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Control of Surface Functionality in Poly(phenylenevinylene) Dendritic Architectures

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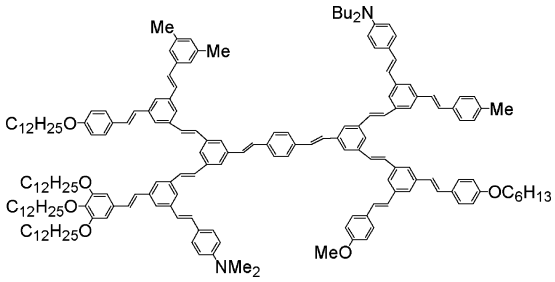

The efficient synthesis of new asymmetric poly(phenylenevinylene) dendritic macromolecules using a stepwise convergent-growth approach is described. By an iterative methodology that made use of the Horner−Wadsworth−Emmons (HWE) reaction, dendrons and dendrimers up to the third generation, with eight different functional groups located at the periphery, were prepared in good yields. Both the number and placement of functionalities can be accurately controlled to afford a large variety of dendritic architectures.

Introduction

In the past two decades a large number of functional dendrimers have been developed. Synthetic methodologies for their preparation, involving convergent and divergent methods, are well established,[1] but the wide scope of their applications is continuously growing.[2] This further increases the burden of synthesis. The convergent approach appears ideally suited for the preparation of dendrimers in which control over both the number and the placement of end functionalities is achieved. Thus, this methodology has been widely used by different authors for the synthesis of highly asymmetrical dendrimers containing a predetermined and well-defined number and arrangement of functional groups at their periphery.[3] Thayumanavan et al. were the first to build dendrons and dendrimers in which all the monomer units are different from each other.[4] They prepared benzyl ether-based dendritic structures, although the synthesis of dendrimers based on melamine with multifunctional periphery has also been achieved.[5] Diversity in functional group display has been also performed through divergent approaches;[6] however, their inherent nature does not allow generating structures in which every peripheral unit is different.

Dendritic poly(phenylenevinylene)s (PPVs), also called stilbenoid dendrimers, represent an important group within this class of material. Different studies have been published to date concerning their synthesis and properties.[7] For example, such compounds have been used successfully as charge transporting,[8]

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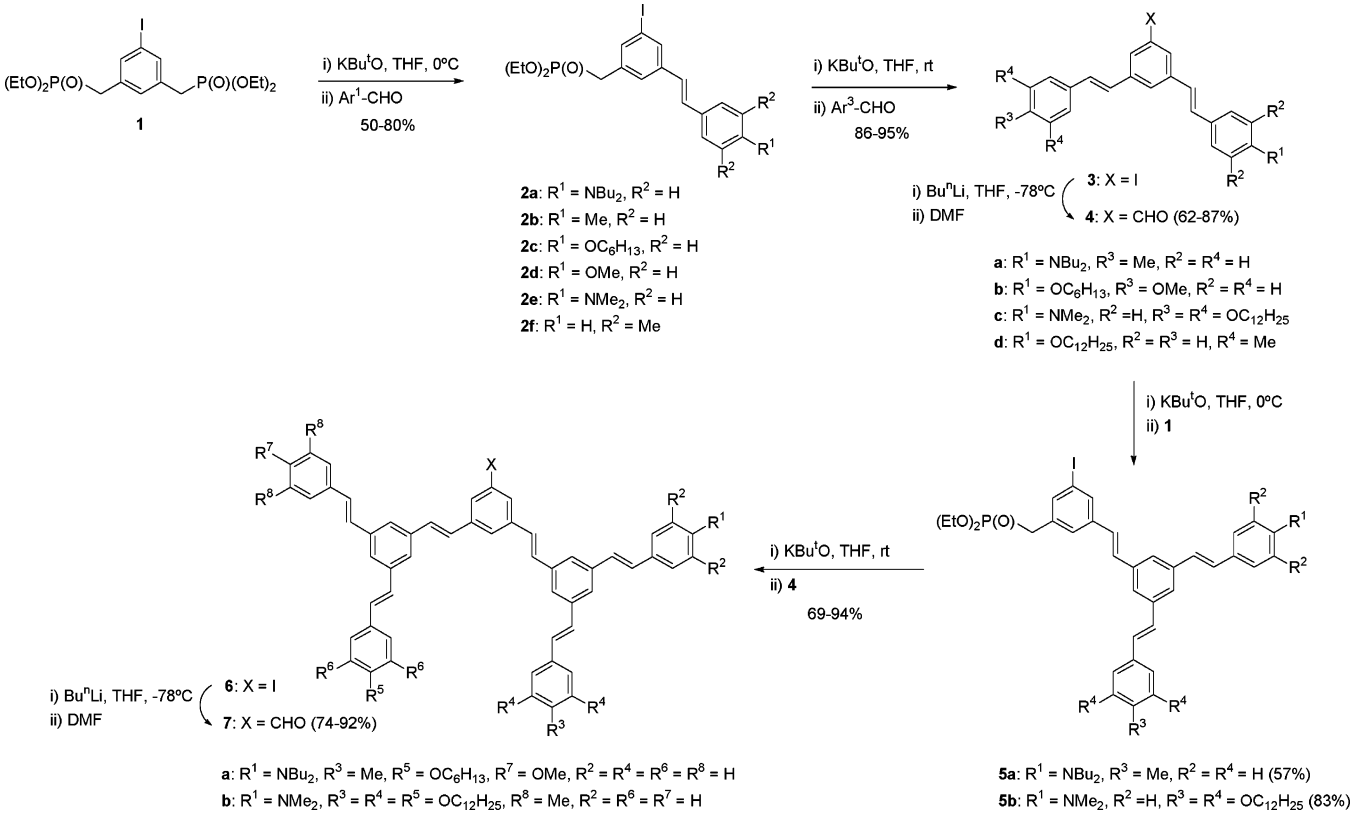
SCHEME 1. Synthesis of Asymmetrical First and Second Generation Dendrons



light-emitting,[9] and electron-transfer materials.[10] It has also been demonstrated that phenylenevinylene dendritic arms can function as light-harvesting antennae.[9b] Nevertheless, the routes that afford the buildup of this class of materials in an asymmetrically surface-functionalized fashion are exceedingly few.[11]

In this context and as a part of our research program aimed at the construction of extended and cross-conjugated π-electronic systems,[11a] we planned to develop an efficient orthogonal and convergent-growth methodology of new asymmetric dendrimer architectures containing phenylenevinylene chromophores within the branches. This has been achieved by the stepwise incorporation of functionalities in a controlled manner onto an AB_2-type monomer unit, using the Horner−Wadsworth−Emmons (HWE) reaction. This reaction has already produced interesting results when applied to the synthesis of dendrimers.[7a−i,9a,b,10,12] In this way, a large variety of dendritic structures were prepared in good yields, including dendrons and dendrimers up to the third generation with eight different functional groups located at the periphery.

Results and Discussion

Our plan was based on our previous work directed toward symmetrical or uniformly functionalized PPV dendrimers[11a] and

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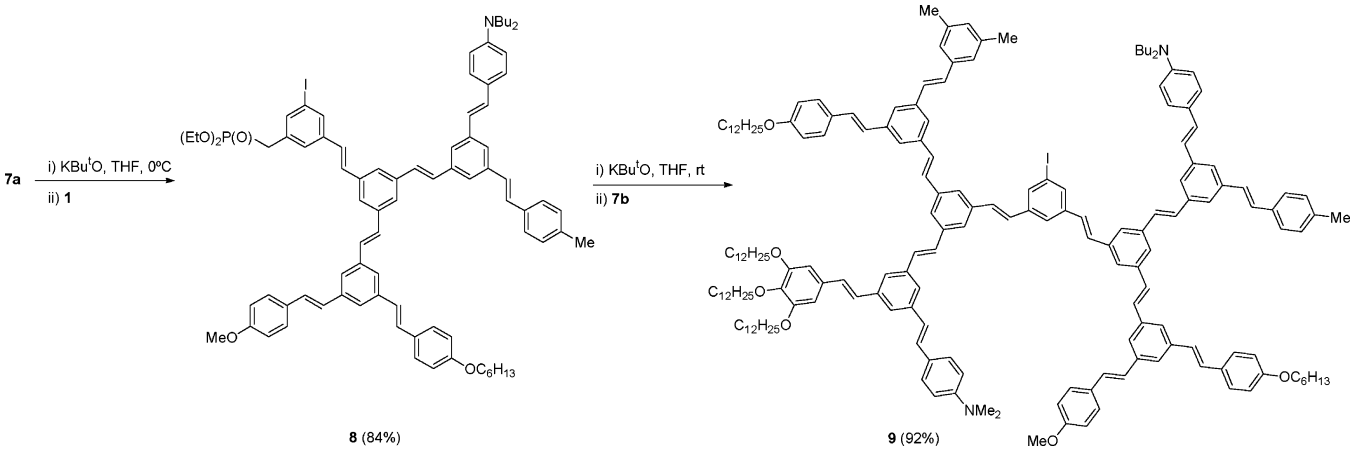
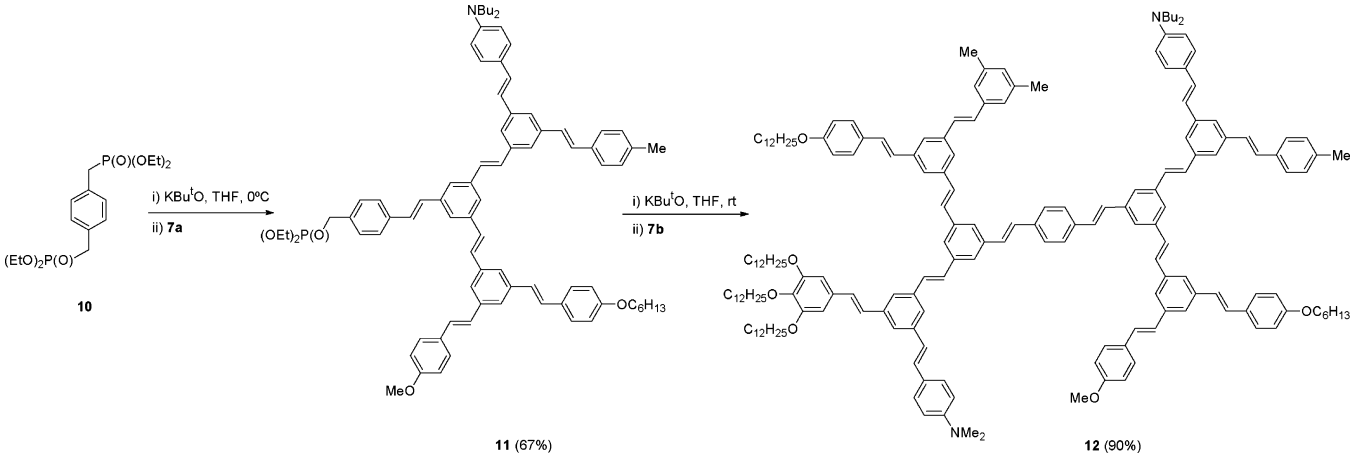
SCHEME 2. Synthesis of Asymmetrical Third Generation Dendron 9



SCHEME 3. Synthesis of Asymmetrical Dendrimer 12



made use of the HWE reaction. Diphosphonate **1** was required as starting material,[13] which contains two coupling sites, as well as a set of either commercially or easily available differently substituted benzaldehyde derivatives.

Scheme 1 shows our iterative approach to obtain homogeneous single functionality dendrons, which contained either an iodo or formyl group at the focal point. The first reaction sequence involved the HWE reaction of one molecule of a benzaldehyde derivative with monomer **1** to form compounds **2a**−**f**, having a free reactive phosphonate group for further coupling. The synthesis was carried out by using only 1.2 equiv of **1** and K^{t}BuO in THF at 0 °C. Although the presence of starting material **1** and the corresponding dicoupled products were also observed in the crude mixture, all of the monophosphonates **2** could be easily separated by column chromatography (silica gel) in good yields (50−80%). A second HWE reaction with a different benzaldehyde derivative gave the desired asymmetrical, first-generation dendrons, **3a**−**d**. Ultimately, two different functional groups are located at the periphery or chain end of the final branched molecules.[14]

The selectivity of the HWE reactions was sufficiently high to generate all-*trans* isomers within the limits of NMR detection. This stereochemistry for the double bonds was unequivocally established on the basis of the coupling constant of the vinylic protons in the ^{1}H NMR spectra ($J \approx 16$ Hz).

Subsequent treatment of dendrons **3** with ^{n}BuLi at −78 °C followed by reaction with DMF gave the corresponding first-generation compounds **4a**−**d** bearing a formyl group at the focal point. These aldehydes are the precursors of the next generation dendrons **6**, which were synthesized by a two-step iterative procedure. Thus, in a similar way as above, compounds **4a** and **4c** were coupled with a slight excess of diphosphonate **1** to afford the monocoupled products **5a** and **5b**, respectively, which after a new HWE reaction with a different first-generation aldehyde **4** formed the asymmetric second-generation dendritic wedges **6a,b**. Transformation into the corresponding aldehyde derivatives **7a,b** could be also obtained in good yields.

Proceeding to generation three, the synthesis of compound **9** was taken as a model, in which all eight branches are different. Its preparation involved the HWE reaction of the second-generation dendron **7a** with a slight excess of monomer **1**. In this way, monophosphonate derivative **8** was isolated in 84% yield after purification. Then, its coupling with the second-generation aldehyde **7b** led to the desired target with a wide variety of peripheral groups (Scheme 2).

In principle, these reaction sequences could be further progressed through multiple cycles, although in practice one would expect that higher molecules would be difficult to prepare because of the well-documented progressive reduction in the reactivity of the focal point in successive generations.[13,15]

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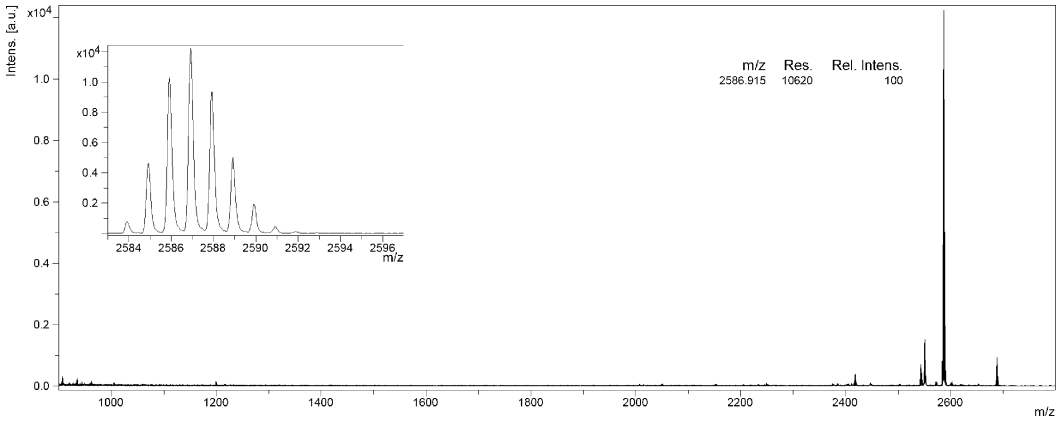

FIGURE 1. MALDI-TOF mass spectrum of compound **12** in a matrix of dithranol.

The groups selected in this work provided good control of the solubility. Indeed, all new molecules prepared are highly soluble in THF as well as in chlorinated solvents such as dichloromethane and chloroform, thus allowing purification by conventional silica gel chromatography. A suitable choice of starting materials could provide a wide variety of dendritic architectures with different peripheral moieties, although peripheral pendant groups should be adequately chosen in order to impart solubility. An example of this potential is shown by the synthesis of the third generation dendrimer **12** starting from the nucleus **10** and the dendrons **7a,b** (Scheme 3).

All compounds were characterized using various analytical techniques. MS and NMR experiments proved very useful to confirm the structures of the compounds (see Experimental Section and Supporting Information). Assessment of the overall purity of these molecules proved difficult. The ^{1}H NMR spectra of dendrons up to generation two are well-resolved in $CDCl_3$ and do not reveal impurities, but the high number of lines in the 7−8 ppm zone could obscure the presence of small amounts of other compounds. Compounds **9** and **12** showed considerable line broadening at 25 °C, which has its origin in reduced segment mobility, a behavior that has been previously observed in high generation PPV dendrimers.[7b,e] However, their spectra were temperature-dependent, and quite normally resolved signals were obtained by heating the sample at 72 °C. The MALDI-TOF technique proved to be very useful for the identification of the higher structures. All of the spectra registered for the higher generations showed peaks matching the calculated molecular weights. As an example, the MALDI-TOF mass spectrum for the third generation dendrimer **12** is given in Figure 1, showing a perfect agreement between the calculated and experimentally determined *m*/*z* ratio and demonstrating the absence of molecules that contain only one dendron.

The size exclusion chromatography elution profile of compound **12** is also shown in Figure 2. It confirms that this molecule is clean and obtained in good purity.

The UV−vis absorption and photoluminescence (PL) spectra of compounds **9** and **12** were recorded in CH_2Cl_2 at room temperature (Figure 3). Owing to the *meta* arrangement through which the stilbene units are linked, it was expected that the absorption spectra would consist of a simple superposition of the absorptions due to the constituent independent chromophores. Indeed, strong bands with maxima at 325 nm for **9** and 329 nm for **12** and large extinction coefficients (ϵ = 348000 and 355300 M^{-1} cm^{-1}, respectively) are observed. The molecules are absolutely transparent above 440 nm. They are also fluorescent and emit strong light when irradiated at the absorption maxima, showing a typical response for the PPV dendrimers,[11a] with a maximum at 509 nm and a shoulder at ca. 434 nm for **9** and a maximum at 510 nm and shoulders at ca. 412 and 434 nm for **12**. The emission spectra obtained by irradiation at different wavelengths are the same regardless of the excitation frequency.

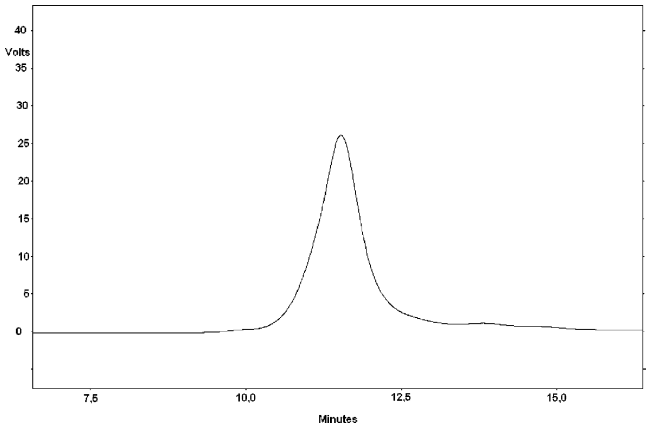

FIGURE 2. Elution profile in size exclusion chromatography for dendrimer **12**.

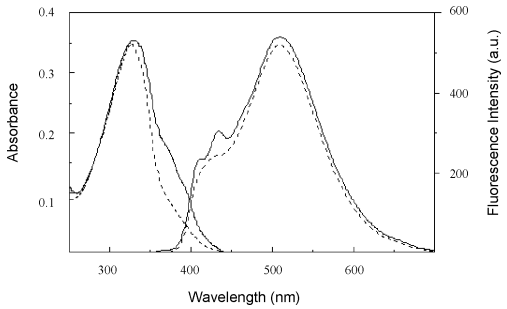

FIGURE 3. UV−vis absorption and fluorescence spectra of dendron **9** (dotted line, λ_{exc} = 325 nm) and dendrimer **12** (solid line, λ_{exc}= 329 nm) ($c = 10^{-6}$ M in CH_2Cl_2 at room temperature).

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Conclusions

New PPV dendritic structures with differentiated surface functionalities have been effectively synthesized up to the third generation using an orthogonal, convergent-growth sequencing methodology based on the HWE reaction. This iterative strategy is extremely general, permitting not only the use of a wide variety of functional groups but also an exquisite control over their placement. The stepwise incorporation of functionalities onto an AB_2 monomer unit proceeds with good yields in the desired product. This approach has its obvious drawback: the desired monosubstituted product is obtained in statistical yield together with the corresponding undesired disubstituted byproduct. However, it avoids the need for protection-deprotection steps that are much more time-consuming. Thus, the methodology reported here may be used as an accelerated access to a wide range of asymmetrically conjugated dendritic architectures. With this methodology the synthesis of many PPV dendrimers with specific substitution patterns would become possible.

Experimental Section

General Procedures for Horner−Wadsworth−Emmons Reactions. Method A (Synthesis of Monosubstituted Phosphonates). To a stirred solution of diphosphonate **1** (1.2 mmol) in anhydrous THF (15 mL), under argon at 0 °C, was added potassium *tert*-butoxide in small portions (1.2 mmol). Ten minutes later the corresponding aromatic aldehyde (1 mmol) dissolved in THF was added, and the reaction mixture was stirred at that temperature for 2 h. After hydrolysis with water, the mixture was extracted with EtAcO (×3). The combined organic layers were successively washed with water and brine and then dried ($MgSO_4$). The solution was filtered, and the solvent was evaporated under reduced pressure. The crude products were purified by column chromatography (silica gel) as indicated. **Method B (Synthesis of Dendritic Iodides).** All operations were identical with those described for method A except that the corresponding monosubstituted phosphonate was used as starting material (1 mmol/mmol of aldehyde). The reactions were carried out at room temperature. After hydrolysis with water, the mixture was extracted with CH_2Cl_2 (×3). The combined organic layers were successively washed with water and brine and then dried ($MgSO_4$). The solution was filtered, and the solvent was evaporated under reduced pressure. The crude products were purified by column chromatography (silica gel) and/or crystallization as indicated.

General Procedure for the Synthesis of Dendritic Aldehydes. To a stirred solution of the corresponding iodide derivative in anhydrous THF (15 mL per mmol), under argon at −78 °C, was added dropwise ^{n}BuLi (1.1 equiv). After 10 min, 3 equiv of DMF was added to quench the reaction mixture, which was then allowed to reach room temperature over a period of 3 h. The mixture was concentrated, taken up in chloroform, washed with water twice, and dried ($MgSO_4$). The solution was filtered, and the solvent was evaporated under reduced pressure. The crude products were purified by column chromatography (silica gel) and/or crystallization as indicated.

Representative examples for the preparation of different dendrons and dendrimers are described below.

Compound 2e. Purified by column chromatography (SiO_2, hexanes/EtAcO, 1:1). Yield: 67%. Yellow oil. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 1.25 (t, 6H, J = 7.0 Hz), 2.94 (s, 6H), 3.04 (d, 2H, J = 21.5 Hz), 4.00−4.10 (m, 4H, J = 7.0 Hz), 6.67 (A of AB_q, 2H, J = 8.5 Hz), 6.72 (A of AB_q, 1H, J = 16.5 Hz), 6.99 (B of AB_q, 1H, J = 16.0 Hz), 7.32 (br s, 1H), 7.35 (B of AB_q, 2H, J = 8.5 Hz), 7.42 (br s, 1H), 7.67 (br s, 1H). ^{13}C NMR and DEPT ($CDCl_3$, 125 MHz) δ: 150.0 (C), 140.2 (d, J = 3.2 Hz, C), 136.1 (d, J = 6.4 Hz, CH), 133.7 (d, J = 9.6 Hz, C), 132.9 (d, J = 3.1 Hz, CH), 130.1 (CH), 127.5 (CH), 126.5 (d, J = 7.2 Hz, CH), 124.7 (C), 121.8 (CH), 112.1 (CH), 94.4 (d, J = 4.0 Hz, C), 62.0 (d, J = 7.2 Hz, CH_2), 40.1 (CH_3), 32.9 (d, J = 137.0 Hz, CH_2), 16.2 (d, J = 5.6 Hz, CH_3). MS (EI) *m*/*e* 499.1 (100). HRMS, *m*/*e* calcd for $C_{21}H_{27}INO_3P$ 499.0773; found 499.0765.

Compound 3b. Purified by column chromatography (SiO_2, hexanes/EtAcO, 9:1) and washed with cold ethanol. Yield: 86%. Colorless solid. Mp 84−86 °C. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 0.91 (t, 3H, J = 7.0 Hz), 1.32−1.38 (m, 4H), 1.43−1.50 (m, 2H), 1.79 (m, 2H), 3.83 (s, 3H), 3.98 (t, 2H, J = 6.5 Hz), 6.85 (A of AB_q, 1H, J = 16.5 Hz), 6.86 (A of AB_q, 1H, J = 16.5 Hz), 6.89 (A of AB_q, 2H, J = 9.0 Hz), 6.91 (A of AB_q, 2H, J = 9.0 Hz), 7.06 (B of AB_q, 1H, J = 16.5 Hz), 7.06 (B of AB_q, 1H, J = 16.5 Hz), 7.43 (B of AB_q, 2H, J = 9.0 Hz), 7.45 (B of AB_q, 2H, J = 9.0 Hz), 7.48 (broad s, 1H), 7.69 (s, 1H), 7.69 (s, 1H). ^{13}C NMR and DEPT ($CDCl_3$, 125 MHz) δ: 159.6 (C), 159.2 (C), 140.0 (C), 140.0 (C), 133.5 (CH), 133.4 (CH), 129.8 (CH), 129.7 (CH), 129.6 (C), 129.4 (C), 127.9 (CH), 127.9 (CH), 124.8 (CH), 124.6 (CH), 123.7 (CH), 114.8 (CH), 114.2 (CH), 95.2 (C), 68.1 (CH_2), 55.3 (CH_3), 31.6 (CH_2), 29.2 (CH_2), 25.7 (CH_2), 22.6 (CH_2), 14.0 (CH_3). MS (EI) *m*/*e* 538.1 (M^+, 100), 454.0 (53). HRMS, *m*/*e* calcd for $C_{29}H_{31}IO_2$ 538.1369; found 538.1367. Anal. Calcd for $C_{29}H_{31}IO_2$: C, 64.69; H, 5.80; I, 23.57. Found: C, 64.74; H, 5.78; I, 23.32.

Compound 4a. Purified by column chromatography (SiO_2, hexanes/EtAcO, 9.9:0.1). Yield: 87%. Yellow oil that solidified upon standing. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 0.97 (t, 6H, J = 7.5 Hz), 1.30−1.40 (m, 4H), 1.56−1.62 (m, 4H), 2.37 (s, 3H), 3.30 (t, 4H, J = 7.5 Hz), 6.64 (A of AB_q, 2H, J = 9.0 Hz), 6.91 (A of AB_q, 1H, J = 16.5 Hz), 7.10 (A of AB_q, 1H, J = 16.0 Hz), 7.16 (B of AB_q, 1H, J = 16.5 Hz), 7.19 (A of AB_q, 2H, J = 8.0 Hz), 7.21 (B of AB_q, 1H, J = 16.0 Hz), 7.40 (B of AB_q, 2H, J = 9.0 Hz), 7.44 (B of AB_q, 2H, J = 8.0 Hz), 7.78 (s, 1H), 7.81 (s, 1H), 7.84 (s, 1H), 10.05 (s, 1H). ^{13}C NMR and DEPT ($CDCl_3$, 125 MHz) δ: 192.6 (CH), 148.2 (C), 139.8 (C), 138.7 (C), 138.0 (C), 137.1 (C), 134.1 (C), 130.9 (CH), 130.3 (CH), 129.6 (CH), 129.5 (CH), 128.0 (CH), 126.6 (CH), 126.3 (CH), 125.7 (CH), 125.1 (CH), 123.7 (C), 121.7 (CH), 111.6 (CH), 50.8 (CH_2), 29.5 (CH_2), 21.3 (CH_3), 20.3 (CH_2), 14.0 (CH_3). IR ν: 1670 (C═O) cm^{-1}. MS (EI) *m*/*e* 451.3 (M^+, 82), 408.2 (100), 366.2 (41). HRMS, *m*/*e* calcd for $C_{32}H_{37}NO$ 451.2875; found 451.2885. Anal. Calcd for $C_{32}H_{37}NO$: C, 85.10; H, 8.26; N, 3.10. Found: C, 84.89; H, 8.27; N, 3.12.

Compound 5b. Purified by column chromatography (SiO_2, hexanes/EtAcO, 1:1, then EtAcO). Yield: 83%. Yellow oil. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 0.88 (t, 6H, J = 7.0 Hz), 0.89 (t, 3H, J = 7.0 Hz), 1.20−1.40 (m, 54H), 1.45−1.53 (m, 6H), 1.76 (m, 2H, J = 7.0 Hz), 1.84 (m, 4H, J = 7.0 Hz), 3.01 (s, 6H), 3.11 (d, 2H, J = 21.6 Hz), 3.98 (t, 2H, J = 6.6 Hz), 4.03−4.10 (m, 8H), 6.75 (broad s, 4H), 6.94 (A of AB_q, 1H, J = 16.3 Hz), 7.00 (A of AB_q, 1H, J = 16.2 Hz), 7.05 (A of AB_q, 1H, J = 16.3 Hz), 7.09 (B of AB_q, 1H, J = 16.3 Hz), 7.13 (B of AB_q, 1H, J = 16.5 Hz), 7.13 (B of AB_q, 1H, J = 16.3 Hz), 7.35−7.54 (m, 7H), 7.79 (d, 1H, J = 1.6 Hz). ^{13}C NMR and DEPT ($CDCl_3$, 125 MHz) δ: 153.3 (C), 150.1 (C), 139.5 (d, J = 3.1 Hz, C), 138.9 (C), 139.3 (C), 138.0 (C), 137.4 (d, J = 6.8 Hz, CH), 137.2 (C), 134.1 (d, J = 8.9 Hz, C), 133.8 (d, J = 3.0 Hz, CH), 132.4 (C), 130.2 (CH), 129.4 (CH), 129.3 (CH), 127.7 (CH), 127.4 (d, J = 6.4 Hz, CH), 127.3 (CH), 126.9 (CH), 125.5 (C), 123.9 (CH), 123.5 (CH), 122.8 (CH), 120.6 (CH), 112.4 (CH), 105.1 (CH), 94.6 (d, J = 3.5 Hz, C), 73.5 (CH_2), 69.1 (CH_2), 62.3 (d, J = 6.8 Hz, CH_2), 40.4 (CH_3), 33.2 (d, J = 138.4 Hz, CH_2), 31.9 (CH_2), 31.9 (CH_2), 30.3 (CH_2), 29.7 (CH_2), 29.7 (CH_2), 29.7 (CH_2), 29.7 (CH_2), 29.6 (CH_2), 29.6 (CH_2), 29.4 (CH_2), 29.4 (CH_2), 29.4 (CH_2), 29.3 (CH_2), 26.1 (CH_2), 22.7 (CH_2), 22.6 (CH_2), 16.4 (d, J = 5.9 Hz, CH_3), 14.1 (CH_3). ^{31}P NMR ($CDCl_3$, 162 MHz) δ: 26.1. MS (MALDI) *m*/*e* 1256.7 (MH^+), 1129.8 (MH^+ − 127). HRMS, *m*/*e* calcd for $C_{73}H_{111}INO_6P$: 1255.7194; found 1255.7206.

Compound 6b. Purified by washing with methanol. Yield: 94%. Yellow solid. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 0.85−0.90 (m, 12H), 1.20−1.40 (m, 64H), 1.43−1.53 (m, 8H), 1.73−1.87 (m, 8H), 2.36 (s, 6H), 3.00 (s, 6H), 3.98 (t, 2H, J = 6.6 Hz), 3.99 (t, 2H, J = 6.6 Hz), 4.04 (t, 4H, J = 6.5 Hz), 6.75 (broad s, 4H), 6.91 (A of AB_q,

2H, J = 9.0 Hz), 6.92−7.22 (m including AB systems, 15H, J = 16.0 Hz, J = 16.5 Hz), 7.45 (B of AB_q, 2H, J = 8.8 Hz), 7.47 (B of AB_q, 2H, J = 8.8 Hz), 7.50−7.55 (m, 6H), 7.60 (broad s, 1H), 7.78 (broad s, 2H). ^{13}C NMR and DEPT ($CDCl_3$, 125 MHz) δ: 159.0 (C), 153.3 (C), 150.1 (broad, C), 139.7 (C), 139.6 (C), 138.9 (C), 138.5(C), 138.4 (C), 138.2 (C), 138.1 (C), 138.1 (C), 137.4 (C), 137.3 (C), 137.1 (C), 134.3 (CH), 134.2 (CH), 132.4 (C), 130.2 (CH), 130.1 (CH), 129.7 (C), 129.6 (CH), 129.5 (CH), 129.4 (CH), 129.0 (CH), 127.9 (CH), 127.8 (CH), 127.7 (CH), 127.4 (CH), 127.2 (CH), 127.1 (CH), 125.9 (CH), 124.5 (CH), 124.2 (CH), 123.9 (CH), 123.7 (CH), 123.5 (CH), 123.5 (CH), 123.0 (CH), 114.7 (CH), 112.5 (broad, CH), 105.2 (CH), 95.2 (C), 73.6 (CH_2), 69.2 (CH_2), 68.1 (CH_2), 40.5 (broad, CH_3), 31.9 (CH_2), 31.9 (CH_2), 30.4 (CH_2), 29.8 (CH_2), 29.7 (CH_2), 29.7 (CH_2), 29.7 (CH_2), 29.7 (CH_2), 29.6 (CH_2), 29.6 (CH_2), 29.6 (CH_2), 29.5 (CH_2), 29.5 (CH_2), 29.4 (CH_2), 29.4 (CH_2), 29.4 (CH_2), 29.3 (CH_2), 29.3 (CH_2), 26.2 (CH_2), 26.1 (CH_2), 22.7 (CH_2), 21.3 (CH_3), 14.1 (CH_3). MS (MALDI) *m*/*e* 1625.0 (MH^+), 1498.0 ($MH^+ - 127$). HRMS, *m*/*e* calcd for $C_{106}H_{146}INO_4$ 1624.0297; found 1624.0269.

Compound 7a. Purified by column chromatography (SiO_2, hexanes/CH_2Cl_2, 1:1, then CH_2Cl_2). Yield: 92%. Yellow solid. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 0.92 (t, 3H, J = 7.0 Hz), 0.97 (t, 6H, J = 7.0 Hz), 1.30−1.40 (m, 6H), 1.45 (m, 2H), 1.58 (m, 4H), 1.77 (m, 2H), 2.35 (s, 3H), 3.28 (t, 4H, J = 7.5 Hz), 3.79 (s, 3H), 3.92 (t, 2H, J = 7.0 Hz), 6.62 (A of AB_q, 2H, J = 9.0 Hz), 6.82−6.92 (m, 7H), 6.99−7.17 (m, 11H), 7.36−7.45 (m, 14H), 7.73 (br s, 1H), 7.79 (br s, 2H), 9.96 (s, 1H). ^{13}C NMR and DEPT ($CDCl_3$, 125 MHz) δ: 192.2 (CH), 159.3 (C), 159.0 (C), 147.9 (C), 138.9 (C), 138.5 (C), 138.4 (C), 138.3 (C), 138.2 (C), 138.0 (C), 137.5 (C), 137.1 (C), 137.0 (C), 134.4 (C), 130.4 (CH), 130.2 (CH), 130.1 (CH), 129.9 (C), 129.7 (C), 129.4 (CH), 128.8 (CH), 128.7 (CH), 128.6 (CH), 127.9 (CH), 127.8 (CH), 127.8 (CH), 127.4 (CH), 127.1 (CH), 126.9 (CH), 126.5 (CH), 126.4 (CH), 126.2 (CH), 126.1 (CH), 125.9 (CH), 124.2 (C), 124.0 (CH), 123.9 (CH), 123.4 (CH), 123.0 (CH), 122.8 (CH), 114.7 (CH), 114.1 (CH), 111.6 (CH), 68.0 (CH_2), 55.2 (CH_3), 50.7 (CH_2), 31.6 (CH_2), 29.5 (CH_2), 29.2 (CH_2), 25.7 (CH_2), 22.6 (CH_2), 21.2 (CH_3), 20.3 (CH_2), 14.0 (CH_3), 14.0 (CH_3). IR ν: 1697 (C═O) cm^{-1}. MS (MALDI) *m*/*e* 990.5 (MH^+). HRMS, *m*/*e* calcd for $C_{71}H_{75}NO_3$ 989.5746; found 989.5738.

Compound 8. Purified by column chromatography (SiO_2, CH_2Cl_2, then CH_2Cl_2/EtOAc 1:1). Yield: 84%. Yellow solid. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 0.92 (t, 3H, J = 7.0 Hz), 0.97 (t, 6H, J = 7.5 Hz), 1.28 (t, 6H, J = 7.0 Hz), 1.30−1.40 (m, 6H), 1.46 (m, 2H), 1.59 (m, 4H), 1.78 (m, 2H), 2.37 (s, 3H), 3.06 (d, 2H, J = 21.5 Hz), 3.29 (t, 4H, J = 7.5 Hz), 3.82 (s, 3H), 3.92 (t, 2H, J = 7.0 Hz), 4.06 (m, 4H), 6.64 (A of AB_q, 2H, J = 8.5 Hz), 6.86−7.20 (m, 20H), 7.40−7.52 (m, 18H), 7.57 (br s, 1H), 7.77 (br s, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 159.3, 159.0, 147.9, 139.5 (d, J = 2.8 Hz), 139.0, 138.3, 138.2, 138.1, 138.0, 138.0, 137.6, 137.5 (d, J = 3.1 Hz), 137.3, 134.5, 134.2 (d, J = 8.7 Hz), 133.8, 130.0, 129.9, 129.8, 129.4, 129.4, 129.3, 129.1, 128.8, 128.7, 128.6, 128.3, 128.2, 127.9, 127.8, 127.8, 127.6, 127.5 (d, J = 6.4 Hz), 127.1, 126.5, 126.3, 126.1, 124.5, 124.3, 124.1, 124.0, 123.8, 123.7, 123.3, 123.2, 122.8, 114.7, 114.1, 111.6, 94.7 (d, J = 3.5 Hz), 68.0, 62.3 (d, J = 6.9 Hz), 55.3, 50.7, 33.2 (d, J = 137.0 Hz), 31.6, 29.5, 29.2, 25.7, 22.6, 21.3, 20.3, 16.4 (d, J = 6.0 Hz), 14.0, 14.0. ^{31}P NMR ($CDCl_3$, 162 MHz) δ: 26.1. MS (MALDI) *m*/*e* 1340.9 (MH^+), 1213.9 ($MH^+ - 127$).

Compound 9. Purified by column chromatography (SiO_2, hexanes/CH_2Cl_2 1:1, then CH_2Cl_2). Yield: 92%. Yellow solid. ^{1}H NMR ($CDCl_3$, 72 °C, 500 MHz) δ: 0.85−0.91 (m, 15H), 0.94 (t, 6H, J = 7.5 Hz), 1.20−1.38 (m, 72H, J = 7.5 Hz), 1.40−1.50 (m, 10H), 1.58 (m, 4H), 1.72−1.82 (m, 10H), 2.31 (s, 6H), 2.32 (s, 3H), 2.93 (s, 6H), 3.26 (t, 4H, J = 7.5 Hz), 3.77 (s, 3H), 3.93 (t, 4H, J = 7.0 Hz), 3.96−4.02 (m, 6H), 6.69−6.72 (m including s and A of AB_q, 6H, J = 8.5 Hz), 6.84−7.21 (m, 39H), 7.37−7.58 (m, 31H), 7.75 (s, 2H). ^{13}C NMR and DEPT ($CDCl_3$, 72 °C, 125 MHz) δ: 159.7 (C), 159.3 (C), 159.3 (C), 153.6 (C), 150.4 (C), 148.1 (C), 139.8 (C), 139.8 (C), 139.3 (C), 139.2 (C), 138.7 (C), 138.6 (C), 138.6 (C), 138.4 (C), 138.4 (C), 138.4 (C), 138.4 (C), 138.3 (C), 138.1 (C), 138.0 (C), 137.9 (C), 137.9 (C), 137.8 (C), 137.8 (C), 137.7, (C), 137.5 (C), 137.4 (C), 137.3 (C), 134.9 (C), 134.6 (CH), 132.7 (C), 130.4 (C), 130.2 (C), 130.1 (CH), 129.6 (CH), 129.6 (CH), 129.5 (CH), 129.2 (CH), 129.1 (CH), 129.0 (CH), 128.9 (CH), 128.7(CH), 128.6 (CH), 128.6 (CH), 128.5 (CH), 128.2 (CH), 128.0 (CH), 127.9 (CH), 127.9 (CH), 127.8 (CH), 127.7 (CH), 127.6 (CH), 127.5 (CH), 126.6 (CH), 126.4 (CH), 126.4 (CH), 124.7 (CH), 124.4 (CH), 124.3 (CH), 124.2 (CH), 124.1 (CH), 124.0 (CH), 124.0 (CH), 123.9 (CH), 123.9 (CH), 123.6 (CH), 123.6 (CH), 123.5 (CH), 123.2 (CH), 115.1 (CH), 114.4 (CH), 112.8 (CH), 106.2 (CH), 95.2 (C), 73.7 (CH_2), 69.7 (CH_2), 68.4 (CH_2), 55.3 (CH_3), 51.4 (broad, CH_2), 40.5 (CH_3), 32.0 (CH_2), 32.0 (CH_2), 31.7 (CH_2), 30.5 (CH_2), 29.8 (CH_2), 29.7 (CH_2), 29.7 (CH_2), 29.7 (CH_2), 29.7 (CH_2), 29.6 (CH_2), 29.6 (CH_2), 29.5 (CH_2), 29.5 (CH_2), 29.5 (CH_2), 29.4 (CH_2), 29.4 (CH_2), 29.4 (CH_2), 29.3 (CH_2), 26.3 (CH_2), 26.2 (CH_2), 25.8 (CH_2), 22.7 (CH_2), 22.6 (CH_2), 21.3 (CH_3), 21.2 (CH_3), 20.4 (CH_2), 14.0 (CH_3), 13.9 (CH_3), 13.8 (CH_3). MS (MALDI) *m*/*e* 2712.7 (MH^+), 2585.7 ($MH^+ - 127$).

Compound 11. Purified by column chromatography (SiO_2, CH_2Cl_2, then CH_2Cl_2/EtOAc 1:1). Yield: 67%. Yellow solid. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 0.92 (t, 3H, J = 7.0 Hz), 0.98 (t, 6H, J = 7.5 Hz), 1.28 (t, 6H, J = 7.0 Hz), 1.30−1.40 (m, 8H), 1.48 (m, 2H), 1.59 (m, 4H), 1.79 (m, 2H), 2.38 (s, 3H), 3.19 (d, 2H, J = 21.5 Hz), 3.31 (broad t, 4H, J = 7.5 Hz), 3.85 (s, 3H), 3.99 (t, 2H, J = 6.5 Hz), 4.05 (m, 4H), 6.66 (A of AB_q, 2H, J = 7.5 Hz), 6.92 (A of AB_q, 2H, J = 9.0 Hz), 6.94 (A of AB_q, 2H, J = 9.0 Hz), 7.03 (A of AB_q, 1H, J = 16.5 Hz),), 7.04 (A of AB_q, 1H, J = 16.5 Hz), 7.10−7.35 (m, 14H), 7.42−7.54 (m, 21H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 159.4, 159.0, 147.9, 139.0, 138.4, 138.3, 138.1, 138.0, 137.8, 137.7, 137.5, 135.9, 134.6, 131.2, 131.1, 130.2, 130.1, 130.1, 129.8, 129.4, 129.3, 129.1, 128.9, 128.8, 128.7, 128.6 128.5, 128.3, 128.1, 127.9, 127.8, 127.8, 127.6, 127.0, 126.9, 126.8, 126.7, 126.7, 126.7, 126.5, 126.3, 126.1, 124.3, 124.1, 124.0, 123.9, 123.7, 123.7, 123.4, 123.4 123.2, 122.8, 114.7, 114.2, 111.6, 68.1 (OCH_2), 62.2 (d, J = 6.8 Hz), 55.3, 50.8, 33.6 (d, J = 137.5 Hz), 31.6, 29.5, 29.2, 25.7, 22.6, 21.3, 20.3, 16.4 (d, J = 6.0 Hz), 14.0, 14.0. ^{31}P NMR ($CDCl_3$, 162 MHz) δ: 26.8. MS (MALDI) *m*/*e* 1215.0 (MH^+).

Compound 12. Purified by column chromatography (SiO_2, hexanes/CH_2Cl_2, 1:1, then CH_2Cl_2). Yield: 90%. Yellow solid. ^{1}H NMR ($CDCl_3$, 72 °C, 500 MHz) δ: 0.85−0.93 (m, 15H), 0.96 (t, 6H, J = 7.5 Hz), 1.20−1.40 (m, 66H), 1.49 (m, 12H), 1.61 (m, 6H), 1.72−1.85 (m, 12H), 2.35 (s, 6H), 2.36 (s, 3H), 2.98 (s, 6H), 3.30 (t, 4H, J = 7.0 Hz), 3.82 (s, 3H), 3.97−4.01 (m, 4H), 4.04 (t, 6H, J = 7.0 Hz), 6.74−6.76 (A of AB_q and s, 6H), 6.89−7.23 (m, 39H), 7.42−7.61 (m, 34H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 159.3, 159.0, 153.3, 150.1, 147.9, 138.4, 138.3, 138.2, 138.1, 138.0, 137.9, 137.7, 137.7, 137.2, 136.7, 134.6, 132.5, 130.1, 129.8, 129.8, 129.5, 129.4, 129.3, 128.9, 128.8, 128.7, 128.6, 128.5, 128.5, 128.3, 128.0, 127.9, 127.8, 127.7, 127.5, 127.0, 126.5, 126.3, 126.1, 126.1, 126.1, 124.5, 124.2, 123.9, 123.7, 123.6, 123.5, 123.4, 123.0, 114.7, 114.2, 112.5, 111.6, 105.2, 73.5, 69.1, 68.1, 55.3, 50.8, 40.5, 32.0, 31.9, 31.6, 30.4, 29.8, 29.7, 29.7, 29.6, 29.6, 29.5, 29.5, 29.4, 29.4, 29.3, 29.3, 26.2, 26.1, 25.7, 22.7, 22.6, 21.4, 21.3, 20.3, 14.1, 14.1, 14.0. MS (MALDI) *m*/*e* 2586.9 (MH^+).

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Supporting Information Available: Compound characterization data and copies of ^{1}H NMR and ^{13}C NMR spectra for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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