme 2.



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Conclusions

We have presented a simplified approach to disassembling compounds that allows the more facile study of different trigger groups and disassembling pathways in model compounds **1–4**, a family of linear analogs of previously prepared disassembling dendrimers. Disassembly of **1–4** occurs with a chemically active trigger (allyloxy) and with a photolytically active trigger (*o*-nitrobenzyl) in good to excellent yields. These analogs provide a facile route to the synthesis of new systems for the purpose of testing potential trigger groups and disassembly conditions prior to dendrimer synthesis.

Experimental procedures

General experimental

NMR spectroscopy and mass spectrometry (MS) were obtained using commercially available instrumentation. 4-Dodecyloxy-5-methoxy-2-nitrobenzyl bromide was prepared as detailed in the Electronic Supplementary Information. Tetrahydrofuran (THF) was distilled under N_2 from potassium-benzophenone ketyl. Acetone, DMF, DMSO, and methanol were dried over crushed 3 Å molecular sieves. Potassium carbonate (granular, J. T. Baker) was dried at 100 °C at reduced pressure and stored in a vacuum oven. All needed reagents were purchased from commercial suppliers and used as received. Flash chromatography was performed by the method of Still *et al.*[31] using silica gel (32–63μ, Scientific Adsorbants, Inc., Atlanta GA). Thin-layer chromatography (TLC) was performed on precoated plates (Silica Gel HLO, F-254, Scientific Adsorbants, Inc.).

Procedures for disassembly

Disassembly procedure for allyl trigger (Method A). To 2.0 mL of solution of $NaBH_4$ in DMF (1.0 mg mL^{-1}) in a quartz cuvette was added 20 μL of a solution of substrate in DMF (3 mM) and 20 μL of a solution of $Pd(PPh_3)_4$ in DMF (4.0 mg mL^{-1}). UV spectra were recorded at regular intervals on an Ocean Optics CCD Array Spectrometer.

Disassembly procedure for allyl trigger (Method B). Stock solutions of the substrate (2.17 mM in DMF), KBH_4 (1 mg mL^{-1} in DMF), $PdCl_2(PPh_3)_2$ (1 mg mL^{-1} in DMSO) were prepared. Disassembly trials were performed by adding 30 μL of the stock substrate solution to 1.7 mL of the stock KBH_4 solution in a UV cuvette and shaking vigorously. 100 μL of MeOH was then added to the mixture and again the mixture was mixed thoroughly *via* shaking. The UV instrument was then auto-zeroed to this mixture, after which 20 μL of the stock catalyst solution was added. A final mixing of the solution by shaking the cuvette preceded initiation of the UV time-course experiment. Absorbance data points were collected at 421 nm every 0.1 s.

General disassembly procedure for *o*-nitrobenzyl trigger followed by UV-Vis. To 2.0 mL of solution of $NaBH_4$ in DMF (1.0 mg mL^{-1}) in a quartz cuvette was added 20 μL of a solution of substrate in DMF (3 mM) and 20 μL of a solution of $Pd(PPh_3)_4$ in DMF (4.0 mg mL^{-1}). UV spectra were recorded at regular intervals. Irradiation for UV-Vis experiments was carried out in a quartz cuvette using a Photon Technology International Xenon arc lamp at the appropriate λ_{max} (~315 nm) and an irradiation slit width of 10 nm.

General disassembly procedure for *o*-nitrobenzyl trigger followed by NMR. ^{1}H NMR solutions of substrate in DMF-d_7 were prepared (5 mM) with $NaBH_4$ (2.0 mg). Irradiation in a Kontes Glass Company 5 mm × 8 in NMR tube was carried out with Hg lamps in a Rayonet photoreactor.

Synthesis

4-(4-Allyloxy-3-methoxybenzyloxy)nitrobenzene (1a). A mixture of *p*-nitrophenol (0.501 g, 3.60 mmol), K_2CO_3 (2.04 g, 14.8 mmol), **10a** (0.865 g, 3.36 mmol), 18-crown-6 (85 mg, 0.32 mmol), and acetone (20 mL) was maintained at reflux for 24 h. The mixture was filtered and concentrated. Water (100 mL) was added to the residue and the solution was extracted with CH_2Cl_2 (3 × 50 mL), dried ($MgSO_4$), filtered, concentrated, and recrystallized (1 : 1 EtOH-H_2O) to afford **1a** (1.04 g, 98%) as a tan solid: ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.21 and 7.03 (AA′BB′ pattern J = 7.1 Hz, 4 H); 6.96–6.87 (m, 3 H); 6.14–6.00 (m, 1 H); 5.41 (dd, J = 1.5, 17.2 Hz, 1 H); 5.30 (dd, J = 1.5, 10.4 Hz, 1 H); 5.08 (s, 2 H); 4.64 (dt, J = 1.4, 5.4 Hz, 2 H); 3.90 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ163.7, 149.7, 148.2, 141.6, 133.1, 128.1, 125.9, 120.3, 118.1, 114.8, 113.3, 111.3, 70.8, 69.9, 56.0; MS (FAB$^+$) m/z 315.08 (M^+, $C_{17}H_{17}NO_5$ calcd 315.11). Anal. Calcd for $C_{17}H_{17}NO_5$: C, 64.75; H, 5.43; N, 4.56; Found: C, 64.61; H, 5.66; N, 4.56.

4-(4-(4-Allyloxy-3-methoxybenzyloxy)-3-methoxybenzyloxy)nitrobenzene (1b). A mixture of *p*-nitrophenol (1.52 g, 10.9 mmol), K_2CO_3 (4.27 g, 30.9 mmol), **10b** (4.27 g, 10.8 mmol), 18-crown-6 (94 mg, 0.36 mmol), and acetone (20 mL) was maintained at reflux for 24 h. The mixture was filtered and concentrated. Water (100 mL) was added to the residue and the solution was extracted with CH_2Cl_2 (4 × 25 mL), dried ($MgSO_4$), filtered, concentrated, and recrystallized (1 : 1 EtOH-H_2O) to afford **1b** (4.55 g, 93%) as a tan solid: ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.21 and 7.03 (AA′BB′ pattern J = 7.1 Hz, 4 Hz); 7.00–6.84 (m, 6 H); 6.13–6.00 (m, 1 H); 5.40 (dd, J = 1.5, 17.2 Hz, 1 H); 5.28 (dd, J = 1.5, 10.4 Hz, 1 H); 5.09 (s, 2 H); 5.07 (s, 2 H); 4.61 (dt, J = 1.4, 5.4 Hz, 2 H); 3.90 (s, 3 H); 3.88 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ163.7, 150.0, 149.5, 148.4, 147.8, 141.6, 133.2, 129.7, 128.4, 125.9, 120.3, 119.9, 118.0, 114.8, 114.1, 113.2, 111.4, 111.1, 71.2, 70.7, 69.9, 56.0, 55.9; MS (FAB$^+$) m/z 451.17 (M^+, $C_{25}H_{25}NO_7$ calcd 451.16). Anal. Calcd for $C_{25}H_{25}NO_7$: C, 65.51; H, 5.58; N, 3.10; Found: C, 65.41; H, 5.77; N, 3.19.

4-(4-(4-(4-Allyloxy-3-methoxybenzyloxy)-3-methoxybenzyloxy)-3-methoxybenzyloxy)nitrobenzene (1c). A mixture of *p*-nitrophenol (138 mg, 0.992 mmol), K_2CO_3 (421 mg, 3.05 mmol), **10c** (522 mg, 0.99 mmol), 18-crown-6 (20 mg, 0.07 mmol), and acetone (10 mL) was maintained at reflux for 24 h. The mixture was filtered and concentrated. Water (30 mL) was added to the residue and the solution was extracted with CH_2Cl_2 (4 × 10 mL), dried ($MgSO_4$), filtered, concentrated, and purified by flash chromatography (SiO_2, 6 : 4 hexanes-EtOAc) to afford **1c** (553 mg, 95%) as a tan solid: ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.21 and 7.02 (AA′BB′ pattern J = 7.1 Hz, 4 Hz); 6.99–6.83 (m, 9 H); 6.13–6.00 (m, 1 H); 5.40 (dd, J = 1.5, 17.2 Hz, 1 H); 5.28 (dd, J = 1.5, 10.4 Hz, 1 H); 5.08 (s, 2 H); 5.07 (s, 4 H); 4.61 (dt, J = 1.4, 5.4 Hz, 2 H); 3.90 (s, 3 H); 3.88 (s, 3 H); 3.87 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ163.7, 150.0, 149.9, 149.6, 148.5, 148.0, 147.7, 141.6, 133.3, 130.0, 130.0, 128.4, 125.9, 120.3, 119.9, 119.9, 118.0, 114.8, 114.2, 114.1, 113.3, 111.4, 111.2, 111.1, 71.2, 71.2, 70.8, 69.9, 56.0, 56.0, 55.9; MS (FAB$^+$) m/z 587.29 (M^+, $C_{33}H_{33}NO_9$ calcd 587.21). Anal. Calcd for $C_{33}H_{33}NO_9$: C, 67.45; H, 5.66; N, 2.38; Found: C, 67.45; H, 6.06; N, 2.38.

4-(4-(4-(4-(4-Allyloxy-3-methoxybenzyloxy)-3-methoxybenzyloxy)-3-methoxybenzyloxy)-3-methoxybenzyloxy)nitrobenzene (1d). A mixture of *p*-nitrophenol (0.90 g, 0.65 mmol), K_2CO_3 (0.274 g, 1.98 mmol), **10d** (0.42 g, 0.63 mmol), 18-crown-6 (35 mg, 0.13 mmol), and acetone (15 mL) was maintained at reflux for 24 h. The mixture was filtered and concentrated. Water (30 mL) was added to the residue and the solution was extracted with CH_2Cl_2 (4 × 10 mL), dried ($MgSO_4$), filtered, concentrated, and purified by flash chromatography (SiO_2, 6 : 4 hexanes-EtOAc) to afford **1d** (1.04 g, 98%) as a tan solid: ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.21 and 7.03 (AA′BB′ pattern J = 7.1 Hz, 4 H); 7.00–6.83 (m, 12 H); 6.13–6.00 (m, 1 H); 5.40 (dd, J = 1.5, 17.2 Hz, 1 H); 5.28 (dd, J = 1.5, 10.4 Hz, 1 H); 5.08 (s, 6 H); 5.07 (s, 2 H); 4.61 (dt, J = 1.4, 5.4 Hz, 2 H); 3.89 (s, 6 H); 3.88 (s, 3 H); 3.87 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 163.7, 150.0, 149.9, 147.9, 147.7, 141.6, 133.3, 130.3, 130.0, 128.4, 125.9, 120.3, 119.9, 119.9, 119.9, 118.0, 114.8, 114.2, 114.1, 113.2, 111.4, 111.2, 111.1, 71.3, 71.2, 70.8, 70.1, 69.9, 56.0, 56.0, 55.9; MS (FAB$^+$) m/z 723.43 (M^+, $C_{41}H_{41}NO_{11}$ calcd 723.27). Anal. Calcd for $C_{41}H_{41}NO_{11}$: C, 68.04; H, 5.71; N, 1.94; Found: C, 67.69; H, 6.10; N, 2.16.

4-(4-(2-Nitro-4-dodecyloxy-5-methoxybenzyloxy)-3-methoxybenzyloxy)-nitrobenzene (2a). A mixture of *p*-nitrophenol (0.12 g, 0.87 mmol), K_2CO_3 (0.36 g, 2.6 mmol), **11a** (0.45 g, 0.80 mmol), and DMF (10 mL) was maintained at 35 °C for 24 h. Water (50 mL) was added and the solution was extracted with CH_2Cl_2 (5 × 15 mL), dried ($MgSO_4$), filtered, concentrated, and purified by flash chromatography (SiO_2, 100% CH_2Cl_2) to afford **2a** (0.31 g, 63%) as a pale yellow solid: ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.22 and 7.02 (AA′BB′ pattern J = 7.1 Hz, 4 H); 7.75 (s, 1 H); 7.47 (s, 1 H); 7.00–6.83 (m, 3 H); 5.57 (s, 2 H); 5.09 (s, 2 H); 4.08 (t, J = 6.8 Hz, 2 H); 3.95 (s, 3 H); 3.93 (s, 3 H); 1.87 (quintet, J = 7.9 Hz, 2 H); 1.50–1.26 (m, 18 H); 0.88 (t, J = 6.2 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 163.6, 154.3, 150.3, 147.9, 147.4, 141.7, 138.9, 129.2, 129.2, 125.9, 120.5, 114.8, 114.5, 111.5, 109.6, 109.0, 70.6, 69.5, 68.5, 56.3, 56.1, 31.9, 29.65, 29.63, 29.57, 29.52, 29.3, 28.9, 25.9, 22.7, 14.1; MS (FAB$^+$) m/z 624.35 (M^+, $C_{34}H_{44}N_2O_9$ calcd 624.30). Anal. Calcd for $C_{34}H_{44}N_2O_9$: C, 65.37; H, 7.10; N, 4.48; Found: C, 64.98; H, 7.24; N, 4.58.

4-(4-(4-(2-Nitro-4-dodecyloxy-5-methoxybenzyloxy)-3-methoxybenzyloxy)-3-methoxybenzyloxy)-nitrobenzene (2b). A mixture of *p*-nitrophenol (73 mg, 0.53 mmol), K_2CO_3 (0.30 g, 2.2 mmol), **11b** (0.34 g, 0.49 mmol), and DMF (5 mL) was maintained at 35 °C for 24 h. Water (50 mL) was added and the solution was extracted with CH_2Cl_2 (5 × 20 mL), dried ($MgSO_4$), filtered, concentrated, and purified by flash chromatography (SiO_2, 7 : 3 hexanes-EtOAc) to afford **2b** (0.31 g, 81%) as a pale yellow solid: ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.22 and 7.04 (AA′BB′ pattern J = 7.1 Hz, 4 H); 7.75 (s, 1 H); 7.46 (s, 1 H); 7.01–6.87 (m, 6 H); 5.55 (s, 2 H); 5.10 (s, 2 H); 5.07 (s, 2 H) 4.08 (t, J = 6.8 Hz, 2 H); 3.94 (s, 3 H); 3.91 (s, 3 H); 3.90 (s, 3 H); 1.87 (quintet, J = 7.9 Hz, 2 H); 1.50–1.26 (m, 18 H); 0.88 (t, J = 6.2 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 163.7, 154.3, 150.0, 149.9, 148.4, 147.4, 147.3, 141.6, 138.8, 130.8, 129.5, 128.5, 125.9, 120.3, 120.1, 114.8, 114.4, 114.1, 111.4, 111.3, 109.6, 109.0, 71.1, 70.7, 69.5, 68.5, 56.3, 56.0, 56.0, 31.9, 29.65, 29.63, 29.5, 29.3, 28.9, 25.9, 22.7, 14.1; MS (FAB$^+$) m/z 760.42 (M^+, $C_{42}H_{52}N_2O_{11}$ calcd 760.36). Anal. Calcd for $C_{42}H_{52}N_2O_{11}$: C, 66.30; H, 6.59; N, 3.68; Found: C, 66.30; H, 6.59; N, 3.68.

4-(4-(4-(4-(2-Nitro-4-dodecyloxy-5-methoxybenzyloxy)-3-methoxybenzyloxy)-3-methoxybenzyloxy)-3-methoxybenzyloxy)-nitrobenzene (2c). A mixture of *p*-nitrophenol (49 mg, 0.35 mmol), K_2CO_3 (0.16 g, 1.2 mmol), **11c** (0.26 g, 0.31 mmol), and DMF (5 mL) was maintained at 35 °C for 24 h. Water (50 mL) was added and the solution was extracted with CH_2Cl_2 (4 × 10 mL), dried ($MgSO_4$), filtered, concentrated, and purified by flash chromatography (SiO_2, 7 : 3 hexanes-EtOAc gradient to 100% CH_2Cl_2) to afford **2c** (0.17 g, 61%) as a pale yellow solid: ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.21 and 7.04 (AA′BB′ pattern J = 7.1 Hz, 4 H); 7.75 (s, 1 H); 7.46 (s, 1 H); 7.01–6.88 (m, 9 H); 5.55 (s, 2 H); 5.08 (s, 4 H); 5.07 (s, 2 H) 4.08 (t, J = 6.8 Hz, 2 H); 3.94 (s, 3 H); 3.91 (s, 3 H); 3.90 (s, 3 H); 3.88 (s, 3 H); 1.87 (quintet, J = 7.9 Hz, 2 H); 1.50–1.26 (m, 18 H); 0.88 (t, J = 6.2 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 163.7, 154.4, 150.0, 149.9, 149.8, 148.4, 147.9, 147.4, 147.3, 138.8, 131.0, 130.1, 129.5, 128.4, 125.9, 120.3, 120.1, 119.9, 114.8, 114.7, 114.3, 114.2, 114.1, 111.4, 111.3, 111.2, 109.6, 109.9, 71.2, 71.1, 70.8, 69.5, 68.5, 56.3, 56.0, 56.0, 56.0, 31.9, 29.65, 29.63, 29.57, 29.52, 29.3, 29.2, 28.9, 25.9, 22.7, 14.1; MS (FAB$^+$) m/z 896.50 (M^+, $C_{50}H_{60}N_2O_{13}$ calcd 896.41). Anal. Calcd for $C_{50}H_{60}N_2O_{13}$: C, 66.95; H, 6.74; N, 3.12; Found: C, 67.06; H, 7.13; N, 3.18.

4-(2-Allyloxy-3-methoxybenzyloxy)-nitrobenzene (3a). A mixture of *p*-nitrophenol (281 mg, 2.02 mmol), K_2CO_3 (0.857 g, 6.20 mmol), **17a** (0.513 g, 1.99 mmol), 18-crown-6 (36 mg, 0.13 mmol), and acetone (5 mL) was maintained at reflux for 24 h after which the mixture was filtered and concentrated. Water (20 mL) was added and the solution was extracted with CH_2Cl_2 (3 × 10 mL), dried ($MgSO_4$), filtered, concentrated, and purified by flash chromatography (SiO_2, 100% CH_2Cl_2) to afford **3a** (0.62 g, 99%) as an orange oil: ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.20 (AA′BB′ pattern J = 7.1 Hz, 2 H); 7.12–6.92 (m, 5 H); 6.10–5.97 (m, 1 H); 5.33 (dd, J = 1.5, 17.2 Hz, 1 H); 5.22–5.17 (m, 3 H); 4.58 (dt, J = 1.4, 5.4 Hz, 2 H); 3.89 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ163.7, 152.6, 145.7, 141.5, 133.9, 129.5, 125.9, 124.3, 120.7, 118.0, 114.8, 112.6, 74.2, 66.0, 55.8; MS (FAB$^+$) m/z 315.15 (M^+, $C_{17}H_{17}NO_5$ calcd 315.11). Anal. Calcd for $C_{17}H_{17}NO_5$: C, 64.75; H, 5.43; N, 4.44; Found: C, 64.37; H, 5.71; N, 4.54.

4-(2-(2-Allyloxy-3-methoxybenzyloxy)-3-methoxybenzyloxy)-nitrobenzene (3b). A mixture of *p*-nitrophenol (0.40 g, 2.8 mmol), K_2CO_3 (1.07 g, 7.74 mmol), **17b** (1.11 g, 2.83 mmol), 18-crown-6 (34 mg, 0.13 mmol), and acetone (10 mL) was maintained at reflux for 5 h after which the mixture was filtered and concentrated. Water (50 mL) was added and the solution was extracted with CH_2Cl_2 (4 × 5 mL), dried ($MgSO_4$), filtered, concentrated, and purified by flash chromatography (SiO_2, 8 : 2 hexanes-EtOAc) to afford **3b** (1.03 g, 81%) as a colorless solid: ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.12 (AA′BB′ pattern J = 7.1 Hz, 2 Hz); 7.11–6.84 (m, 8 H); 6.10–5.96 (m, 1 H); 5.29 (dd, J = 1.5, 17.2 Hz, 1 H); 5.22–5.12 (m, 3 H); 5.06 (s, 2 H); 4.46 (dt, J = 1.4, 5.4 Hz, 2 H); 3.92 (s, 3 H); 3.84 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ163.7, 152.7, 152.5, 146.0, 145.6, 141.3, 134.2, 131.4, 130.0, 125.7, 124.3, 124.0, 121.9, 120.2, 117.3, 114.8, 112.4, 112.4, 74.1, 70.1, 65.8, 55.8, 55.7; MS (FAB$^+$) m/z 451.16 (M^+, $C_{25}H_{25}NO_7$ calcd 451.16). Anal. Calcd for $C_{25}H_{25}NO_7$: C, 65.51 H, 5.58; N, 3.10; Found: C, 65.48; H, 5.70; N, 3.27.

4-(2-(2-(2-Allyloxy-3-methoxybenzyloxy)-3-methoxybenzyloxy)-3-methoxybenzyloxy)-nitrobenzene (3c). A mixture of *p*-nitrophenol (0.29 g, 2.1 mmol), K_2CO_3 (0.98 g, 7.1 mmol), **17c** (1.08 g, 2.04 mmol), 18-crown-6 (31 mg, 0.12 mmol), and acetone (10 mL) was maintained at reflux for 8 h after which the mixture was filtered and concentrated. Water (30 mL) was added and the solution was extracted with CH_2Cl_2 (4 × 5 mL), dried ($MgSO_4$), filtered, concentrated, and purified by flash chromatography (SiO_2, 7 : 3 hexanes-EtOAc) to afford **3c** (1.01 g, 84%) as a colorless oil: ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.06 (AA′BB′ pattern J = 7.1 Hz, 2 Hz); 7.10–6.81 (m, 11 H); 6.05–5.93 (m, 1 H); 5.26 (dd, J = 1.5, 17.2 Hz, 1 H); 5.12–5.07 (m, 5 H); 5.02 (s, 2 H); 4.44 (dt, J = 1.4, 5.4 Hz, 2 H); 3.85 (s, 3 H); 3.84 (s, 3 H); 3.83 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ163.7, 152.7, 152.7, 152.4, 146.2, 145.5, 134.3, 131.9, 131.7, 130.1, 125.7, 124.2, 124.0, 123.9, 121.9, 121.2, 120.1, 117.1, 114.7, 114.7, 112.5, 112.2, 111.9, 74.0, 70.0, 69.9, 65.8, 55.8, 55.7, 55.7; MS (FAB$^+$) m/z 587.36 (M^+, $C_{33}H_{33}NO_9$ calcd 587.21). Anal. Calcd for $C_{33}H_{33}NO_9$: C, 67.45; H, 5.66; N, 2.38; Found: C, 67.46; H, 6.00; N, 2.36.

4-(2-(2-(2-(2-Allyloxy-3-methoxybenzyloxy)-3-methoxybenzyloxy)-3-methoxybenzyloxy)-3-methoxybenzyloxy)-nitrobenzene (3d). A mixture of *p*-nitrophenol (0.82 g, 5.1 mmol), K_2CO_3 (2.52 g, 18.2 mmol), **17d** (3.91 g, 5.88 mmol), 18-crown-6 (78 mg, 0.29 mmol), and acetone (20 mL) was maintained at reflux for 8 h after which the mixture was filtered and concentrated. Water (100 mL) was added and the solution was extracted with CH_2Cl_2 (4 × 25 mL), dried ($MgSO_4$), filtered, concentrated, and purified by flash chromatography (SiO_2, 7 : 3 hexanes-EtOAc) to afford **3d** (4.06 g, 95%) as a colorless oil: ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.03 (AA′BB′ pattern J = 7.1 Hz); 7.11–6.78 (m, 14 H); 6.05–5.93 (m, 1 H); 5.24 (dd, J = 1.5, 17.2 Hz, 1 H); 5.10–5.03 (m, 7 H); 4.98 (s, 2 H); 4.42 (dt, J = 1.4, 5.4 Hz, 2 H); 3.84 (s, 3 H); 3.82 (s, 3 H); 3.76 (s, 3 H); 3.75 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 163.7, 152.6, 152.5, 152.3, 146.3, 145.5, 145.5, 145.4, 141.2, 134.3, 132.2, 132.0, 131.5, 130.1, 125.7, 124.1, 124.0, 123.9, 123.8, 121.9, 121.2, 120.9, 120.0, 117.1, 114.7, 112.4, 112.2, 111.9, 111.8, 74.0, 70.0, 69.9, 69.6, 65.7, 55.7, 55.7, 55.6; MS (FAB$^+$) m/z 723.43 (M^+, $C_{41}H_{41}NO_{11}$ calcd 723.27). Anal. Calcd for $C_{41}H_{41}NO_{11}$: C, 68.04; H, 5.71; N, 1.94; Found: C, 67.65; H, 6.04; N, 2.29.

4-(2-(2-Nitro-4-dodecyloxy-5-methoxybenzyloxy)-3-methoxybenzyloxy)-nitrobenzene (4a). A mixture of *p*-nitrophenol (66 mg, 0.47 mmol), K_2CO_3 (0.18 g, 1.3 mmol), **18a** (0.24 g, 0.45 mmol), and DMF (4 mL) was maintained at ambient temperature for 24 h. Water (100 mL) was added and the solution was extracted with CH_2Cl_2 (4 × 25 mL), washed with H_2O (100 mL), brine (100 mL), dried ($MgSO_4$), filtered, and concentrated. Flash chromatography (SiO_2, 7 : 3 hexanes-CH_2Cl_2) afforded **4a** (0.21 g, 75%) as a yellow solid: ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.14 and 6.93 (AA′BB′ pattern J = 7.1 Hz, 4 H); 7.66 (s, 1 H); 7.45 (s, 1 H); 7.16–6.99 (m, 3 H); 5.45 (s, 2 H); 5.16 (s, 2 H); 4.03 (t, J = 6.8 Hz, 2 H); 3.88 (s, 3 H); 3.87 (s, 3 H); 1.88 (quintet, J = 7.9 Hz, 2 H); 1.50–1.26 (m, 18 H); 0.88 (t, J = 6.2 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 163.6 154.0, 152.8, 147.3, 146.0, 141.5, 138.9, 129.5, 129.4, 125.8, 124.9, 121.4, 114.5, 113.0, 109.7, 108.7, 71.8, 69.5, 66.3, 56.3, 55.8, 31.9, 29.65, 29.63, 29.57, 29.52, 29.3, 28.9, 25.9, 22.7, 14.1; MS (FAB$^+$) m/z 624.37 (M^+, $C_{34}H_{44}N_2O_9$ calcd 624.30). Anal. Calcd for $C_{34}H_{44}N_2O_9$: C, 65.37; H, 7.10; N, 4.48; Found: C, 65.51; H, 7.36; N, 4.61.

4-(2-(2-(2-Nitro-4-dodecyloxy-5-methoxybenzyloxy)-3-methoxybenzyloxy)-3-methoxybenzyloxy)-nitrobenzene (4b). A mixture of

p-nitrophenol (0.10 g, 0.73 mmol), K_2CO_3 (0.41 g, 3.0 mmol), **18b** (0.49 g, 0.70 mmol), and DMF (5 mL) was maintained at ambient temperature for 24 h. Water (30 mL) was added and the solution was extracted with CH_2Cl_2 (4 × 10 mL), washed with H_2O (2 × 30 mL), brine (50 mL), dried ($MgSO_4$), filtered, and concentrated. Flash chromatography (SiO_2, 8 : 2 hexanes-EtOAc) afforded **4b** (0.35 g, 66%) as a yellow solid: ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.07 and 6.80 (AA′BB′ pattern J = 7.1 Hz, 4 H); 7.69 (s, 1 H); 7.59 (s, 1 H); 7.06–6.88 (m, 6 H); 5.30 (s, 2 H); 5.18 (s, 2 H); 4.95 (s, 2 H); 4.08 (t, J = 6.8 Hz, 2 H); 3.92 (s, 3 H); 3.80 (s, 3 H); 3.76 (s, 3 H); 1.88 (quintet, J = 7.9 Hz, 2 H); 1.50–1.26 (m, 18 H); 0.88 (t, J = 6.2 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 163.6 154.1, 152.6, 152.5, 147.0, 145.9, 145.4, 141.3, 138.5, 131.3, 130.3, 129.9, 125.7, 124.6, 124.3, 122.4, 120.4, 114.6, 112.5, 112.3, 109.5, 108.7, 71.6, 70.1, 69.5, 65.8, 56.4, 55.7, 55.7 31.9, 29.65, 29.63, 29.57, 29.52, 29.4, 29.3, 28.9, 25.9, 22.7, 14.1; MS (FAB$^+$) m/z 759.49 (M-H$^+$). Anal. Calcd for $C_{42}H_{52}N_2O_{11}$: C, 66.30; H, 6.89; N, 3.68; Found: C, 66.06; H, 7.22; N, 3.92.

4-(2-(2-(2-(2-Nitro-4-dodecyloxy-5-methoxybenzyloxy)-3-methoxybenzyloxy)-3-methoxybenzyloxy)-3-methoxybenzyloxy)-nitrobenzene (4c). A mixture of *p*-nitrophenol (0.42 g, 3.0 mmol), K_2CO_3 (1.60 g, 11.6 mmol), **18c** (2.49 g, 2.97 mmol), and DMF (20 mL) was maintained at ambient temperature for 24 h. Water (100 mL) was added and the solution was extracted with CH_2Cl_2 (4 × 25 mL), washed with H_2O (100 mL), brine (100 mL), dried ($MgSO_4$), filtered, and concentrated. Flash chromatography (SiO_2, 8 : 2 hexanes-EtOAc) afforded **4c** (2.42 g, 91%) as a yellow oil: ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.05 and 6.80 (AA′BB′ pattern J = 7.1 Hz, 4 H); 7.66 (s, 1 H); 7.56 (s, 1 H); 7.11–6.86 (m, 9 H); 5.30 (s, 2 H); 5.11 (s, 2 H); 5.02 (s, 2 H); 4.94 (s, 2 H); 4.06 (t, J = 6.8 Hz, 2 H); 3.86 (s, 3 H); 3.81 (s, 3 H); 3.80 (s, 3 H); 3.70 (s, 3 H); 1.88 (quintet, J = 7.9 Hz, 2 H); 1.50–1.26 (m, 18 H); 0.88 (t, J = 6.2 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 163.7, 154.1, 152.6, 152.5, 152.4, 146.9, 146.0, 145.4, 145.3, 141.3, 138.4, 131.8, 131.6, 130.5, 129.9, 125.7, 124.5, 124.2, 124.0, 121.9, 121.5, 120.0114.7, 112.4, 112.2, 112.0, 109.4, 108.7, 71.4, 70.0, 69.9, 69.5, 65.7, 56.3, 55.7, 55.7, 55.6, 31.9, 29.65, 29.63, 29.57, 29.52, 29.4, 29.3, 28.9, 25.9, 22.7, 14.1; MS (FAB$^+$) m/z 895.58 (M-H$^+$). Anal. Calcd for $C_{50}H_{60}N_2O_{13}$: C, 66.95; H, 6.74; N, 3.12; Found: C, 67.11; H, 7.10; N, 3.23.

4-Allyloxy-3-methoxybenzaldehyde (6a). A mixture of vanillin (102 g, 0.67 mol), K_2CO_3 (50.2 g, 0.36 mol), allyl bromide (82.5 g, 0.68 mol), and DMF (600 mL) was maintained at 70 °C for 24 h after which the mixture was filtered and concentrated to afford a dark oil. Water (300 mL) was added and the solution was extracted with CH_2Cl_2 (4 × 50 mL), washed with brine (2 × 200 mL), dried ($MgSO_4$), filtered, and concentrated to afford **6a** as a dark oil (123 g, 96%): ^{1}H NMR (250 MHz, $CDCl_3$) δ 9.85 (s, 1 H); 7.45–7.41 (m, 2 H); 6.98 (dd, J = 2.0 Hz, 1 H); 6.17–6.01 (m, 1 H); 5.44 (dd, J = 1.4, 17.2 Hz, 1 H); 5.34 (dd, J = 1.4, 10.5 Hz, 1 H); 4.71 (dt, J = 1.5, 5.4 Hz, 2 H); 3.94 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 190.7, 153.4, 149.8, 132.1, 130.1, 126.5, 118.6, 111.8, 109.2, 69.7, 55.9; MS (FAB$^+$) m/z 192.16 (M$^+$, $C_{11}H_{12}O_3$ calcd 192.08).

4-(4-Allyloxy-3-methoxybenzyloxy)-3-methoxybenzaldehyde (6b). A mixture of vanillin (8.19 g, 53.8 mmol), K_2CO_3 (22.6 g, 0.163 mmol), **10a** (13.8 g, 53.7 mmol), 18-crown-6 (0.36 g, 1.4 mmol), and acetone (100 mL) was maintained at reflux for 24 h. The mixture was filtered and concentrated. Water (100 mL) was added to the residue and the solution was extracted with CH_2Cl_2 (4 × 25 mL), dried ($MgSO_4$), filtered, concentrated, and recrystallized in EtOAc to afford **6b** (10.8 g, 62%) as a colorless solid: ^{1}H NMR (250 MHz, $CDCl_3$) δ 9.84 (s, 1 H); 7.43–7.38 (m, 2 H); 7.03–6.85 (m, 4 H); 6.14–6.00 (m, 1 H); 5.40 (dd, J = 1.5, 17.2 Hz, 1 H); 5.29 (dd, J = 1.5, 10.5 Hz, 1 H); 4.62 (dt, J = 1.5, 5.4 Hz, 2 H); 3.94 (s, 3 H); 3.89 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 190.8, 153.6, 150.0, 149.6, 148.0, 133.1, 130.2, 128.7, 126.5, 120.0, 118.0, 113.2, 112.4, 111.0, 109.2, 71.0, 69.8, 56.0, 55.9; MS (FAB$^+$) m/z 328.13 (M$^+$, $C_{19}H_{20}O_5$ calcd 328.13).

4-(4-(4-Allyloxy-3-methoxybenzyloxy)-3-methoxybenzyloxy)-3-methoxybenzaldehyde (6c). A mixture of vanillin (5.23 g, 34.4 mmol), K_2CO_3 (17.5 g, 126 mmol), **10b** (13.5 g, 34.3 mmol), 18-crown-6 (0.14 g, 0.52 mmol), and acetone (100 mL) was maintained at reflux for 24 h. The mixture was filtered and concentrated. Water (100 mL) was added to the residue and the solution was extracted with CH_2Cl_2 (4 × 25 mL), dried ($MgSO_4$), filtered, concentrated, and purified by flash chromatography (SiO_2, 5 : 4 : 1 CH_2Cl_2-hexanes-Et_2O) to afford **6c** (5.38 g, 34%) as a colorless solid: ^{1}H NMR (250 MHz, $CDCl_3$) δ 9.84 (s, 1 H); 7.43–7.38 (m, 2 H); 7.03–6.83 (m, 7 H); 6.13–6.00 (m, 1 H); 5.40 (dd, J = 1.5, 17.2 Hz, 1 H); 5.28 (dd, J = 1.5, 10.5 Hz, 1 H); 5.16 (s, 2 H); 5.08 (s, 2 H); 4.61 (dt, J = 1.4, 5.4 Hz, 2 H); 3.94 (s, 3 H); 3.88 (s, 3 H); 3.87 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 190.9, 153.7, 150.1, 150.0, 149.6, 148.2, 147.8, 133.3, 130.0, 129.9, 129.0, 126.6, 120.0, 119.9, 118.0, 114.2, 113.3, 112.5, 111.2, 109.3, 71.2, 71.0, 69.9, 56.0, 56.0, 55.9; MS (FAB$^+$) m/z 465.45 (M + H$^+$).

4-(4-(4-(4-Allyloxy-3-methoxybenzyloxy)-3-methoxybenzyloxy)-3-methoxybenzyloxy)-3-methoxybenzaldehyde (6d). A mixture of vanillin (0.745 g, 4.89 mmol), K_2CO_3 (2.48 g, 18.0 mmol), **10c** (2.58 g, 4.88 mmol), 18-crown-6 (0.22 g, 0.82 mmol), and acetone (100 mL) was maintained at reflux for 2 days. The mixture was filtered and concentrated. Water (100 mL) was added to the residue and the solution was extracted with CH_2Cl_2 (4 × 25 mL), dried ($MgSO_4$), filtered, concentrated, and purified by flash chromatography (SiO_2, 100% CH_2Cl_2 gradient to 100% EtOAc gradient to 100% MeOH) to afford **6d** (1.84 g, 63%) as a colorless solid: ^{1}H NMR (250 MHz, $CDCl_3$) δ 9.84 (s, 1 H); 7.43–7.38 (m, 2 H); 7.03–6.81 (m, 10 H); 6.15–6.00 (m, 1 H); 5.40 (dd, J = 1.5, 17.2 Hz, 1 H); 5.28 (dd, J = 1.5, 10.5 Hz, 1 H); 5.16 (s, 2 H); 5.11 (s, 2 H); 5.07 (s, 2 H); 4.61 (dt, J = 1.4, 5.4 Hz, 2 H); 3.94 (s, 3 H); 3.91 (s, 3 H); 3.88 (s, 3 H); 3.87 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 190.8, 153.6, 150.0, 149.9, 149.8, 149.5, 148.2, 147.7, 133.3, 130.3, 130.1, 130.0, 129.0, 126.5, 120.0, 119.9, 119.9, 117.9, 114.2, 114.1, 113.2, 112.4, 111.2, 111.2, 111.1, 109.3, 71.2, 71.2, 71.0, 69.9, 56.0, 56.0, 55.9, 55.9; MS (FAB$^+$) m/z 600.56 (M$^+$, $C_{35}H_{36}O_9$ calcd 600.23).

4-(2-Nitro-4-dodecyloxy-5-methoxybenzyloxy)-3-methoxybenzyaldehyde (7a). A mixture of vanillin (4.48 g, 29.4 mmol), K_2CO_3 (12.3 g, 88.8 mmol), 4-dodecyloxy-5-methoxy-2-nitrobenzyl bromide (12.7 g, 29.5 mmol), 18-crown-6 (0.29 g, 1.1 mmol), and acetone (30 mL) was maintained at ambient temperature for 5 h. The mixture was filtered and concentrated. Water (200 mL) was added to the residue and the solution was extracted with CH_2Cl_2

(4 × 50 mL), dried ($MgSO_4$), filtered, concentrated, and purified by flash chromatography (SiO_2, 8 : 2 hexanes-EtOAc) to afford **7a** (11.6 g, 78%) as a red solid: ^{1}H NMR (250 MHz, $CDCl_3$) δ 9.87 (s, 1 H); 7.77 (s, 1 H); 7.47–7.43 (m, 3 H); 7.05 (d, J = 8.0 Hz, 1 H); 5.63 (s, 2 H); 4.09 (t, J = 6.8 Hz, 2 H); 3.98 (s, 3 H); 3.95 (s, 3 H); 1.88 (quintet, J = 7.9 Hz, 2 H); 1.50–1.26 (m, 18 H); 0.88 (t, J = 6.2 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 190.8, 154.4, 152.9, 150.1, 147.5, 138.8, 130.8, 128.1, 126.7, 112.7, 109.4, 109.4, 109.0, 69.5, 68.0, 56.3, 56.1, 31.9, 29.62, 29.60, 29.55, 29.50, 29.3, 28.8, 25.8, 22.7, 14.1; MS (FAB$^+$) m/z 501.57 (M^+, $C_{28}H_{39}NO_7$ calcd 501.27).

4-(4-(2-Nitro-4-dodecyloxy-5-methoxybenzyloxy)-3-methoxybenzyloxy)-3-methoxybenzaldehyde (7b). A mixture of vanillin (1.19 g, 7.80 mmol), K_2CO_3 (3.05 g, 22.1 mmol), **11a** (4.40 g, 7.77 mmol), 18-crown-6 (0.18 g, 0.69 mmol), and acetone (100 mL) was maintained at ambient temperature for 24 h after which the mixture was concentrated. Water (100 mL) was added to the residue and the solution was extracted with CH_2Cl_2 (4 × 20 mL), dried ($MgSO_4$), filtered, concentrated, and recrystallized (95 : 5 hexanes-CH_2Cl_2) to afford **7b** (4.52 g, 91%) as a pale yellow solid: ^{1}H NMR (250 MHz, $CDCl_3$) δ 9.85 (s, 1 H); 7.75 (s, 1 H); 7.46–7.38 (m, 3 H); 7.05–6.89 (m, 4 H); 5.56 (s, 2 H); 5.18 (s, 2 H); 4.08 (t, J = 6.8 Hz, 2 H); 3.95 (s, 3 H); 3.94 (s, 3 H); 3.91 (s, 3 H); 1.88 (quintet, J = 7.9 Hz, 2 H); 1.50–1.26 (m, 18 H); 0.88 (t, J = 6.2 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 190.8, 154.3, 153.5, 150.1, 150.0, 149.8, 147.7, 147.3, 138.8, 130.3, 129.8, 129.3, 126.5, 120.2, 114.4, 112.5, 111.3, 109.6, 109.3, 109.0, 70.9, 69.5, 68.5, 56.3, 56.1, 56.0, 31.9, 29.65, 29.63, 29.57, 29.52, 29.3, 28.9, 25.9, 22.7, 14.1; MS (FAB$^+$) m/z 637.64 (M^+, $C_{36}H_{47}NO_9$ calcd 637.32).

4-(4-(4-(2-Nitro-4-dodecyloxy-5-methoxybenzyloxy)-3-methoxybenzyloxy)-3-methoxybenzyloxy)-3-methoxybenzaldehyde (7c). A mixture of vanillin (0.62 g, 4.1 mmol), K_2CO_3 (3.49 g, 25.3 mmol), **11b** (2.83 g, 4.03 mmol), 18-crown-6 (0.16 g, 0.62 mmol), and acetone (40 mL) was maintained at ambient temperature for 24 h after which the mixture was concentrated. Water (100 mL) was added to the residue and the solution was extracted with CH_2Cl_2 (4 × 40 mL), dried ($MgSO_4$), filtered, concentrated. Flash chromatography (SiO_2, 7 : 3 hexanes-EtOAc) to afford **7c** (3.00 g, 96%) as a yellow solid: ^{1}H NMR (250 MHz, $CDCl_3$) δ 9.84 (s, 1 H); 7.75 (s, 1 H); 7.46 (s, 1 H); 7.43–7.38 (m, 2 H); 7.05–6.90 (m, 7 H); 5.55 (s, 2 H); 5.16 (s, 2 H); 5.08 (s, 2 H); 4.08 (t, J = 6.8 Hz, 2 H); 3.94 (s, 6 H); 3.91 (s, 3 H); 3.89 (s, 3 H); 1.87 (quintet, J = 7.9 Hz, 2 H); 1.50–1.26 (m, 18 H); 0.88 (t, J = 6.2 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 190.8, 154.3, 153.6, 150.0, 149.9, 149.8, 148.1, 147.4, 147.3, 138.8, 130.9, 130.2, 129.5, 129.1, 126.5, 120.1, 120.0, 114.3, 114.1, 112.4, 111.3, 111.2, 109.6, 109.3, 109.0, 71.1, 70.9, 69.5, 68.5, 56.3, 56.0, 56.0, 31.9, 29.65, 29.63, 29.57, 29.52, 29.3, 28.9, 25.9, 22.7, 14.1; MS (FAB$^+$) m/z 773.79 (M^+, $C_{44}H_{55}NO_{11}$ calcd 773.38).

4-Allyloxy-3-methoxybenzyl alcohol (8a). A solution of **6** (121 g, 0.63 mol), $NaBH_4$ (47.2 g, 1.25 mol), and THF (550 mL) was maintained at reflux for 24 h after which the solution was concentrated and ice (200 mL) and 10% HCl (500 mL) were added. The solution was extracted with EtOAc (4 × 150 mL), washed with saturated $NaHCO_3$ (500 mL), dried ($MgSO_4$), filtered, and concentrated to afford **8a** (119 g, 97%) as a colorless solid: ^{1}H NMR (250 MHz, $CDCl_3$) δ 6.94 (s, 1 H); 6.86 (s, 2 H); 6.16–6.01 (m, 1 H); 5.40 (dd, J = 1.4, 17.2 Hz, 1 H); 5.29 (dd, J = 1.4, 10.5 Hz, 1 H); 4.63–4.61 (m, 4 H); 3.89 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 149.5, 147.5, 133.9, 133.2, 119.2, 117.9, 113.3, 110.8, 69.9, 65.3, 55.9; MS (FAB$^+$) m/z 194.20 (M^+, $C_{11}H_{14}O_3$ calcd 194.09).

4-(4-Allyloxy-3-methoxybenzyloxy)-3-methoxybenzyl alcohol (8b). A solution of **6b** (9.35 g, 28.5 mmol), $NaBH_4$ (2.24 g, 59.4 mmol), and THF (100 mL) was maintained at reflux for 24 h after which ice (100 mL) and 10% HCl (50 mL) were added. The solution was extracted with EtOAc (4 × 25 mL), washed with saturated $NaHCO_3$ (500 mL), dried ($MgSO_4$), filtered, concentrated, and recrystallized in EtOH to afford **8b** (8.77 g, 93%) as a colorless solid: ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.01–6.81 (m, 6 H); 6.13–6.00 (m, 1 H); 5.39 (dd, J = 1.5, 17.2 Hz, 1 H); 5.28 (dd, J = 1.5, 10.4 Hz, 1 H); 5.07 (s, 2 H); 4.62–4.59 (m, 4 H); 3.89 (s, 3 H); 3.87 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ149.9, 149.5, 147.7, 134.2, 133.3, 130.0, 119.9, 119.3, 117.9, 114.3, 113.2, 111.1, 110.9, 71.3, 69.9, 65.3, 55.9; MS (FAB$^+$) m/z 330.26 (M^+, $C_{19}H_{22}O_5$ calcd 330.15).

4-(4-(4-Allyloxy-3-methoxybenzyloxy)-3-methoxybenzyloxy)-3-methoxybenzyl alcohol (8c). A solution of **6c** (5.17 g, 11.1 mmol), $NaBH_4$ (0.862 g, 22.9 mmol), and THF (100 mL) was maintained at reflux for 24 h after which ice (100 mL) and 10% HCl (50 mL) were added. The solution was extracted with EtOAc (4 × 75 mL), washed with saturated $NaHCO_3$ (150 mL), dried ($MgSO_4$), filtered, and concentrated to afford **8c** (5.19 g, 100%) as a colorless solid: ^{1}H NMR (250 MHz, $CDCl_3$) δ7.01–7.79 (m, 9 H); 6.13–6.00 (m, 1 H); 5.40 (dd, J = 1.5, 17.2 Hz, 1 H); 5.28 (dd, J = 1.5, 10.5 Hz, 1 H); 5.06 (s, 4 H); 4.62–4.59 (m, 4 H); 3.89 (s, 3 H); 3.88 (s, 3 H); 3.87 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 149.9, 149.9, 149.6, 147.9, 147.7, 134.2, 133.3, 130.3, 130.0, 119.9, 119.9, 119.3, 118.0, 114.3, 114.2, 113.3, 111.2, 111.1, 110.9, 71.2, 69.9, 65.3, 55.9, 55.9; MS (FAB$^+$) m/z 466.46 (M^+, $C_{27}H_{30}O_7$ calcd 466.20).

4-(4-(4-(4-Allyloxy-3-methoxybenzyloxy)-3-methoxybenzyloxy)-3-methoxybenzyloxy)-3-methoxybenzyl alcohol (8d). A solution of **6d** (1.59 g, 2.65 mmol), $NaBH_4$ (224 mg, 5.94 mmol), and THF (100 mL) was maintained at reflux for 24 h after which ice (100 mL) and 10% HCl (50 mL) were added. The solution was extracted with EtOAc (4 × 20 mL), washed with saturated $NaHCO_3$ (100 mL), dried ($MgSO_4$), filtered, and concentrated to afford **8d** (0.935 g, 58%) as a colorless solid: ^{1}H NMR (250 MHz, $CDCl_3$) δ7.01–6.80 (m, 12 H); 6.13–6.00 (m, 1 H); 5.40 (dd, J = 1.5, 17.2 Hz, 1 H); 5.28 (dd, J = 1.5, 10.5 Hz, 1 H); 5.07 (s, 6 H); 4.62–4.59 (m, 4 H); 3.91 (s, 3 H); 3.89 (s, 3 H); 3.88 (s, 3 H); 3.87 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 149.9, 149.9, 149.6, 147.9, 147.7, 134.2, 133.3, 130.3, 130.0, 119.9, 119.9, 119.3, 118.0, 114.3, 114.2, 114.1, 113.3, 111.2, 111.1, 110.9, 71.3, 71.2, 69.9, 65.3, 56.0, 55.9; MS (FAB$^+$) m/z 602.61 (M^+, $C_{35}H_{38}O_9$ calcd 602.25).

4-(2-Nitro-4-dodecyloxy-5-methoxybenzyloxy)-3-methoxybenzyl alcohol (9a). A solution of **7a** (10.88 g, 21.68 mmol), $NaBH_4$ (1.65 g, 43.77 mmol), and THF (150 mL) was maintained at 60 °C for 3 h after which ice (100 mL) and 10% HCl (30 mL) were added. The solution was extracted with CH_2Cl_2 (4 × 70 mL),

washed with saturated $NaHCO_3$ (100 mL), dried ($MgSO_4$), filtered, concentrated, and recrystallized (EtOH) to afford **9a** (9.92 g, 91%) as a pink solid: ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.75 (s, 1 H); 7.47 (s, 1 H); 7.00 (d, J = 1.5 Hz, 1 H); 6.88–6.86 (m, 2 H); 5.56 (s, 2 H); 4.64 (d, J = 5.4 Hz, 2 H); 4.08 (t, J = 6.8 Hz, 2 H); 3.94 (s, 3 H); 3.93 (s, 3 H); 1.87 (quintet, J = 7.9 Hz, 2 H); 1.50–1.26 (m, 18 H); 0.88 (t, J = 6.2 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 154.3, 149.8, 147.3, 147.2, 138.8, 134.9, 129.5, 119.5, 114.4, 111.0, 109.6, 109.0, 69.5, 68.5, 65.2, 56.3, 56.0, 31.9, 29.65, 29.63, 29.57, 29.52, 29.3, 28.9, 25.9, 22.7, 14.1; MS (FAB^+) m/z 503.58 (M^+, $C_{28}H_{41}NO_7$ calcd 503.29).

4-(4-(2-Nitro-4-dodecyloxy-5-methoxybenzyloxy)-3-methoxybenzyloxy)-3-methoxybenzyl alcohol (9b). A solution of **7b** (4.29 g, 6.73 mmol), $NaBH_4$ (0.51 g, 13.7 mmol), and THF (80 mL) was maintained at ambient temperature for 24 h after which ice (30 mL) and 10% HCl (50 mL) were added. The solution was extracted with CH_2Cl_2 (4 × 25 mL), washed with saturated $NaHCO_3$ (100 mL), dried ($MgSO_4$), filtered, and concentrated to afford **9b** (4.22 g, 98%) as a yellow solid: ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.74 (s, 1 H); 7.45 (s, 1 H); 7.06 (d, J = 1.7 Hz, 1 H); 6.95–6.83 (m, 5 H); 5.55 (s, 2 H); 5.08 (s, 2 H); 4.61 (s, 2 H); 4.07 (t, J = 6.8 Hz, 2 H); 3.93 (s, 3 H); 3.91 (s, 3 H); 3.90 (s, 3 H); 1.87 (quintet, J = 7.9 Hz, 2 H); 1.50–1.26 (m, 18 H); 0.88 (t, J = 6.2 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 154.3, 149.9, 149.8, 147.6, 147.3, 147.3, 138.8, 134.3, 131.0, 129.5, 120.1, 119.3, 114.3, 114.3, 111.3, 110.9, 109.6, 109.0, 71.2, 69.5, 68.5, 65.3, 56.3, 56.0, 55.9, 31.9, 29.65, 29.63, 29.57, 29.52, 29.3, 28.9, 25.9, 22.7, 14.1; MS (FAB^+) m/z 639.62 (M^+, $C_{36}H_{49}NO_9$ calcd 639.34).

4-(4-(4-(2-Nitro-4-dodecyloxy-5-methoxybenzyloxy)-3-methoxybenzyloxy)-3-methoxybenzyloxy)-3-methoxybenzyl alcohol (9c). A solution of **7c** (2.64 g, 3.41 mmol), $NaBH_4$ (0.31 g, 8.24 mmol), and THF (70 mL) was maintained at ambient temperature for 24 h after which ice (100 mL) and 10% HCl (50 mL) were added. The solution was extracted with CH_2Cl_2 (4 × 25 mL), washed with saturated $NaHCO_3$ (100 mL), dried ($MgSO_4$), filtered, and concentrated. Flash chromatography (SiO_2, 1 : 1 hexanes-EtOAc gradient to 100% CH_2Cl_2 gradient to 100% EtOAc) to yield **9c** (2.30 g, 87%) as a yellow solid: ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.75 (s, 1 H); 7.45 (s, 1 H); 7.05–6.83 (m, 9 H); 5.55 (s, 2 H); 5.07 (s, 2 H); 5.07 (s, 2 H); 4.62 (d, J = 5.8 Hz, 2 H); 4.07 (t, J = 6.8 Hz, 2 H); 3.93 (s, 3 H); 3.90 (s, 3 H); 3.89 (s, 3 H); 3.88 (s, 3 H); 1.87 (quintet, J = 7.9 Hz, 2 H); 1.50–1.26 (m, 18 H); 0.88 (t, J = 6.2 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 154.4, 149.8, 149.8, 147.8, 147.7, 147.3, 147.3, 138.8, 134.2, 131.0, 130.4, 129.6, 120.1, 119.9, 119.3, 114.3, 114.2, 114.2, 111.3, 111.2, 110.9, 109.6, 109.0, 71.2, 71.1, 69.5, 68.5, 65.3, 56.3, 56.0, 55.9, 55.9, 31.9, 29.65, 29.63, 29.57, 29.52, 29.3, 28.9, 25.9, 22.7, 14.1; MS (FAB^+) m/z 775.85 (M^+, $C_{44}H_{57}NO_{11}$ calcd 775.39).

4-Allyloxy-3-methoxybenzyl bromide (10a). To a cold (0 °C), stirred solution of **8a** (20.4 g, 0.105 mmol), PPh_3 (38.5 g, 0.15 mmol), and CH_2Cl_2 (300 mL) was added NBS (26.3 g, 0.15 mmol) over a 90 min period. A solution of saturated $NaHCO_3$ (300 mL) was added to the reaction and a dark green color arose. The solution was extracted with CH_2Cl_2 (4 × 25 mL), dried ($MgSO_4$), filtered, and concentrated to a dark oil. Flash chromatography of the crude product (SiO_2, 8 : 2 hexanes-EtOAc) afforded **10a** as a yellow oil (13.8 g, 51%): ^{1}H NMR (250 MHz, $CDCl_3$) δ 6.93–6.79 (m, 3 H); 6.14–5.99 (m, 1 H); 5.40 (dd, J = 1.6, 17.4 Hz, 1 H); 5.29 (dd, J = 1.6, 10.4 Hz, 1 H); 4.61 (dt, J = 1.4, 5.4 Hz, 2 H); 4.78 (s, 2 H); 3.88 (s, 3 H).

4-(4-Allyloxy-3-methoxybenzyloxy)-3-methoxybenzyl bromide (10b). To a cold (0 °C), stirred solution of **8b** (21.0 g, 63.4 mmol), PPh_3 (23.3 g, 88.7 mmol), and CH_2Cl_2 (200 mL) was added NBS (15.9 g, 89.2 mmol) over a 30 min period. A solution of saturated $NaHCO_3$ (200 mL) was added to the reaction and a dark green color arose. The solution was extracted with CH_2Cl_2 (4 × 25 mL), dried ($MgSO_4$), filtered, and concentrated to a dark oil. Flash chromatography of the crude product (SiO_2, 8 : 2 hexanes-EtOAc) afforded **10b** as a colorless solid (13.5 g, 54%): ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.00–6.82 (m, 6 H); 6.13–6.00 (m, 1 H); 5.40 (dd, J = 1.5, 17.2 Hz, 1 H); 5.28 (dd, J = 1.5, 10.5 Hz, 1 H); 5.07 (s, 2 H); 4.64 (dt, J = 1.4, 5.4 Hz, 2 H); 4.49 (s, 2 H); 3.89 (s, 3 H); 3.87 (s, 3 H).

4-(4-(4-Allyloxy-3-methoxybenzyloxy)-3-methoxybenzyloxy)-3-methoxybenzyl bromide (10c). To a cold (0 °C), stirred solution of **8c** (4.83 g, 10.4 mmol), PPh_3 (3.80 g, 14.5 mmol), and CH_2Cl_2 (100 mL) was added NBS (2.60 g, 14.6 mmol) over a 10 min period. A solution of saturated $NaHCO_3$ (100 mL) was added to the reaction and a dark green color arose. The solution was extracted with CH_2Cl_2 (4 × 25 mL), dried ($MgSO_4$), filtered, and concentrated to a dark oil. Flash chromatography of the crude product (SiO_2, 100% CH_2Cl_2) afforded **10c** as a colorless solid (3.11 g, 57%): ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.00–6.81 (m, 9 H); 6.14–6.02 (m, 1 H); 5.40 (dd, J = 1.6, 17.3 Hz, 1 H); 5.28 (dd, J = 1.6, 10.4 Hz, 1 H); 5.07 (s, 2 H); 5.06 (s, 2 H); 4.61 (dt, J = 1.4, 5.4 Hz, 2 H); 4.49 (s, 2 H); 3.89 (s, 3 H); 3.88 (s, 3 H); 3.87 (s, 3 H).

4-(4-(4-(4-Allyloxy-3-methoxybenzyloxy)-3-methoxybenzyloxy)-3-methoxybenzyloxy)-3-methoxybenzyl bromide (10d). To a cold (0 °C), stirred solution of **8d** (0.730 g, 1.21 mmol), PPh_3 (0.441 g, 1.68 mmol), and CH_2Cl_2 (25 mL) was added NBS (0.319 g, 1.79 mmol) over a 15 min period. A solution of saturated $NaHCO_3$ (50 mL) was added to the reaction and a dark green color arose. The solution was extracted with CH_2Cl_2 (4 × 10 mL), dried ($MgSO_4$), filtered, and concentrated to a dark oil. Flash chromatography of the crude product (SiO_2, 4 : 6 hexanes-EtOAc gradient to 100% CH_2Cl_2) afforded **10d** as a colorless solid (0.422 g, 52%): ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.00–6.82 (m, 12 H); 6.13–6.00 (m, 1 H); 5.40 (dd, J = 1.5, 17.2 Hz, 1 H); 5.28 (dd, J = 1.5, 10.5 Hz, 1 H); 5.06 (s, 6 H); 4.61 (dt, J = 1.4, 5.4 Hz, 2 H); 4.48 (s, 2 H) 3.91 (s, 3 H); 3.89 (s, 3 H); 3.87 (s, 3 H); 3.87 (s, 3 H).

4-(2-Nitro-4-dodecyloxy-5-methoxybenzyloxy)-3-methoxybenzyl bromide (11a). To a cold (0 °C), stirred solution of **9a** (9.54 g, 19.0 mmol), PPh_3 (6.96 g, 26.5 mmol), and CH_2Cl_2 (300 mL) was added NBS (4.76 g, 26.8 mmol) over a 10 min period. A solution of saturated $NaHCO_3$ (100 mL) was added to the reaction and a dark green color arose. The solution was extracted with CH_2Cl_2 (4 × 50 mL), dried ($MgSO_4$), filtered, and concentrated to a dark oil. Flash chromatography of the crude product (SiO_2, 1 : 1 hexanes-CH_2Cl_2 gradient to 100% CH_2Cl_2) afforded **11a** as a yellow solid (5.20 g, 48%): ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.75 (s, 1 H); 7.44 (s, 1 H); 6.97–6.83 (m, 3 H); 5.55 (s, 2 H); 4.50 (s, 2 H);

4.08 (t, J = 6.8 Hz, 2 H); 3.94 (s, 3 H); 3.93 (s, 3 H); 1.87 (quintet, J = 7.9 Hz, 2 H); 1.50–1.26 (m, 18 H); 0.88 (t, J = 6.2 Hz, 3 H).

4-(4-(2-Nitro-4-dodecyloxy-5-methoxybenzyloxy)-3-methoxybenzyloxy)-3-methoxybenzyl bromide (11b). To a cold (0 °C), stirred solution of **9b** (4.00 g, 6.17 mmol), PPh_3 (2.27 g, 8.65 mmol), and CH_2Cl_2 (50 mL) was added NBS (1.56 g, 8.78 mmol) over a 15 min period. A solution of saturated $NaHCO_3$ (100 mL) was added to the reaction and a dark green color arose. The solution was extracted with CH_2Cl_2 (4 × 25 mL), dried ($MgSO_4$), filtered, and concentrated to a dark oil. Flash chromatography of the crude product (SiO_2, 6 : 4 hexanes-EtOAc) afforded **11b** as a yellow solid (5.20 g, 48%): ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.75 (s, 1 H); 7.45 (s, 1 H); 7.04 (d, J = 1.6 Hz, 1 H); 6.93–6.81 (m, 5 H); 5.56 (s, 2 H); 5.08 (s, 2 H); 4.49 (s, 2 H); 4.08 (t, J = 6.8 Hz, 2 H); 3.93 (s, 3 H); 3.91 (s, 3 H); 3.90 (s, 3 H); 1.87 (quintet, J = 7.9 Hz, 2 H); 1.50–1.26 (m, 18 H); 0.88 (t, J = 6.2 Hz, 3 H).

4-(4-(4-(2-Nitro-4-dodecyloxy-5-methoxybenzyloxy)-3-methoxybenzyloxy)-3-methoxybenzyloxy)-3-methoxybenzyl bromide (11c). To a cold (0 °C), stirred solution of **9c** (0.29 g, 0.37 mmol) and THF (5 mL) was added PBr_3 (0.07 g, 0.74 mmol) over a 5 min period and maintained for 10 min. Water (10 mL) was added and the resultant solution was extracted with CH_2Cl_2 (4 × 10 mL), washed with saturated $NaHCO_3$ (30 mL), dried ($MgSO_4$), filtered, and concentrated to afford **11c** as a yellow solid (0.26 g, 84%): ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.75 (s, 1 H); 7.46 (s, 1 H); 7.05–6.84 (m, 9 H); 5.55 (s, 2 H); 5.07 (s, 2 H); 5.06 (s, 2 H); 4.48 (s, 2 H); 4.07 (t, J = 6.8 Hz, 2 H); 3.93 (s, 3 H); 3.90 (s, 3 H); 3.89 (s, 3 H); 3.88 (s, 3 H); 1.87 (quintet, J = 7.9 Hz, 2 H); 1.50–1.26 (m, 18 H); 0.88 (t, J = 6.2 Hz, 3 H).

2-Allyloxy-3-methoxybenzaldehyde (13a). A mixture of *o*-vanillin (40 g, 0.26 mol), K_2CO_3 (82 g, 0.59 mol), allyl bromide (32 g, 0.26 mol), and DMF (200 mL) was maintained at ambient temperature for 24 h after which the mixture was concentrated. Water (300 mL) was added to the residue and the solution was extracted with CH_2Cl_2 (4 × 60 mL), washed with brine (2 × 300 mL), dried ($MgSO_4$), filtered, and concentrated to afford **13a** (47.7 g, 94%) as a dark oil: ^{1}H NMR (250 MHz, $CDCl_3$) δ 10.44 (s, 1 H); 7.43–7.38 (m, 1 H); 7.17–7.09 (m, 2 H); 6.16–6.00 (m, 1 H); 5.36 (dd, J = 1.5, 17.2 Hz, 1 H); 5.27 (dd, J = 1.5, 10.2 Hz, 1 H); 4.67 (dt, J = 1.2, 6.2 Hz, 2 H); 3.90 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 190.3, 152.9, 151.1, 133.0, 130.0, 124.0, 118.9, 118.8, 117.9, 15.1, 55.9; MS (FAB$^+$) m/z 192.16 (M^+, $C_{11}H_{12}O_3$ calcd 192.08).

2-(2-Allyloxy-3-methoxybenzyloxy)-3-methoxybenzyaldehyde (13b). A mixture of *o*-vanillin (12.5 g, 82.4 mmol), K_2CO_3 (32.9 g, 0.238 mol), **17a** (21.2 g, 82.4 mmol), and DMF (100 mL) was maintained at 50 °C for 24 h. Water (300 mL) was added and the solution was extracted with CH_2Cl_2 (5 × 50 mL), washed with H_2O (5 × 200 mL), brine (300 mL), dried ($MgSO_4$), filtered, and concentrated. Flash chromatography (SiO_2 8 : 2 hexanes-EtOAc) afforded **13b** (22.5 g, 83%) as a yellow solid: ^{1}H NMR (250 MHz, $CDCl_3$) δ 10.23 (s, 1 H); 7.41–7.37 (m, 1 H); 7.19–7.01 (m, 4 H); 6.93–6.89 (m, 1 H); 6.10–5.97 (m, 1 H); 5.31 (dd, J = 1.5, 17.2 Hz, 1 H); 5.24 (s, 2 H); 5.19 (dd, J = 1.5, 10.5 Hz, 1 H); 4.55 (dt, J = 1.5, 5.4 Hz, 2 H); 3.93 (s, 3 H); 3.86 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 190.6, 153.2, 152.6, 151.5, 146.2, 134.1, 130.5, 130.4, 124.1, 124.1, 122.0, 118.8, 117.9, 117.4, 112.9, 74.1, 71.3, 56.1, 55.8; MS (FAB$^+$) m/z 328.30 (M^+, $C_{19}H_{20}O_5$ calcd 328.13).

2-(2-(2-Allyloxy-3-methoxybenzyloxy)-3-methoxybenzyloxy)-3-methoxybenzaldehyde (13c). A mixture of *o*-vanillin (6.60 g, 43.4 mmol), K_2CO_3 (17.5 g, 0.126 mol), **17b** (17.0 g, 43.3 mmol), and DMF (100 mL) was maintained at 50 °C for 5 h. Water (700 mL) was added and the solution was extracted with CH_2Cl_2 (5 × 50 mL), washed with brine (2 × 200 mL), dried ($MgSO_4$), filtered, and concentrated. Flash chromatography (SiO_2 8 : 2 hexanes-EtOAc gradient to 7 : 3 hexanes-EtOAc) afforded **13c** (17.6 g, 87%) as a yellow oil: ^{1}H NMR (250 MHz, $CDCl_3$) δ 10.17 (s, 1 H); 7.37–7.34 (m, 1 H); 7.11–6.84 (m, 8 H); 6.05–6.5.94 (m, 1 H); 5.27 (dd, J = 1.5, 17.2 Hz, 1 H); 5.17 (s, 2 H); 5.12 (dd, J = 1.5, 10.5 Hz, 1 H); 5.06 (s, 2 H); 4.44 (dt, J = 1.4, 5.4 Hz, 2 H); 3.89 (s, 3 H); 3.87 (s, 3 H); 3.84 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 190.5, 153.1, 152.7, 152.4, 151.5, 146.2, 145.6, 134.3, 131.9, 130.9, 130.3, 124.1, 123.9, 123.9, 121.6, 121.3, 118.7, 117.7, 117.1, 112.8, 112.0, 74.0, 71.2, 69.8, 55.9, 55.9, 55.8; MS (FAB$^+$) m/z 464.44 (M^+, $C_{27}H_{28}O_7$ calcd 464.18).

2-(2-(2-(2-Allyloxy-3-methoxybenzyloxy)-3-methoxybenzyloxy)-3-methoxybenzyloxy)-3-methoxybenzaldehyde (13d). A mixture of *o*-vanillin (2.83 g, 18.6 mmol), K_2CO_3 (8.03 g, 58.1 mmol), **17c** (9.83 g, 18.6 mmol), and DMF (100 mL) was maintained at 50 °C for 8 h. Water (250 mL) was added and the solution was extracted with CH_2Cl_2 (4 × 50 mL), washed with H_2O (2 × 200 mL), brine (200 mL), dried ($MgSO_4$), filtered, and concentrated. Flash chromatography (SiO_2 7 : 3 hexanes-EtOAc gradient to 7 : 3 hexanes-EtOAc) afforded **13d** (7.75 g, 70%) as a colorless oil: ^{1}H NMR (250 MHz, $CDCl_3$) δ 10.14 (s, 1 H); 7.36–7.32 (m, 1 H); 7.10–6.83 (m, 11 H); 6.10–5.95 (m, 1 H); 5.25 (dd, J = 1.5, 17.2 Hz, 1 H); 5.13–5.03 (m,7 H); 4.43 (dt, J = 1.4, 5.4 Hz, 2 H); 3.84 (s, 3 H); 3.82 (s, 3 H); 3.77 (s, 3 H); 3.77 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 190.5, 153.0, 152.6, 152.5, 152.3, 151.5, 146.2, 145.6, 145.4, 134.3, 132.2, 132.1, 130.8, 130.2, 124.0, 123.9, 123.9, 121.6, 121.2, 121.0, 118.6, 117.7, 117.1, 112.7, 112.0, 111.8, 74.0, 71.1, 69.8, 69.6, 55.8, 55.8, 55.7, 55.7; MS (FAB$^+$) m/z 600.57 (M^+, $C_{35}H_{36}O_9$ calcd 600.23).

2-(2-Nitro-4-dodecyloxy-5-methoxybenzyloxy)-3-methoxybenzyaldehyde (14a). A mixture of *o*-vanillin (4.47 g, 29.4 mmol), K_2CO_3 (12.4 g, 89.7 mmol), 4-dodecyloxy-5-methoxy-2-nitrobenzyl bromide (12.7 g, 29.4 mmol), 18-crown-6 (0.34 g, 1.3 mmol), and acetone (180 mL) was maintained at ambient temperature for 6 h after which the mixture was filtered and concentrated. Water (200 mL) was added and the solution was extracted with CH_2Cl_2 (4 × 50 mL), dried ($MgSO_4$), filtered, concentrated, and purified by flash chromatography (SiO_2, 9 : 1 hexanes-CH_2Cl_2) to afford **14a** (11.3 g, 77%) as a red solid: ^{1}H NMR (250 MHz, $CDCl_3$) δ 10.40 (s, 1 H); 7.74 (s, 1 H); 7.55 (s, 1 H); 7.48–7.44 (m, 1 H); 7.22–7.20 (m, 2 H); 5.56 (s, 2 H); 4.10 (t, J = 6.8 Hz, 2 H); 4.02 (s, 3 H); 3.89 (s, 3 H); 1.88 (quintet, J = 7.9 Hz, 2 H); 1.50–1.26 (m, 18 H); 0.88 (t, J = 6.2 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 189.7, 154.3, 152.9, 150.6, 147.4, 138.8, 129.9, 129.0, 124.7, 119.8, 118.0, 109.7, 108.9, 72.7, 69.5, 56.5, 56.0, 31.9, 29.65, 29.63, 29.57, 29.52, 29.3, 28.9, 25.9, 22.7, 14.1; MS (FAB$^+$) m/z 501.54 (M^+, $C_{28}H_{39}NO_7$ calcd 501.27).

2-(2-(2-Nitro-4-dodecyloxy-5-methoxybenzyloxy)-3-methoxybenzyloxy)-3-methoxybenzaldehyde (14b). A mixture of *o*-vanillin (1.82 g, 12.0 mmol), K_2CO_3 (4.96 g, 35.91 mmol), **18a** (6.75 g, 11.91 mmol), and DMF (60 mL) was maintained at ambient temperature for 24 h. Water (100 mL) was added and the solution was extracted with CH_2Cl_2 (4 × 50 mL), washed with H_2O (100 mL), brine (100 mL), dried ($MgSO_4$), filtered, and concentrated. Flash chromatography (SiO_2, 8 : 2 hexanes-EtOAc) afforded **14b** (6.88 g, 91%) as a yellow solid: ^{1}H NMR (250 MHz, $CDCl_3$) δ 10.20 (s, 1 H); 7.72 (s, 1 H); 7.58 (s, 1 H); 7.34–7.30 (m, 1 H); 7.11–6.96 (m, 4 H); 5.30 (s, 2 H); 5.26 (s, 2 H); 4.09 (t, J = 6.8 Hz, 2 H); 3.98 (s, 3 H); 3.83 (s, 3 H); 3.78 (s, 3 H); 1.88 (quintet, J = 7.9 Hz, 2 H); 1.50–1.26 (m, 18 H); 0.88 (t, J = 6.2 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 190.4, 154.3, 153.0, 152.6, 151.1, 147.0, 146.0, 138.5, 130.4, 130.3, 130.2, 124.7, 124.1, 122.4, 118.9, 117.7, 113.0, 109.6, 108.8, 71.5, 71.1, 69.5, 56.4, 55.9, 55.8, 31.9, 29.65, 29.63, 29.57, 29.52, 29.3, 29.2, 28.9, 25.9, 22.7, 14.1; MS (FAB$^+$) m/z 637.67 (M$^+$, $C_{36}H_{47}NO_9$ calcd 637.32).

2-(2-(2-(2-Nitro-4-dodecyloxy-5-methoxybenzyloxy)-3-methoxybenzyloxy)-3-methoxybenzyloxy)-3-methoxybenzaldehyde (14c). A mixture of *o*-vanillin (1.04 g, 6.83 mmol), K_2CO_3 (3.09 g, 22.4 mmol), **18b** (4.82 g, 6.85 mmol), and DMF (20 mL) was maintained at ambient temperature for 20 h. Water (100 mL) was added and the solution was extracted with CH_2Cl_2 (5 × 20 mL), washed with H_2O (100 mL), brine (100 mL), dried ($MgSO_4$), filtered, and concentrated. Flash chromatography (SiO_2, 8 : 2 hexanes-EtOAc) afforded **14c** (6.88 g, 91%) as a yellow solid: ^{1}H NMR (250 MHz, $CDCl_3$) δ 10.08 (s, 1 H); 7.66 (s, 1 H); 7.57 (s, 1 H); 7.32–7.28 (m, 1 H); 7.09–6.82 (m, 8 H); 5.30 (s, 2 H); 5.11 (s, 2 H); 5.07 (s, 1 H); 4.05 (t, J = 6.8 Hz, 2 H); 3.89 (s, 3 H); 3.82 (s, 3 H); 3.78 (s, 3 H); 3.72 (s, 3 H); 1.88 (quintet, J = 7.9 Hz, 2 H); 1.50–1.26 (m, 18 H); 0.88 (t, J = 6.2 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 190.3, 154.2, 152.9, 152.5, 152.4, 151.4, 146.9, 146.1, 145.4, 138.3, 131.7, 130.7, 130.6, 130.2, 124.5, 124.1, 123.9, 121.8, 121.6, 118.6, 117.6, 112.7, 112.1, 109.4, 108.7, 71.4, 71.2, 69.9, 69.4, 56.3, 55.8, 55.7, 55.7, 31.9, 29.65, 29.63, 29.57, 29.52, 29.3, 29.2, 28.9, 25.9, 22.7, 14.1; MS (FAB$^+$) m/z 773.83 (M$^+$, $C_{44}H_{55}NO_{11}$ calcd 773.38).

2-Allyloxy-3-methoxybenzyl alcohol (15a). A solution of **13a** (6.03 g, 31.4 mmol), $NaBH_4$ (2.06 g, 54.72 mmol), and THF (50 mL) was maintained at reflux for 24 h after which ice (100 mL) and 10% HCl (50 mL) were added. The solution was extracted with EtOAc (4 × 10 mL), washed with saturated $NaHCO_3$ (50 mL), dried ($MgSO_4$), filtered, and concentrated to yield **15a** (5.84 g, 96%) as a colorless oil: ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.08–7.02 (m, 1 H); 6.94–6.86 (m, 2 H); 6.16–6.00 (m, 1 H); 5.36 (dd, J = 1.5, 17.2 Hz, 1 H); 5.27 (dd, J = 1.5, 10.2 Hz, 1 H); 4.69 (d, J = 5.7 Hz, 2 H); 4.58 (dt, J = 1.3, 5.8 Hz, 2 H); 3.86 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 152.3, 145.5, 134.7, 134.0, 124.0, 120.4, 117.7, 111.9, 73.9, 61.4, 55.7; MS (FAB$^+$) m/z 194.19 (M$^+$, $C_{11}H_{14}O_3$ calcd 194.09).

2-(2-Allyloxy-3-methoxybenzyloxy)-3-methoxybenzyl alcohol (15b). A solution of **13b** (22.5 g, 68.5 mmol), $NaBH_4$ (5.20 g, 0.138 mol), and THF (100 mL) was maintained at reflux for 24 h after which ice (100 mL) and 10% HCl (100 mL) were added. The solution was extracted with EtOAc (4 × 50 mL), washed with saturated $NaHCO_3$ (200 mL), dried ($MgSO_4$), filtered, and concentrated to yield **15b** (21.7 g, 96%) as a colorless solid: ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.10–7.02 (m, 3 H); 6.92–6.90 (m, 3 H); 6.10–6.00 (m, 1 H); 32 (dd, J = 1.5, 17.0 Hz, 1 H); 5.20 (dd, J = 1.5, 10.5 Hz, 1 H); 5.14 (s, 2 H); 4.55 (dt, J = 1.5, 5.4 Hz, 2 H); 4.52 (d, J = 1.3 Hz, 2 H); 3.90 (s, 3 H); 3.87 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 152.6, 152.6, 146.0, 135.1, 134.1, 131.5, 124.1, 124.1, 122.1, 121.0, 117.6, 112.6, 112.2, 74.2, 69.9, 61.7, 55.9, 55.8; MS (FAB$^+$) m/z 330.34 (M$^+$, $C_{19}H_{22}O_5$ calcd 330.15).

2-(2-(2-Allyloxy-3-methoxybenzyloxy)-3-methoxybenzyloxy)-3-methoxybenzyl alcohol (15c). A solution of **13c** (16.8 g, 36.1 mmol), $NaBH_4$ (2.76 g, 73.2 mmol), and THF (100 mL) was maintained at reflux for 24 h after which ice (30 mL) and 10% HCl (30 mL) were added. The solution was extracted with EtOAc (4 × 25 mL), washed with saturated $NaHCO_3$ (100 mL), dried ($MgSO_4$), filtered, and concentrated. Flash chromatography (SiO_2, 7 : 3 hexanes-EtOAc) yielded **15c** (11.5 g, 68%) as a colorless solid: ^{1}H NMR (250 MHz, $CDCl_3$) δ7.12–6.83 (m, 9 H); 6.06–5.96 (m, 1 H); 5.26 (dd, J = 1.5, 17.2 Hz, 1 H); 5.14–5.08 (m, 5 H); 4.51 (s, 2 H); 4.45 (dt, J = 1.4, 5.4 Hz, 2 H); 3.90 (s, 3 H); 3.85 (s, 3 H); 3.82 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 152.7, 152.4, 152.4, 146.1, 146.0, 145.5, 135.1, 134.3, 131.9, 131.9, 124.2, 123.9, 121.7, 121.4, 120.8, 117.2, 112.5, 112.0, 112.0, 74.1, 69.9, 61.4, 55.8, 55.8, 55.7; MS (FAB$^+$) m/z 466.47 (M$^+$, $C_{27}H_{30}O_7$ calcd 466.20).

2-(2-(2-(2-Allyloxy-3-methoxybenzyloxy)-3-methoxybenzyloxy)-3-methoxybenzyloxy)-3-methoxybenzyl alcohol (15d). A solution of **13d** (6.57 g, 10.9 mmol), $NaBH_4$ (0.85 g, 22.6 mmol), and THF (500 mL) was maintained at reflux for 24 h after which ice (20 mL) and 10% HCl (50 mL) were added. The solution was extracted with EtOAc (4 × 20 mL), washed with saturated $NaHCO_3$ (100 mL), dried ($MgSO_4$), filtered, and concentrated. Flash chromatography (SiO_2, 7 : 3 hexanes-EtOAc) yielded **15d** (4.82 g, 73%) as a colorless solid: ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.15–6.81 (m, 12 H); 6.10–5.93 (m, 1 H); 5.26 (dd, J = 1.5, 17.2 Hz, 1 H); 5.11–5.04 (m,7 H); 4.48 (s, 2 H); 4.43 (dt, J = 1.4, 5.4 Hz, 2 H); 3.85 (s, 3 H); 3.82 (s, 3 H); 3.78 (s, 3 H); 3.77 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 152.6, 152.5, 152.4, 152.3, 146.2, 145.9, 145.5, 145.4, 135.1, 134.3, 132.3, 132.1, 131.8, 124.0, 123.9, 121.7, 121.3, 121.0, 120.7, 117.1, 112.4, 111.9, 111.9, 111.9, 74.0, 69.9, 69.9, 69.8, 69.7, 61.3, 55.8, 55.8, 55.7, 55.7; MS (FAB$^+$) m/z 602.50 (M$^+$, $C_{35}H_{38}O_9$ calcd 602.25).

2-(2-Nitro-4-dodecyloxy-5-methoxybenzyloxy)-3-methoxybenzyl alcohol (16a). A solution of **14a** (10.4 g, 20.8 mmol), $NaBH_4$ (1.57 g, 41.6 mmol), and THF (100 mL) was maintained at 60 °C for 3 h after which ice (100 mL) and 10% HCl (50 mL) were added. The solution was extracted with CH_2Cl_2 (4 × 50 mL), washed with saturated $NaHCO_3$ (100 mL), dried ($MgSO_4$), filtered, concentrated, and recrystallized (EtOH) to yield **16a** (8.28 g, 79%) as a red solid: ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.74 (s, 1 H); 7.59 (s, 1 H); 7.15–7.09 (m, 1 H); 7.01–6.92 (m, 2 H); 5.45 (s, 2 H); 4.72 (d, J = 6.2 Hz, 2 H); 4.09 (t, J = 6.8 Hz, 2 H); 4.1 (s, 3 H); 3.85 (s, 3 H); 1.87 (quintet, J = 7.9 Hz, 2 H); 1.50–1.26 (m, 18 H); 0.88 (t, J = 6.2 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 154.2, 152.5, 147.2, 145.5, 138.8, 134.6, 130.0, 124.7, 120.7, 112.2, 109.8, 108.9, 71.6, 69.5, 61.4, 56.5, 55.8, 31.9, 29.65, 29.63, 29.57, 29.52, 29.3, 28.9, 25.9, 22.7, 14.1; MS (FAB$^+$) m/z 503.54 (M$^+$, $C_{28}H_{41}NO_7$ calcd 503.29).

2-(2-(2-Nitro-4-dodecyloxy-5-methoxybenzyloxy)-3-methoxybenzyloxy)-3-methoxybenzyl alcohol (16b). A solution of **14b** (6.77 g, 10.6 mmol), $NaBH_4$ (0.82 g, 21.8 mmol), and THF (60 mL) was maintained at 60 °C for 6 h after which ice (75 mL) and 10% HCl (25 mL) were added. The solution was extracted with EtOAc (4 × 25 mL), washed with saturated $NaHCO_3$ (100 mL), dried ($MgSO_4$), filtered, and concentrated. Flash chromatography (SiO_2 7 : 3 hexanes-EtOAc) yielded **16b** (5.18 g, 76%) as a yellow solid: ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.73 (s, 1 H); 7.64 (s, 1 H); 7.14–7.11 (m, 2 H); 6.98–6.94 (m, 2 H); 6.86–6.76 (m, 2 H); 5.34 (s, 2 H); 5.17 (s, 2 H); 4.47 (d, J = 6.6 Hz, 2 H); 4.08 (t, J = 6.8 Hz, 2 H); 3.99 (s, 3 H); 3.84 (s, 3 H); 3.74 (s, 3 H); 2.15 (t, J = 6.6, 1 H); 1.88 (quintet, J = 7.9 Hz, 2 H); 1.50–1.26 (m, 18 H); 0.88 (t, J = 6.2 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 154.3, 152.6, 152.3, 147.0, 145.9, 145.7, 138.5, 134.9, 131.4, 130.5, 124.7, 124.1, 122.3, 120.8, 112.6, 112.0, 109.6, 108.8, 71.7, 69.8, 69.5, 61.7, 56.5, 55.8, 55.7, 31.9, 29.65, 29.63, 29.57, 29.52, 29.3, 29.2, 28.9, 25.9, 22.7, 14.1; MS (FAB$^+$) m/z 639.68 (M^+, $C_{36}H_{49}NO_9$ calcd 639.34).

2-(2-(2-(2-Nitro-4-dodecyloxy-5-methoxybenzyloxy)-3-methoxybenzyloxy)-3-methoxybenzyloxy)-3-methoxybenzyl alcohol (16c). A solution of **14c** (4.00 g, 5.17 mmol), $NaBH_4$ (0.49 g, 12.9 mmol), and THF (25 mL) was maintained at 60 °C for 5 h after which ice (100 mL) and 10% HCl (50 mL) were added. The solution was extracted with EtOAc (4 × 25 mL), washed with saturated $NaHCO_3$ (100 mL), dried ($MgSO_4$), filtered, and concentrated. Flash chromatography (SiO_2 7 : 3 hexanes-EtOAc) yielded **16c** (3.44 g, 86%) as a yellow solid: ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.66 (s, 1 H); 7.58 (s, 1 H); 7.14–6.78 (m, 9 H); 5.31 (s, 2 H); 5.15 (s, 2 H); 4.98 (s, 2 H); 4.45 (d, J = 6.5 Hz, 2 H); 4.06 (t, J = 6.8 Hz, 2 H); 3.88 (s, 3 H); 3.82 (s, 3 H); 3.75 (s, 3 H); 3.72 (s, 3 H); 2.19 (t, J = 6.5, 1 H); 1.88 (quintet, J = 7.9 Hz, 2 H); 1.50–1.26 (m, 18 H); 0.88 (t, J = 6.2 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 154.1, 152.5, 152.4, 152.3, 146.8, 146.0, 145.7, 145.3, 138.4, 134.9, 131.8, 131.7, 130.6, 124.5, 124.1, 123.9, 121.8, 121.7, 120.6, 112.4, 112.0, 111.8, 109.5, 108.7, 71.4, 69.9, 69.8, 69.4, 61.2, 56.3, 55.7, 55.7, 55.6, 31.9, 29.65, 29.63, 29.57, 29.52, 29.3, 29.2, 28.9, 25.9, 22.7, 14.1; MS (FAB$^+$) m/z 775.86 (M^+, $C_{44}H_{57}NO_{11}$ calcd 775.39).

2-Allyloxy-3-methoxybenzyl bromide (17a). To a cold (0 °C), stirred solution of **15a** (32.5 g, 0.17 mol), PPh_3 (61.2 g, 0.23 mol), and CH_2Cl_2 (200 mL) was added NBS (41.7 g, 0.24 mol) over a 90 min period. A solution of saturated $NaHCO_3$ (300 mL) was added to the reaction and a dark green color arose. The solution was extracted with CH_2Cl_2 (4 × 50 mL), dried ($MgSO_4$), filtered, and concentrated to a dark oil. Flash chromatography of the crude product (SiO_2, 7 : 3 hexanes-EtOAc) afforded **17a** as a yellow oil (21.6 g, 50%): ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.06–6.94 (m, 2 H); 6.89–6.85 (m, 2 H); 6.24–6.08 (m, 1 H); 5.43 (dd, J = 1.5, 17.2 Hz, 1 H); 5.26 (dd, J = 1.5, 10.2 Hz, 1 H); 4.63 (dt, J = 1.3, 5.8 Hz, 2 H); 4.57 (s, 2 H); 3.85 (s, 3 H).

2-(2-Allyloxy-3-methoxybenzyloxy)-3-methoxybenzyl bromide (17b). To a cold (0 °C), stirred solution of **15b** (21.2 g, 64.2 mmol), PPh_3 (23.6 g, 89.8 mmol), and CH_2Cl_2 (150 mL) was added NBS (16.0 g, 89.9 mmol) over a 30 min period. A solution of saturated $NaHCO_3$ (150 mL) was added to the reaction and a dark green color arose. The solution was extracted with CH_2Cl_2 (4 × 20 mL), dried ($MgSO_4$), filtered, and concentrated to a dark oil. Flash chromatography of the crude product (SiO_2, 7 : 3 hexanes-EtOAc) afforded **17b** as a colorless solid (18.2 g, 72%): ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.26–7.23 (m, 1 H); 7.14–6.88 (m, 5 H); 6.16–6.05 (m, 1 H); 5.36 (dd, J = 1.5, 17.2 Hz, 1 H); 5.23–5.18 (m, 3 H); 4.54 (dt, J = 1.5, 5.4 Hz, 2 H); 4.51 (s, 2 H); 3.90 (s, 3 H); 3.88 (s, 3 H).

2-(2-(2-Allyloxy-3-methoxybenzyloxy)-3-methoxybenzyloxy)-3-methoxybenzyl bromide (17c). To a cold (0 °C), stirred solution of **15c** (10.9 g, 23.4 mmol), PPh_3 (8.60 g, 32.8 mmol), and CH_2Cl_2 (100 mL) was added NBS (5.87 g, 33.0 mmol) over a 10 min period. A solution of saturated $NaHCO_3$ (100 mL) was added to the reaction and a dark green color arose. The solution was extracted with CH_2Cl_2 (4 × 20 mL), dried ($MgSO_4$), filtered, and concentrated to a dark oil. Flash chromatography of the crude product (SiO_2, 7 : 3 hexanes-EtOAc) afforded **17c** as a colorless solid (10.9 g, 88%): ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.25–6.83 (m, 9 H); 6.06–5.96 (m, 1 H); 5.27 (dd, J = 1.5, 17.2 Hz, 1 H); 5.17–5.09 (m, 5 H); 4.48–4.45 (m, 4 H); 3.88 (s, 3 H); 3.85 (s, 3 H); 3.77 (s, 3 H).

2-(2-(2-(2-Allyloxy-3-methoxybenzyloxy)-3-methoxybenzyloxy)-3-methoxybenzyloxy)-3-methoxybenzyl bromide (17d). To a cold (0 °C), stirred solution of **15d** (3.78 g, 6.27 mmol), PPh_3 (2.30 g, 8.78 mmol), and CH_2Cl_2 (50 mL) was added NBS (1.57 g, 8.81 mmol) over a 10 min period. A solution of saturated $NaHCO_3$ (100 mL) was added to the reaction and a dark green color arose. The solution was extracted with CH_2Cl_2 (4 × 25 mL), dried ($MgSO_4$), filtered, and concentrated to a dark oil. Flash chromatography of the crude product (SiO_2, 7 : 3 hexanes-EtOAc) afforded **17d** as a colorless solid (3.92 g, 94%): ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.24–6.81 (m, 12 H); 6.10–5.93 (m, 1 H); 5.25 (dd, J = 1.5, 17.2 Hz, 1 H); 5.14–5.06 (m,7 H); 4.45 (s, 2 H); 4.44 (dt, J = 1.4, 5.4 Hz, 2 H); 3.85 (s, 3 H); 3.83 (s, 3 H); 3.77 (s, 3 H); 3.72 (s, 3 H).

2-(2-Nitro-4-dodecyloxy-5-methoxybenzyloxy)-3-methoxybenzyl bromide (18a). To a cold (0 °C), stirred solution of **16a** (1.44 g, 2.85 mmol), PPh_3 (1.05 g, 4.01 mmol), and CH_2Cl_2 (40 mL) was added NBS (0.74 g, 4.14 mmol) over a 5 min period. A solution of saturated $NaHCO_3$ (50 mL) was added to the reaction and a dark green color arose. The solution was extracted with CH_2Cl_2 (4 × 20 mL), dried ($MgSO_4$), filtered, and concentrated to a dark oil. Flash chromatography of the crude product (SiO_2, 7 : 3 hexanes-EtOAc) afforded **18a** as a yellow solid (1.38 g, 85%): ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.76 (s, 1 H); 7.74 (s, 1 H); 7.09–6.92 (m, 3 H); 5.55 (s, 2 H); 4.52 (s, 2 H); 4.08 (t, J = 6.8 Hz, 2 H); 3.98 (s, 3 H); 3.86 (s, 3 H); 1.87 (quintet, J = 7.9 Hz, 2 H); 1.50–1.26 (m, 18 H); 0.88 (t, J = 6.2 Hz, 3 H).

2-(2-(2-Nitro-4-dodecyloxy-5-methoxybenzyloxy)-3-methoxybenzyloxy)-3-methoxybenzyl bromide (18b). To a cold (0 °C), stirred solution of **16b** (4.88 g, 7.62 mmol), PPh_3 (2.80 g, 10.7 mmol), and CH_2Cl_2 (60 mL) was added NBS (1.91 g, 10.7 mmol) over a 10 min period. A solution of saturated $NaHCO_3$ (100 mL) was added to the reaction and a dark green color arose. The solution was extracted with CH_2Cl_2 (4 × 25 mL), dried ($MgSO_4$), filtered, and concentrated to a dark oil. Flash chromatography of the crude product (SiO_2, 8 : 2 hexanes-EtOAc) afforded **18b** as a yellow solid (4.87 g, 91%): ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.73 (s, 1 H); 7.68 (s, 1 H); 7.21–7.15 (m, 2 H); 6.99–6.92 (m, 3 H); 6.81–6.78 (m, 1 H); 5.41 (s, 2 H); 5.22 (s, 2 H); 4.42 (s, 2 H); 4.08 (t, J = 6.8 Hz, 2 H); 3.97 (s, 3 H); 3.85 (s, 3 H); 3.71 (s, 3 H);

1.88 (quintet, J = 7.9 Hz, 2 H); 1.50–1.26 (m, 18 H); 0.88 (t, J = 6.2 Hz, 3 H).

2-(2-(2-(2-Nitro-4-dodecyloxy-5-methoxybenzyloxy)-3-methoxybenzyloxy)-3-methoxybenzyloxy)-3-methoxybenzyl bromide (18c). To a cold (0 °C), stirred solution of **16c** (2.42 g, 3.12 mmol), PPh_3 (1.14 g, 4.36 mmol), and CH_2Cl_2 (50 mL) was added NBS (0.78 g, 4.39 mmol) over a 10 min period. A solution of saturated $NaHCO_3$ (100 mL) was added to the reaction and a dark green color arose. The solution was extracted with CH_2Cl_2 (4 × 25 mL), dried ($MgSO_4$), filtered, and concentrated to a dark oil. Flash chromatography of the crude product (SiO_2, 7 : 3 hexanes-EtOAc) afforded **18c** as a yellow oil (2.51 g, 96%): ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.67 (s, 1 H); 7.59 (s, 1 H); 7.21–6.81 (m, 9 H); 5.35 (s, 2 H); 5.18 (s, 2 H); 5.10 (s, 2 H); 4.40 (s, 2 H); 4.06 (t, J = 6.8 Hz, 2 H); 3.86 (s, 3 H); 3.82 (s, 3 H); 3.73 (s, 3 H); 3.71 (s, 3 H); 1.88 (quintet, J = 7.9 Hz, 2 H); 1.50–1.26 (m, 18 H); 0.88 (t, J = 6.2 Hz, 3 H).

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