Substituted Hexaarylbenzenes

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A Strategy towards the Multigram Synthesis of Uncommon Hexaarylbenzenes

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***Abstract:** A novel rational synthetic pathway—the "functionalization of para-nitroaniline" (FpNA)—provides substituted hexaarylbenzenes (HABs) with uncommon symmetries that bear up to five different substituents, fully avoiding regioisomeric product distributions during the reactions. 4-Nitroaniline is functionalized by a cascade of electrophilic halogenations, Sandmeyer brominations, and Suzuki cross-coupling reactions, leading to 26 substitution geometries, of which 18 structures are not available by the current established techniques. Furthermore, we demonstrate that this method is applicable to the bulk production of such systems on a multigram scale. Regarding optoelectronic properties, we demonstrate how highly functionalized HABs can show strong luminescent behavior, making these molecules very attractive to organic electronic devices.*

Investigations starting in the early 2000s have brought hexaarylbenzenes and their oxidized derivatives—hexa-*peri*-hexabenzocoronenes (HBCs)—tremendous attention in materials chemistry, for example in nano-electronics and nonlinear optics.[1,2] The sixfold symmetry proved to be a key factor in templating nano-ring structures.[3] These compounds with star-like substitution patterns represent extraordinary building blocks in large light-harvesting architectures,[4] and they proved to be versatile backbones for catalytic scaffolds.[5,6] The literature provides a plethora of further examples in which HABs and HBCs have been introduced into highly sophisticated molecules or molecular assemblies. Interestingly, until quite recently, only HABs and HBCs with a rather small variety of symmetries were available—the most prominent being the fully symmetrical $\mathbf{A_6}$ HAB, the mono-substituted $\mathbf{A_5B}$, and the *ortho* and *para* disubstituted HABs with $\mathbf{A_4B_2}$ and $\mathbf{(A_2B)_2}$ patterns (compare structures #1, #2, #3, and #5 in Figure 2). Regrettably, the controlled formation of HABs with specific substitution patterns from unsymmetrical starting materials via standard techniques, such as the [2+2+2] cyclotrimerization of tolans and the Diels–Alder reactions of perarylated cyclopentadienones and acetylenes, is limited. Very often, instead of only one product, mixtures of regioisomers are obtained.[7] As recently as 2015, a spectacular route consisting of a variety of palladium-catalyzed arylation reactions led to the first HAB bearing six different substituents.[8] Despite the great achievement, this eight-step methodology suffers from low overall yields, is not applicable for bulk synthesis, and the final statistical Diels–Alder reaction leading to two regioisomers. Nevertheless, engineering the arylated periphery of benzene results in compounds displaying properties of fundamental importance, for example an outstanding blue emission in organic light-emitting diodes (OLEDs)[9] and detection of H_2S in living cells[10] and of explosives like picric acid and TNT.[11] Importantly, toroidal π-delocalization in HABs, for a long time underestimated, can be fine-tuned by the nature of aryl substituents, strongly suggesting that HABs are candidates for organic electronics.[12] However, HABs with substitution patterns such as those in compounds **1**–**4** have hardly been investigated. In this context, the facile access to larger amounts of these materials is of utmost importance.

Here, we present our own wet-chemical approach, which is quite different to the established methods. Importantly, we wanted this procedure to be simple and applicable towards the preparation of bulk material, without involving highly sophisticated techniques or purification difficulties due to the formation of regioisomers.

Our method, the functionalization of *para*-nitroaniline (F*p*NA), utilizes **5** as a cheap and commercially available starting material, which leads selectively to 26 substitution patterns (Figure 2). Depending on the desired structure, the first step involves the conversion of **5** to bromo species **6**, **7**, or **8** (see Figure 1), which can be conducted on a multiple-hundred-gram scale.[13–15] In this way the pattern of the upper—"northern" hemisphere is determined. As described in Scheme 1, an $\mathbf{A_3}$ hemisphere is generated by the threefold Suzuki cross-coupling reaction of **8** with three equivalents of arylboronic acid in a microwave reactor,[16] or under conventional conditions.[17] An **ABA** hemisphere is derived from **7** by coupling two equivalents of aryl moieties **A**, followed by halogenation of the mid position and a final coupling reaction with aryl moiety **B**. Similarly, an **ABC** hemisphere requires, after the first cross-coupling reaction of **6** with aryl moiety **A,** an aromatic halogenation *ortho* to the amine functionality, followed by the same procedure as described for the **ABA** hemisphere. After the completion of this "northern" hemisphere, the design of the "southern" hemisphere can be addressed. Thus, triarylnitrobenzene is activated by reductive conversion of the nitro moiety to the amine by using either $SnCl_2$ or H_2 and Pd/C. Halogenating agents can be either iodine monochloride or bromine, yielding diodo- and dibro-

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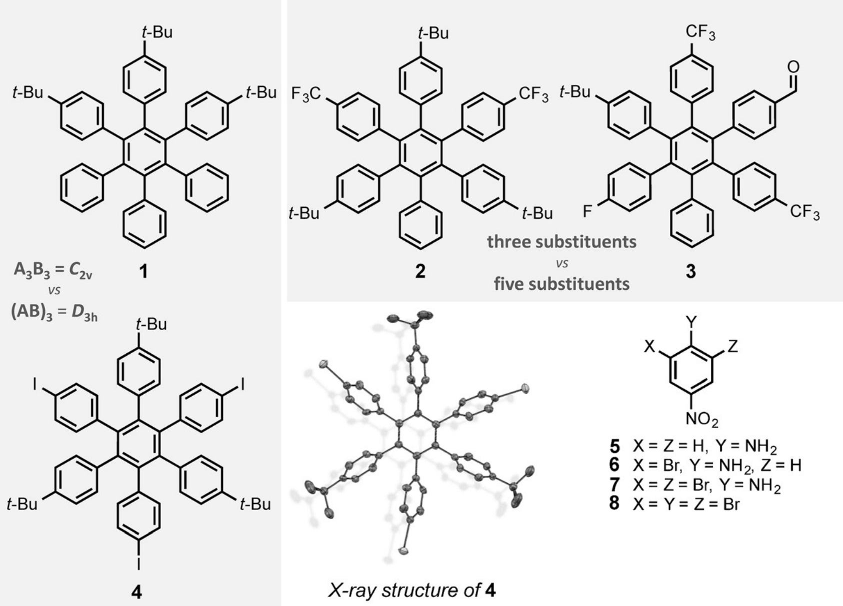


Figure 1. Compounds **1**–**4** are examples of "uncommon" HAB motifs that have been prepared by the herein reported method. The X-ray structure of **4** is depicted as an ORTEP model with 50% thermal ellipsoids; hydrogens are omitted for clarity.[22] Further crystallographic depictions can be extracted from the supporting information in Figure S1.

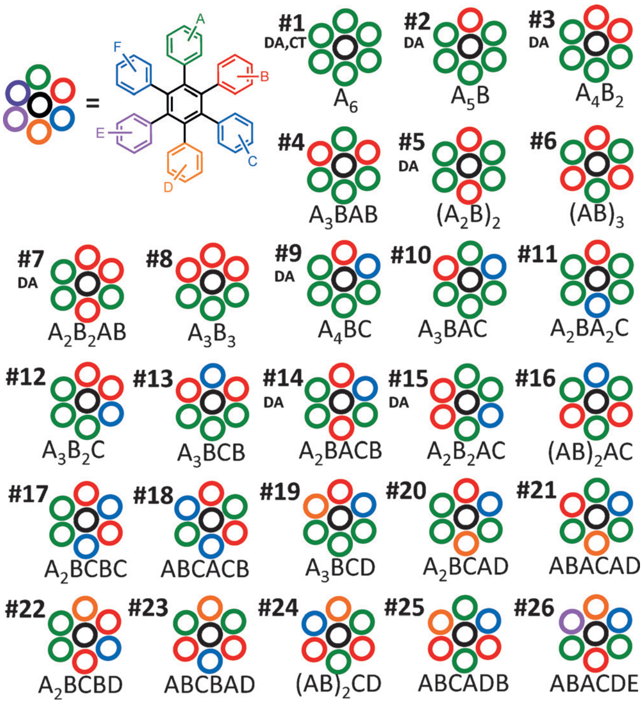
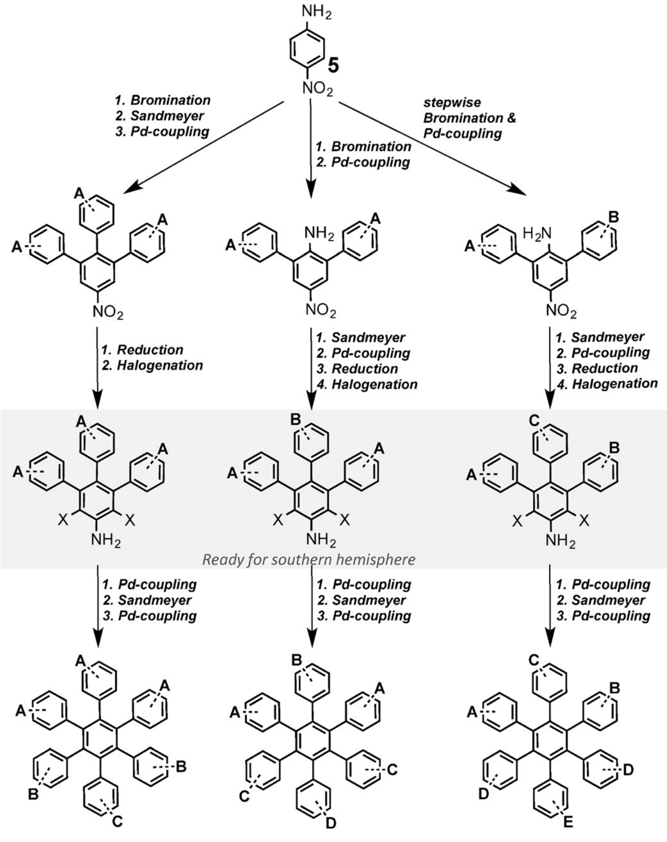


Figure 2. All possible substitution patterns of HABs that can be prepared by the herein reported method; CT = also available by cyclotrimerization, DA = also available by Diels–Alder reaction. The structures are classified as obtainable by the methods, if no regioisomers are formed during the reaction.

moaniline, respectively. Following the "northern" hemisphere strategy, the halogenated aniline can be transformed into the pentaarylaniline. Finally, the amine is converted into a bromide and the hexaarylbenzene synthesis concludes with arylation. All synthetic details can be extracted from the Supporting Information. Following this method, HABs with up to five different substituents can be constructed, avoiding statistical regioisomeric product distributions and concomitant difficulties in purification. Most importantly, the beauty of this strategy lies in its simplicity and the fact that all reaction steps rely on very well-known and well-established reaction procedures.

Of the 36 possible substitution geometries of hexaarylbenzene (Scheme S3 in the Supporting Information), we are able to prepare 26 structures, from which we enlarge the family of HAB substitution geometries by 18 novel structures. These were, to the best of our knowledge, previously unknown or only very difficult to obtain by the common techniques.

We examined the properties of the HABs with uncommon geometries. We observed an outstanding emission behavior of HABs that bear a quadrupole or octupole substitution pattern. In Figure 3, we show synthesized examples (compounds **9**–**12**) and their emission—ranging from dark to bright blue—in solution and more



Scheme 1. Synthesis of the possible HABs starting from 4-nitroaniline (**5**).

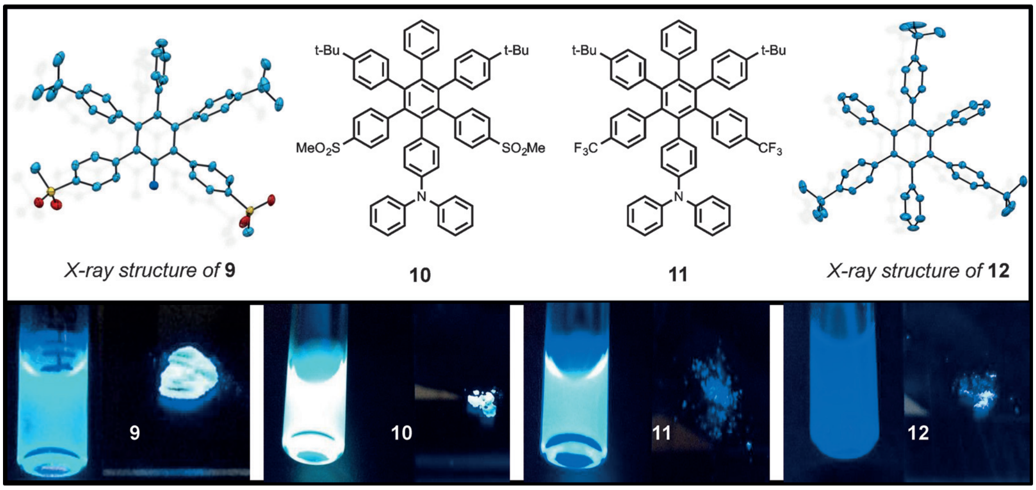


Figure 3. Pictures showing the luminescent behavior in solution (left) and in the solid state (right) of compounds **9**–**12** (solvent: CH_2Cl_2; solid-state emission observed for the powder under ambient conditions; excitation at $\lambda = 366$ nm). X-ray structures of compounds **9** and **12** are depicted as ORTEP models with 50% thermal ellipsoids; hydrogen atoms are omitted for clarity. Further crystallographic depictions can be extracted from the Supporting Information in Figures S2 and S3.

importantly, in the solid state. Their application in light-emitting devices is currently under investigation. Consequently, we are convinced that the toroidal π-delocalization of hexaarylbenzenes, which is responsible for charge delocalization of nonconjugated, but parallel proximate π-systems, will prove to be a potent tool in materials chemistry and the design of functional molecules.[12]

As proof of principle, we decided to prepare an **A_3BCB** system on a decagram scale, in order to show that this method opens the gate towards uncommon HAB motifs in bulk quantities (Scheme 2).[18,19] Therefore, we cross-coupled 10 g of **8** with 4-*tert*-butylphenyl boronic acid, using Pd(dppf)Cl_2 as the catalyst; we obtained **13** in 89% yield after purification by precipitation from methanol. Compound **13** was subsequently reduced and the resulting amine was precipitated from methanol and halogenated with 2.5 equiv of Br_2, providing dibromoaniline **14** in 81% yield over two steps. Next, a twofold Suzuki cross-coupling with phenylboronic acid gave pentaarylaniline **15** in 92% yield, after purification by precipitation from hexanes and methanol. The final and critical Sandmeyer halogenation was carried out using isoamyl nitrite in $CHBr_3$ at 100 °C, which served as excellent solvent and reactant at the same time.[20] Compound **16** was obtained in 75% yield after a short silica gel plug filtration and precipitation from CH_2Cl_2 and methanol. Importantly, conventional Sandmeyer halogenations yielded only little product, or failed completely. Hence, bromoform played the pivotal role as solvent and reagent, leading to the successful bromination of highly arylated and sterically crowded anilines. Lastly, despite the large steric hindrance of the di-*ortho*-substituted bromobenzene **16**, the terminal Suzuki coupling with 4-formylphenylboronic acid under standard conditions generated the desired “uncommon” **A_3BCB**-substituted HAB in 80% yield (the overall yield, starting from **8** was 40%).

Concerning the functional group tolerance of F*p*NA, a wide range of functionalities (F, CF_3, SO_2Me, OMe, SMe, *t*-Bu, Ph_2N, CHO) were successfully introduced to HABs and their precursors (Scheme S1 and Table S1). However, in the case of substituents that are labile under the reaction conditions, a powerful alternative is offered by the post-functionalization of the readily prepared HAB core. Several protocols for the six-fold halogenation of hexaphenylbenzene are available, which can be modified to halogenate only the available *para*-positions of the otherwise unsubstituted phenyl moiety (compare compound **4** in Figure 1 and **S36**–**S39** in Scheme S2).[21]

Overall we demonstrated a novel rational pathway—the functionalization of *para*-nitroaniline (F*p*NA)—to substituted hexaarylbenzenes with uncommon symmetries, avoiding regioisomeric product distributions during the reaction. This was made possible by utilizing 4-nitroaniline (**5**), a cheap and commercially available starting material, and by applying a cascade of electrophilic halogenations, and Suzuki cross-coupling reactions. A successfully mastered obstacle was the Sandmeyer-like bromination of highly crowded pentaarylanilines. Due to the simple and well-established synthetic protocols, we proved that this method is applicable to the bulk production of the final products. Further we demonstrated that these highly functional and complex molecules do not need highly sophisticated synthetic methods, but rather a sophisticated synthetic plan. With this novel tool in hand, we are convinced that the now open gate to the family of new HAB architectures—in total 18 geometries—will lead to a manifold of interesting findings based on HABs, which will be particularly attractive to the fields of molecular materials, nano-electronics and medicine. We are convinced that a new era in materials chemistry of HABs with “uncommon” symmetries and their derivatives is currently evolving, guiding the research community to new and highly exciting results.

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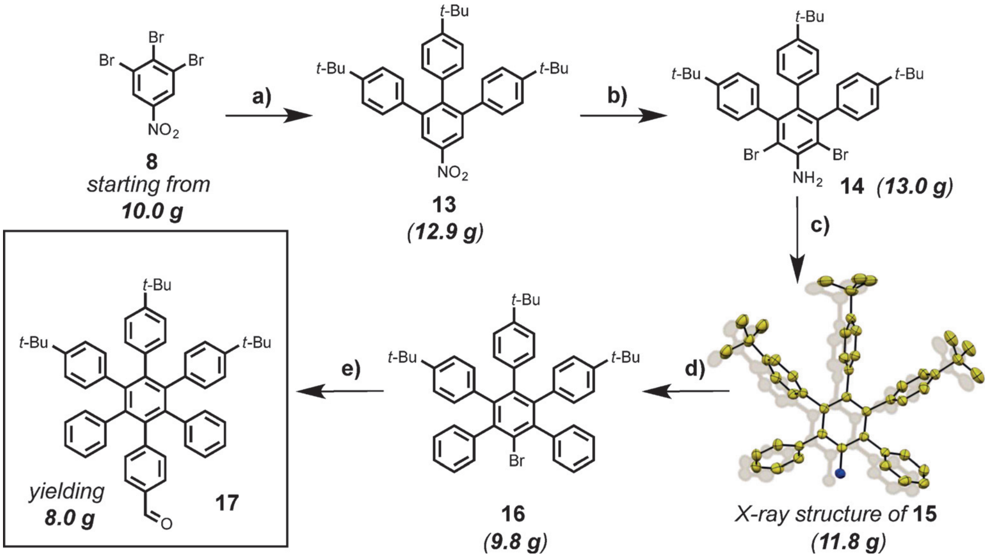

Scheme 2. a) 4-*t*-butylphenylboronic acid, Pd(dppf)Cl$_2$, K$_3$PO$_4$ in toluene/H$_2$O 13:1 (89%); b) 1. SnCl$_2$ in EtOH/EtOAc 1:1, 2. Br$_2$ in CHCl$_3$/AcOH 1:3 (81%); c) phenylboronic acid, Pd(dppf)Cl$_2$, K$_3$PO$_4$ in toluene/H$_2$O 10:1(92%); d) isoamyl nitrite in CHBr$_3$ (75%); e) 4-formylphenylboronic acid, Pd(dppf)Cl$_2$, K$_3$PO$_4$ in toluene/H$_2$O 10:1(80%). The X-ray structure of compound **15** is depicted as an ORTEP model with 50% thermal ellipsoids; hydrogen atoms are omitted for clarity. Further crystallographic depictions can be extracted from the Supporting Information in Figure S4.

Keywords: C–C coupling · halogenation · luminescence · materials · synthetic methods

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