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Iterative Synthesis of 1,3,5-Polyphenylene Dendrons via C−H Activation

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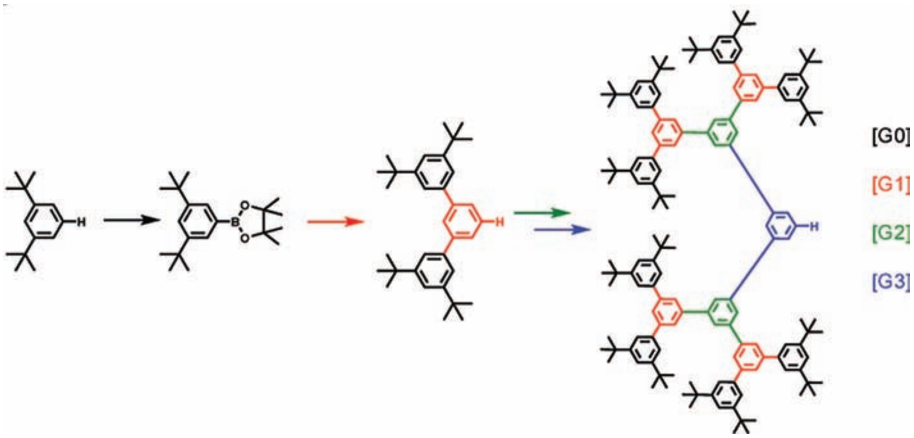
ABSTRACT



An iterative synthesis of 1,3,5-polyphenylene dendrons via C−H activation/Suzuki−Miyaura coupling up to a third generation dendron is described. C−H bonds at the focal points of the dendrons are selectively borylated via iridium-catalyzed borylation, eliminating the need for reactive protecting groups. Sequential additions of low catalyst loadings efficiently borylate higher-generation dendrons, whereas higher initial catalyst loadings are less efficient.

The demand for new, efficient optoelectronic materials has led to a surge of interest in conjugated small molecules.[1] However, the facile preparation of novel organic materials rarely keeps up with their demand, as the preparation of discrete, conjugated organic molecules can be synthetically rigorous. As a result, the need to develop and utilize new synthetic methods in the preparation of novel materials is equally vital to ensure their rapid utilization.

In few areas are these gaps between demand and efficient synthesis more apparent than in the preparation of rigid, fully conjugated dendrimers.[2] Extensive work on rigid conjugated dendrimers has been undertaken with a diverse array of chemistries including phenylacetylene,[3] stilbene,[4] truxene,[5] and phenylene[6] repeat units. Dendrimers containing 1,3,5-polyphenylene linkages constitute one of the simplest yet lesser-utilized rigid dendritic architectures. Since their first reports nearly 20 years ago, dendrimers of this class have

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been used in several photophysical studies[7] and perhaps most notably in the incorporation of highly efficient organic light-emitting diodes.[8] While the optoelectronic properties of these dendrimers are attractive, their preparation and synthetic manipulation are not ideal. Typically limited to convergent methods, the preparation of 1,3,5-polyphenylene dendrons has almost exclusively relied upon the elucidation of a "masked" boronic acid at the focal point prior to Suzuki−Miyaura coupling[9] with an aryl halide and mask-containing branching unit.[10]

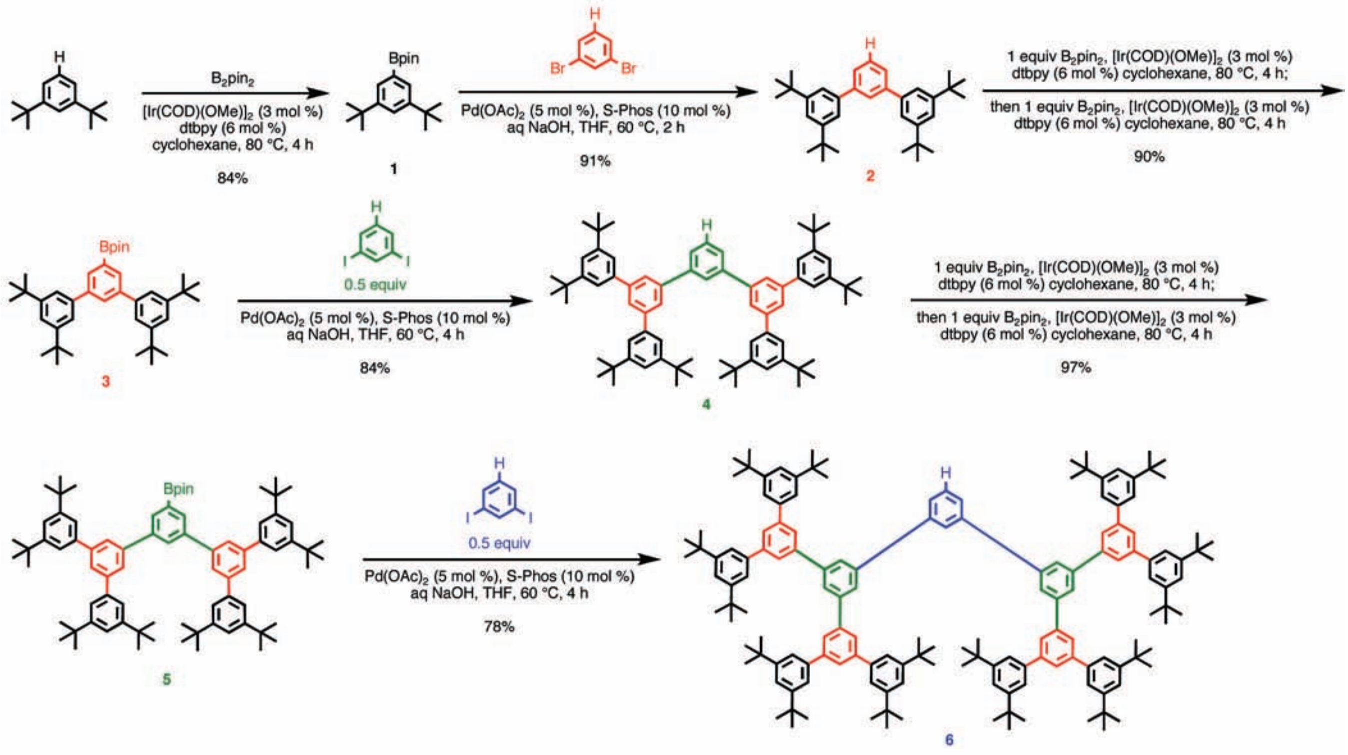
Herein we describe a new method for the iterative assembly of 1,3,5-polyphenylene dendrons incorporating 3,5-di-*tert*-butyl-phenylene containing peripheral groups. The method requires no "masked" focal point; instead, direct and selective borylation of an aryl C−H bond via iridium-catalyzed C−H activation generates the reactive pinacolboronate ester at the focal point. The dendron can then undergo Suzuki−Miyaura coupling with an inexpensive, commercially available 1,3-dihalobenzene to build the higher generations. We show that the process can be iterated to build a third-generation polyphenylene dendron **6** in good yield (Scheme 1). Utilizing highly efficient Suzuki−Miyaura coupling conditions dramatically decreases reaction times and inhibits byproduct formation.

The borylation of aromatic compounds via iridium-catalyzed C−H bond activation has been extensively studied since initial reports by Smith,[11] Hartwig, Ishiyama, and Miyaura.[12] This reaction is unique with respect to other aromatic substitution reactions because regioselectivity is predominantly controlled by sterics rather than electronics.[13] Under these reaction conditions, a 1,3-disubstituted arene preferentially borylates *meta* to both substituents, and typically in excellent yields. This methodology has been extended to the borylation of substituted arenes and aromatic heterocycles,[14] but the borylation of larger aromatics has been limited to porphyrins[15] and simple polycyclic aromatics such as naphthalene, pyrene, and perylene.[16] The implementation of this transformation into iterative methods for the preparation of novel materials has been limited to date, and to our knowledge there are no examples of the Ir-catalyzed borylation of oligoarenes.

The borylation of 1,3-di-*tert*-butylbenzene with bis(pinacolato)diboron (B_2pin_2) as the borylating reagent to form boronate ester **1** occurs in good yield in cyclohexane at 80 °C. It was found that, for all boronate esters in this work, column chromatography on silica gel depreciated the yields considerably, likely as a result of decomposition of the product on silica gel. A short plug of silica gel was sufficient to remove the catalyst, excess B_2pin_2, and boron-containing byproducts, without apparent product decomposition. The crude product, which typically contained small amounts (<5%) of starting material and B_2pin_2, was taken on without further purification and with no detriment to subsequent transformations or purification.

In most previous preparations of 1,3,5-polyphenylene dendrons, Suzuki−Miyaura coupling was undertaken with the standard palladium catalyst $Pd(PPh_3)_4$. However, coupling of **1** with 1,3-diiodobenzene or 1,3-dibromobenzene to form

Scheme 1. Synthesis of Polyphenylene Dendrons

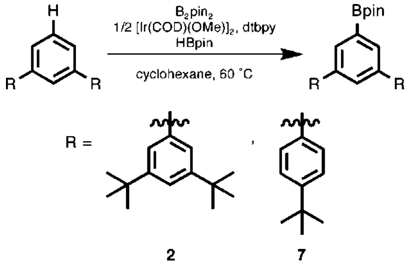


2 was very slow and tended to give significant amounts of byproducts, including homocoupled[17] and deboronated pinacolboronate esters. Effective methods of converting the relatively unreactive pinacolboronate esters to more reactive boronic acids and aryltrifluoroborate salts are available;[18] however, extra synthetic steps are undesirable. Instead, more efficient catalyst systems were screened. The phosphine ligand 2-dicyclohexylphosphino-2′,6′-dimethoxybiphenyl (S-phos) developed by Buchwald[19] is highly active toward Suzuki−Miyaura cross-couplings and is particularly effective in the coupling of sterically hindered boronic acids and aryl halides. The syntheses of dendrons **2**, **4**, and **6** from boronate esters **1**, **3**, and **5** using 5 mol % $Pd(OAc)_2$/10 mol % S-phos and aqueous NaOH in THF proceeded rapidly at 60 °C. All three are readily purified by flash chromatography on silica gel, eluting with hexane/dichloromethane mixtures. Analytical gel permeation chromatograms (GPC) of purified **2**, **4**, and **6** give narrow bands with PDI values below 1.03 (see Supporting Information). The ^1H NMR of **6** was taken in both $CDCl_3$ and benzene-d_6 (see Supporting Information). The aromatic proton chemical shifts appear to have a high degree of solvent dependence, as better dispersion of the aromatic protons can be achieved with benzene as solvent, whereas in $CDCl_3$ there is significant overlap of many peaks. Most notably, the peripheral aromatic protons are fully resolved in benzene, but in $CDCl_3$ both resonances convolute to appear as a singlet.

Although K_3PO_4 is most commonly used as a base with this ligand system, significant amounts of deboronated starting material was generated in the syntheses of **4** and **6** if aqueous K_3PO_4 or K_2CO_3 was used. Homocoupling of the pinacolboronate esters was detrimental to the purification of **4** and **6**, as homocoupled **3** and **5** were difficult to isolate from the desired product by most purification methods. It was found that switching the base to aqueous NaOH and using no more than 2 equiv of **3** or **5** attenuated homocoupling and deboronation, while only marginally lowering the yield.[20] Furthermore, switching to the more reactive 1,3-diiodobenzene for the syntheses of **4** and **6** also decreased byproduct formation.

Initial attempts to borylate dendrons **2** and **4** were slow and did not proceed to complete conversion, even with extended heating and high catalyst loadings. Extensive GC studies on the borylation of **2** were performed (Table 1). Interestingly, it was found that using low catalyst loadings and sequential addition of a premade catalyst stock solution containing $[Ir(COD)(OMe)]_2$, 4,4′-di-*tert*-butyl-2,2′-bipyridine (dtbpy), and pinacolborane (HBpin) (Table 1, entry 3) gave higher conversions than using higher initial catalyst loadings (Table 1, entry 6).[21] Addition of excess B_2pin_2 after 4 h slightly enhanced conversion (Table 1, entry 4).

Table 1. Borylation of Sterically Hindered *m*-Terphenyls[a]



			added after 4 h		% convn (GC)	
entry	arene	initial catalyst[b]	B_2pin_2	catalyst[b]	4h	8h
1	**2**	2 mol %	n/a[d]	n/a[d]	70	74
2	**2**	2 mol %	1 equiv	n/a[d]	70	77
3	**2**	2 mol %	n/a[d]	2 mol %	68	91
4	**2**	2 mol %	1 equiv	2 mol %	67	95
5[c]	**2**	2 mol %	n/a[d]	n/a[d]	70	75
6	**2**	6 mol %	n/a[d]	n/a[d]	nd[e]	91
7	**7**	2 mol %	n/a[d]	n/a[d]	nd[e]	91

[a] Reactions were carried out with 1.0 equiv of arene, 1.0 equiv of B_2pin_2, 20 mol % HBpin, and the specified amount of catalyst. [b] mol % 1/2$[Ir(COD)(OMe)]_2$ and dtbpy added. [c] 2 equiv of B_2pin_2 initally added. [d] Nothing added. [e] Conversion not determined.

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Previous studies on the effects of steric inhibition of borylation by peripheral, non-*ortho* substituents are limited. Borylation of *N*-(triisopropylsilyl)pyrrole occurs at the 3 position, in contrast to unsubstituted pyrrole, which borylates at the 2 position.[13a,22] Elegant studies by Hata demonstrated that a *m*-phenylene-linked Zn-tetraarylporphyrin dimer borylates quantitatively at the focal point, but a similar dimer with peralkylated porphyrins does not undergo borylation.[15] To investigate the role of sterics, dendron **7**, which is less sterically hindered than **2**, was prepared (see Supporting Information) and subsequently borylated (Table 1, entry 7). It was found that no additional catalyst was needed to get high conversions for the borylation of **7** with low catalyst loadings, indicating that steric hindrance from distal moieties plays an important role in the efficiency of borylation. Likewise, dendron **4** also required sequential addition of catalyst to achieve full conversion. At present, we cannot understand why sequential addition of low catalyst loadings led to more effective borylation of sterically hindered arenes. However, these data suggest a complex mechanistic pathway for decomposition of the catalyst that is competitive with C−H activation; the details will be investigated further in subsequent studies.

The potential of these polyphenylene dendrons for use in optoelectronic materials led us to characterize the thermal and photophysical properties of **2**, **4**, and **6**. Like previously synthesized 1,3,5-polyphenylene dendrimers, all three exhibit high thermal stability (see Supporting Information).[11] TGA studies run under N_2 show that **4** and **6** are stable up to nearly 500 °C. Interestingly, DSC studies run under N_2 showed no melting for **4** and **6** up to 400 °C; **6** displays two glass transitions at 230 and 330 °C. Not surprisingly, absorbance and emission spectra of the dendrons show evidence for disrupted conjugation between phenyl rings. Absorbance spectra of the dendrons (Figure 1) indicate a slight redshift in the λ_{max} from 250 nm for **2** to 255 nm for **4** to 257 nm for **6**. Fluorescence quantum yields measured for **4** ($\Phi = 0.16$) and **6** ($\Phi = 0.15$) in methylcyclohexane upon excitation at 250 nm show low fluorescence efficiencies. However, low fluorescence quantum yields do not preclude efficient energy transfer upon covalent attachment of an acceptor moiety.

Crystals suitable for X-ray analysis were grown from slow evaporation of solutions of **1** and **4** in dichloromethane and THF, respectively (Supporting Information). The high degree of biaryl twist in **4** is indicative of low π-overlap between benzene rings, confirmed by the relative lack of redshift in the absorbance spectra with increasing generation of dendron. From these data, we conclude that the cross-conjugated benzene rings in these dendrons are essentially behaving as individual chromophores.

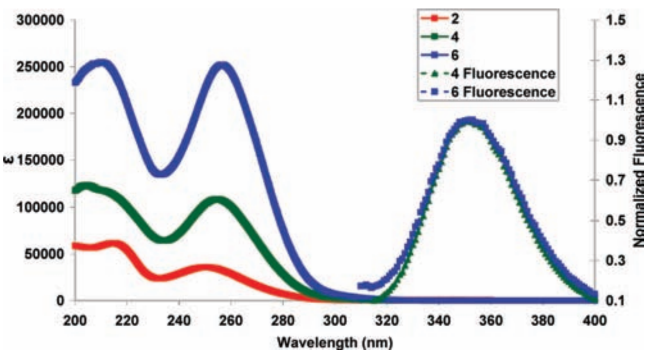

Figure 1. Absorbance and emission spectra of dendrons.

In summary, we have developed a novel method for the preparation of 1,3,5-polyphenylene dendrons with 3,5-di-*tert*-butylphenyl peripheral groups. To our knowledge, this is the first example of an iterative synthetic method that utilizes the direct C−H activation of an arene. For larger generations of dendrons, sequential addition of the iridium catalyst is necessary for high turnovers, presumably due in part to steric hindrance caused by the peripheral *tert*-butyl groups. While it is efficient for this particular example with 3,5-di-*tert*-butyl peripheral groups, this method is generally limited to the construction of 1,3,5-polyphenylene dendrons with peripheral groups unreactive to borylation. Dendrons containing unsubstituted arenes, alkynes, alkenes, nitro groups, phenols, and primary or secondary amines are thus unsuitable. Future work will demonstrate the versatility of this iterative approach, with the preparation of novel architectures that would otherwise be extremely difficult to synthesize.

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Supporting Information Available: Synthetic procedures, spectroscopic and thermal characterization of the new compounds, GPC traces, and crystal structures of **1** and **4**. This material is available free of charge via the Internet at http://pubs.acs.org.

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[21] The formation of the active trisboryl-iridium catalyst is accelerated by addition of HBpin, but the use of HBpin is unnecessary. HBpin is an impractical reagent because of its extreme moisture susceptibility. Sequential addition of the precatalyst, ligand and B_2pin_2 without HBpin gave similar results. Thus, HBpin was not used in the synthesis of **3** and **5**. See refs 13b and 14b and Supporting Information.

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