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Extending the Limits of Precision Polymer Synthesis: Giant Polyphenylene Dendrimers in the Megadalton Mass Range Approaching Structural Perfection

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S *Supporting Information*

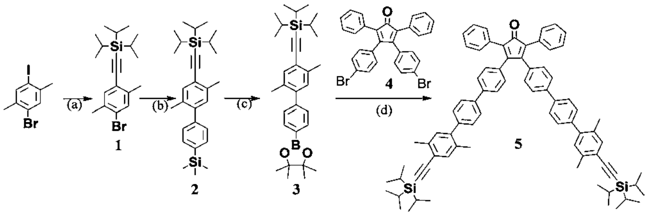
ABSTRACT: The catalyst-free Diels–Alder synthesis of polyphenylene dendrimers with a chromophore core has now been demonstrated to achieve the seventh to ninth generations upon divergent growth. Since standard analytical tools such as size-exclusion chromatography do not provide realistic molecular weights, MALDI-TOF mass spectrometry was applied to characterize the complete series of nine generations. Perfection and monodispersity were thus elucidated at such high masses. Transmission electron microscopy imaging was used to determine the size of these molecularly defined nanosized "particles" with diameters of up to 33 nm.

Among the different synthetic macromolecules in the megadalton mass range that can be prepared on a laboratory or industrial scale, high-generation dendrimers stand out for their well-defined shapes, monodispersity, and structural perfection.[1] Nevertheless, there exist only a few literature reports dealing with the synthesis of very large dendrimers, and many of the reported compounds have not been thoroughly characterized.[2,3] This shortcoming has so far hampered a discussion whether dendrimers are suitable test cases for precision synthesis of high-molecular-weight polymers.

Two problems are commonly encountered during the synthesis of high-generation dendrimers: (i) the occurrence of structural defects and (ii) dendrimer aggregation by interdigitation of dendrimer arms.[4] In regard the first issue, defects in the dendritic structure can arise through incomplete reactions brought about by steric congestion at the periphery,[5] reactions with yields below unity,[2c,3d,6] or backfolding of flexible dendritic branches, which hides their functional groups.[3c,7] The aim of this work was to prepare defect-free polyphenylene dendrimers (PPDs) with diameters of up to 33 nm using a simplified and scalable synthetic procedure. Pushing the limits of polymer chemistry with PPDs as models is a matter of not only redesigning the dendrimer architecture and improving the synthetic techniques applied but also making physical methods of structure proof applicable.

Our approach utilized an easily accessible building block (**5**; Scheme 1) and a large perylenediimide (PDI) core in a repetitive Diels–Alder cycloaddition (Scheme 2). This strategy enabled us for the first time to synthesize and characterize PPDs up to the ninth generation. To the best of our knowledge, these dendrimers are the biggest and best-characterized dendrimers known to date. Theoretically, **G9** has a diameter of ~33 nm and a molecular mass approaching 1.9 MDa. Unlike any other reported large dendrimers,[2c,3c,4,8] those described in this paper (i) are bigger in size; (ii) are almost free of structural defects; (iii) possess a highly luminescent PDI chromophore in the center; and (iv) most importantly, can be isolated and characterized by a series of analytical techniques, including ^{1}H and ^{13}C NMR, FTIR, UV–vis absorption, and luminescence spectroscopy as well as size-exclusion chromatography (SEC) and, as the most powerful tool, matrix-assisted laser desorption ionization mass spectrometry (MALDI-TOF MS). The presence of the PDI core, in addition to allowing optical detection of the dendrimers, is instrumental in the MS detection.

Scheme 1. Synthesis of the Masked AB$_2$ Building Block 5[a]



[a]Reagents and conditions: (a) TIPS-acetylene, [PdCl$_2$(PPh$_3$)$_2$], CuI, PPh$_3$, TEA/toluene (2:1), 0 °C → r.t., 20 h, 70%. (b) 4-(Trimethylsilyl)phenylboronic acid, K$_2$CO$_3$, tetra-*n*-butylammonium bromide (TBAB), [Pd(PPh$_3$)$_4$], toluene/water (2:1), 80 °C, 36 h, 66%. (c) (i) BBr$_3$, dry CH$_2$Cl$_2$, 0 °C → r.t., 3 h; (ii) pinacol, EtOAc, 77% for two steps. (d) K$_2$CO$_3$, TBAB, [Pd(PPh$_3$)$_4$], toluene/water (4:1), 80 °C, 20 h, 50%.

To push the limits of polymer synthesis, PPDs are ideal objects because (i) the reactive groups on the surfaces are sterically accessible as a result of the lack of backfolding of the dendrimer arms and (ii) our repetitive Diels–Alder cycloaddition method for divergent dendrimer growth is high-yielding and irreversible as a result of the extrusion of CO. While this is analogous to that of the parent PPDs,[2a] two key ingredients are now needed: the multiethynyl-functionalized PDI chromophore core **6** (see Scheme 2) and the AB$_2$ building block **5** with extended arms. In principle, one could have considered even more "exploded" AB$_2$ reagents for faster dendrimer growth, but the efficient

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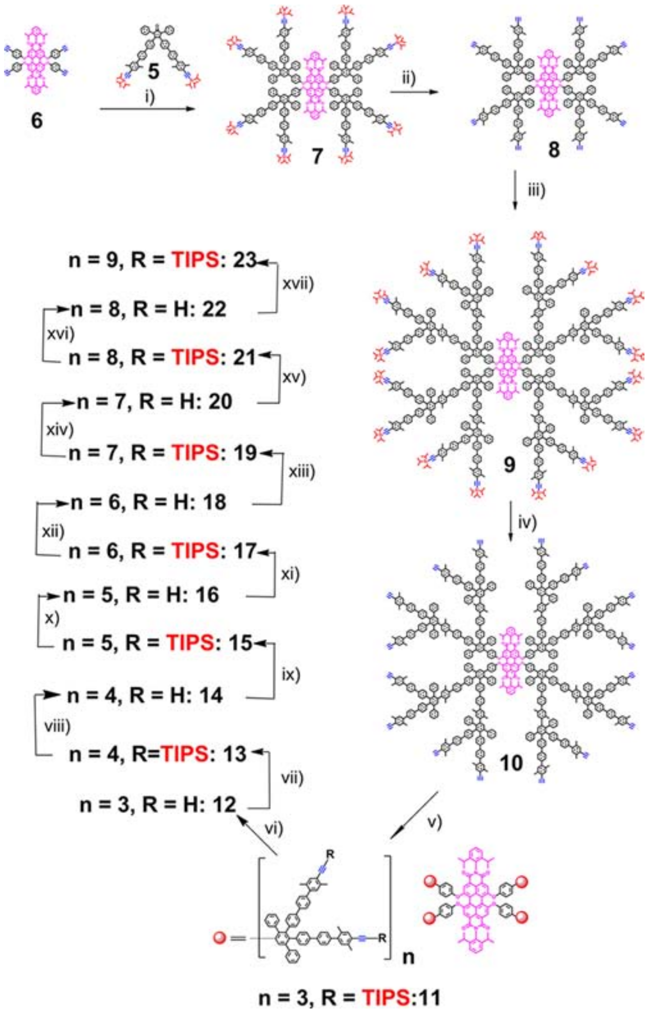
Scheme 2. Synthesis of the G1 through G9 Dendrimers[a]



[a]Reagents and conditions: *o*-Xylene, 145 °C, and tetracyclone **5** for (i), (iii), (v), (vii), (ix), (xi), (xiii), (xv), and (xvii); TBAF, THF, r.t. for (ii), (iv), (vi), (viii), (x), (xii), (xiv), and (xvi). Yields: (i) 95.8%; (ii) 90%; (iii) 91.9%; (iv) 90.5%; (v) 95.4%; (vi) 93.9%; (vii) 95.0%; (viii) 75.0%; (ix) 81.3%; (x) 88.5%; (xi) 82.1%; (xii) 87.3%; (xiii) 85.7%; (xiv) 95.0%; (xv) 78.0%; (xvi) 92.0%; (xvii) 75.3%.

synthesis of **5** in only four steps (Scheme 1) was essential for achieving sufficient amounts of ultrahigh-molecular-weight products. Fourfold Diels–Alder cycloaddition of **5** to **6** afforded the first-generation dendrimer **7** bearing eight triisopropylsilyl (TIPS)-protected ethynyl chain ends. Deprotection of the ethynyl groups was achieved with tetrabutylammonium fluoride trihydrate (TBAF), quantitatively affording pure deprotected dendrimers **G1** (**8**). The reaction cycle was repeated throughout eight generations, and the final coupling yielded the **G9** dendrimer with 2048 TIPS-protected ethynyl chain ends and 18 402 benzene rings! On the experimental side, making such large PPDs accessible required significant improvements over the established techniques. Thus, an additional purification step involving analytical SEC proved to be essential for high-generation dendrimers. Furthermore, to avoid side reactions, the deprotected dendrimers after desilylation had to be kept in the dark at temperatures below 40 °C. Because of the large dihedral angles between adjacent phenyl rings in the semirigid PPDs, all of the synthesized dendrimers, in spite of their high molecular weights, showed good solubility in most common organic solvents (except for alcohols and alkanes). All of the intermediates and final products could thus be characterized completely. Full synthetic details and analytical data for all of the reported compounds can be found in the Supporting Information (SI).

Successful purification of the dendrimers after each synthetic step enabled us to isolate the single dendrimers, as reflected in the relatively well-resolved peaks in the ^{1}H NMR spectra shown in Figure 1. The aromatic resonances from the third- to the ninth-generation dendrimers, however, were virtually identical, as the peaks for the protons from the PDI core (around 8.22 ppm) were "diluted". All of the ^{1}H NMR spectra showed relative signal intensities of aromatic and TIPS protons in agreement with the structural formula. Moreover, no signal at 3.15 ppm originating from unreacted ethynyl groups could be detected after each Diels–Alder cycloaddition providing additional proof that the reactions were quantitative.

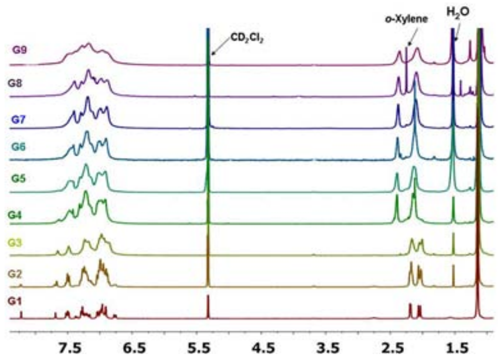


Figure 1. 300 MHz ^{1}H NMR spectra of **G1** and **G2** and 500 MHz ^{1}H NMR spectra of **G3**–**G9** in CD_2Cl_2 at 298 K.

Sharp, narrow SEC traces of all nine dendrimer generations after a second purification by analytical SEC were observed (Figure 2A). Such sharp SEC traces have not been achieved previously for high-generation dendrimers; instead, all of the reported large dendrimers exhibited only very broad peaks. Not surprisingly, the SEC data can be interpreted only qualitatively because linear polystyrene (PS) standards were used. Figure 2B shows a semilogarithmic plot of molecular mass versus elution volume for both the PS standards and dendrimers **G1**–**G9**. The curve for the PS standards is a relatively straight line, whereas that of the dendrimers is linear only up to **G3**, after which the slope starts to increase as a function of the dendrimer size. This increase indicates that bigger dendrimers are delayed longer than expected during SEC elution.

MS analysis was employed to detect the molecular weight and possible structural defects of this dendrimer series. Because of the outstanding purity of the SEC-fractionated dendrimers and the high fragmentation stability of the PDI core upon UV laser irradiation during MALDI analysis, MS could be applied to the whole series. This enabled the first successful analysis of "real" synthetic polymers up to the megadalton range beyond PS standards[9] and dendrimer clusters.[4]

The determined molecular weights of our dendrimers were in perfect agreement with the theoretical values up to **G4**. Slight deviations of the measured values from the calculated ones commenced at **G5** and increased incrementally from one generation to the next. As representative for the higher generations, Figure 3 shows the baseline-corrected mass spectrum of **G7**. The signals can be assigned to dendrimers

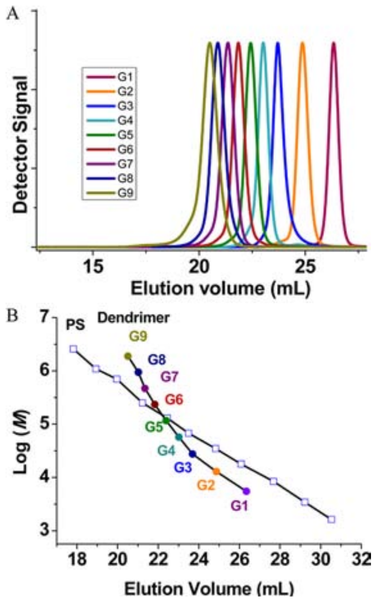


Figure 2. (A) SEC traces obtained for different dendrimer generations **G1**−**G9**. (B) Semilogarithmic plot of average molecular mass vs SEC elution volume for the linear polystyrene standards compared with the theoretical molecular masses of the dendrimers plotted vs their experimental SEC elution volumes. Conditions: THF, 1 mL/min; 500 Å, 10^4 Å, 10^6 Å SDV (Polymer Standard Service Mainz) columns (0.8 cm × 30 cm); ambient temperature.

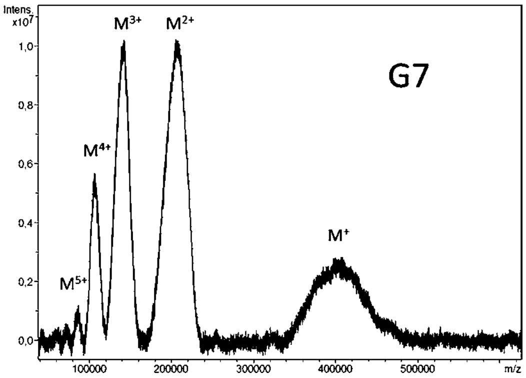


Figure 3. MALDI-TOF mass spectrum of **G7** measured with DCTB as the matrix (smoothed and baseline-corrected).

carrying charges of up to 5+, with a peak maximum of the singly charged molecules at 400 kDa and a peak width of ~100 kDa. The mass deviation of 15% relative to the theoretical value, as well as the fact that the peak width is significantly beyond a mass spectrometric peak broadening, could be interpreted as a mass distribution resulting from a slight chemical heterogeneity. Since the detected mass is lower than the theoretical mass, we conclude that the differences observed above **G4** are generally due missing branches with increasing generation number. The deviation between the experimental and theoretical masses (SI Table 2), however, can only partially be attributed to structural defects because there was also a systematic error during the measurements. Recalculations for the more highly charged states generally provided a smaller deviation with increasing charge size. This suggests that the MS method, which to date is the most precise tool for molecular weight determinations, also reaches its limit, which is most probably due to the very low but detectable polydispersity. In the case of **G7**, the deviation is thus reduced from 15% for the singly charged molecules to only 10% for the species with a charge of 5+. It also follows that the multiply charged molecules provide a more exact molecular weight measurement than the singly charged species because of their higher detection efficiency. For this reason, the measured values in SI Table 2 summarizing the mass spectrometric results (see the SI) were calculated using the highest charge states available and serve as best approximations to the real molecular weights. A similar phenomenon was observed previously for high-mass PS samples. An interpretation of this finding is still missing, most probably because of missing evidence for the exact "true" molecular weights.[10]

The evidence for structural imperfections with an onset at **G5**, corresponding to a molecular weight already above 100 kDa, should not be understood as downgrading the structural purity of our dendrimers. On the contrary, they own superior perfection in comparison with other systems, as otherwise they could not be analyzed by mass spectrometry at all because of the well-known restrictions for polymers with broad molecular weight distributions.[11] Astruc and co-workers, for example, reported the synthesis of nine successive generations of flexible organosilicon dendrimers, but MALDI-TOF mass spectra could be recorded only up to the fourth generation, and defects were found to be present proceeding from the second generation.[3c]

It should be emphasized that the polydispersity of the whole dendrimer series did not exceed a value of 1.005, which still corresponds to a very narrow molecular weight distribution and affirms the extremely high structural perfection of these giant PPDs. Such findings could not be elucidated with comparable exactness by MS previously. For traditional characterization methods such as SEC, NMR spectroscopy, and viscometry, such details are not visible, and the dendrimers would appear as virtually perfect systems.

To obtain direct information on the size of the dendrimers, transmission electron microscopy (TEM) was employed. The samples were obtained by drop-casting of dilute dendrimer solutions [10^{-9} M in tetrahydrofuran (THF)] onto thin carbon substrates (Figure 4). The TEM micrographs of **G8** and **G9** yielded diameters between 23 and 33 nm, in close agreement with the lengths extracted from modeling of linear polyphenylene chains. Thus, the rigid pentaphenylbenzene branching units provide conformational stiffness and directionality to the chain ends similar to that of the nonexpanded PPDs without backfolding.

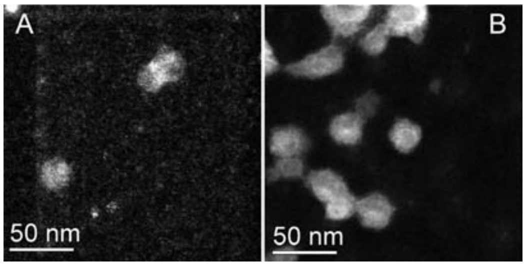


Figure 4. TEM micrographs of (A) **G8** and (B) **G9** dendrimers on carbon substrates.

In conclusion, we have successfully synthesized and comprehensively characterized a series of giant fluorescent polyphenylene dendrimers with hitherto unsurpassed structural perfection. The largest member of this series is the ninth-generation dendrimer (**G9**), with an expected molecular mass of up to 1.9 MDa and a longest-extension diameter of up to 33 nm, as firmly established by TEM imaging. **G9** contains as many as 18 402 benzene rings and an amazing 2048 chain ends. We have thus pushed the synthetic limit, as **G9** represents the biggest aromatic dendrimer reported to date. The entire series of nine rigorously purified dendrimer generations exhibited sharp, narrow SEC traces and could even be characterized by MALDI-TOF mass spectrometry, confirming the structural perfection up to **G4** and indicating a slight increase of chemical heterogeneity from **G5** on. Although it seems to be a contradiction, it can be assumed that MALDI MS could detect these slight structural imperfections at high molecular weights only because of the outstanding structural perfection not obtained previously. The reason that polystyrene was to date the only example of synthetic polymers in the megadalton range to which MS had been applied is an unbeatable structural perfection and polydispersity that to date has been achievable only by anionic polymerization. The fact that our dendrimers can now compete with PS standards can be considered as a breakthrough of our repetitive Diels−Alder cycloaddition reaction and justifies the nomenclature "precision polymers".

The success of our divergent dendrimer synthesis up to these high generations and extremely large molecular sizes relied on three significant improvements: (i) the use of an easily accessible extended dendritic branching unit in combination with a relatively voluminous PDI scaffold; (ii) the careful three-step purification of each; and especially (iii) keeping the deprotected dendrimer solution at low temperature and in the dark while gradually removing the solvent. Because of the fluorescent PDI core, fluorescence correlation spectroscopy could also be applied to obtain size information on the basis of diffusion coefficients. This is particularly important since one and the same PDI chromophore is now encapsulated in shells of widely different thicknesses. All of these optical properties will be reported in a forthcoming paper.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Synthetic details and characterization data. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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