## **Diverse Functionalization of Corannulene:** Easy Access to Pentagonal Superstructure

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## ABSTRACT



A variety of functionalized penta-arylcorannulene derivatives were prepared in high yields and high chemoselectivity by a cross-coupling reaction between sym-pentachlorocorannulene and substituted arylboronic acids using Fu's Pd(0) catalyst. This approach provides a general entry to pentasubstituted corannulene derivatives, which are useful building blocks for various structures of high complexity, such as pentagonal dendrimers, synthetic capsids, and discotic liquid crystals. This was demonstrated here by the facile synthesis of a third generation pentagonal dendrimer.

The notion that molecular containers<sup>1</sup> can be obtained by total synthesis and assembly of small molecules is largely inspired by the fascinating architecture of the virus particles, particularly the spherical viral capsids.<sup>2</sup> We have recently proposed a general strategy to meet the challenge of constructing non-protein molecular capsids having the icosahedral geometry by synthesis and assembly of 12 pentagonal tiles that bear appropriate "sticky" devices.<sup>3</sup> The icosahedron has been extensively used by Nature at all scales for the basic physical property of encapsulation because this architecture exploits the economy of the sphere in terms of both surfacearea-to-volume ratio and genetic efficiency of subunit-based symmetric assembly.<sup>4</sup>

For the synthesis of the desired pentagonal tiles we have chosen the corannulene molecule as the core skeleton due to its bowl shape, rigid polycyclic aromatic nature, and 5-fold symmetry.<sup>5</sup> These properties render corannulene a useful building block not only for the synthesis of chemical capsids but also for the construction of large molecular<sup>6</sup> and

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supramolecular architectures, such as pentagonal dendrimers,<sup>7</sup> single-wall nanotubes, light emitters,<sup>8</sup> and discotic liquid crystals.<sup>9</sup>

The synthetic difficulties en route to penta-functional corannulene derivatives have been significantly reduced owing to the available synthesis of corannulene.<sup>10</sup> Furthermore, the challenge of symmetrical activation of all five edges in the molecule has been satisfactorily met by Scott's discovery that the reaction of corannulene with ICl proceeds with high regioselectivity to produce 1,3,5,7,9-pentachlorocorannulene, 1.10b,11 Consequently, the main challenge became the attachment of the desired functional groups and binding devices onto the corannulene edges. This is a nontrivial task considering the low reactivity of aryl chlorides in cross-coupling reactions<sup>12</sup> and the need to perform the reaction five times on the same molecule.

Previous efforts to meet this challenge were based on various methods of metal-catalyzed cross-coupling reactions. Siegel's protocol, which employs trialkyl aluminum compounds under nickel(II) catalysis, can convert 1 into pentaalkylcorannulenes in 30-50% yields.<sup>14</sup> However, the analogous nickel(II)-catalyzed reactions with metallo-aryl reactants, including those of aluminum, magnesium, boron, and tin, were met with partial success.

Some successful approaches have been found. For example, Siegel has used the Negishi chemistry to achieve several sym-penta-arylcorannulenes in 28-49% yield via nickel-catalyzed cross-coupling of 1 with arylzinc chloride.<sup>13,14</sup> Also Eberhard's pincer catalyst<sup>15</sup> was found useful for these cross-coupling transformations with metallo-alkynyl reactants.<sup>10b,16</sup> Further advances by Scott offered the crosscoupling of 1 with 2-chloroarylboronic acid using the Suzuki–Miyaura protocol under Nolan's conditions.<sup>17,18</sup>

We found that although the above-mentioned methods work well for some aryl groups, their efficiency is limited

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in the synthesis of penta-arylcorannulenes bearing functional groups that are needed to achieve the desired architectures. For example, our attempts to couple 1 with various arylzinc or arylboronic acid partners bearing various functional groups failed to produce the corresponding penta-arylcorannulenes in satisfactory yield. Consequently, we searched for a more general cross-coupling approach.

Here we report that a broad variety of functionalized pentaarylcorannulene derivatives can be obtained in high yields under mild conditions from 1 and the appropriate arylboronic acids using Fu's bulky phosphine ligand, tri(tert-butyl)phosphine.<sup>19</sup>

Our general procedure for the cross-coupling reactions of **1** at 0.1 mmol scale (Scheme 1)<sup>20</sup> employ the substituted arylboronic acid (8 equiv, 1.6 equiv per site), catalytic amounts of Pd[P(t-Bu)<sub>3</sub>]<sub>2</sub> (20%, 4% per site), and CsF (15 equiv, 3 equiv per site) in dioxane at 80 °C. The resulting penta-arylcorannulenes, 2, 5, 8 and 11, were obtained under these conditions in 59-83% yields.

The isolation and characterization of symmetrical corannulene derivatives is not easy because of their low solubility in most organic solvents.<sup>21</sup> A typical example is 1,3,5,7,9penta(4-methoxycarbonylphenyl)corannulene, 2, which is obtained by reacting 1 with 4-(methoxycarbonyl)phenylboronic acid. The procedure reported by Scott for another pentaarylcorannulene,<sup>17</sup> which involves filtration through a short bed of silica-gel, afforded only traces of 2. Nevertheless, avoiding the filtration and chromatographic purification yielded a crude solid product that was purified by recrystallization from chloroform, affording 2 in 41% yield. Significantly higher yields were obtained with Fu's catalytic system,<sup>19</sup> leading to pure **2** in 59% yield without recrystallization (Scheme 1).

Compound 2 was successfully transformed into other useful penta-arylcorannulenes. Thus, hydrolysis with KOT-MS in refluxing THF for 16 h afforded 1,3,5,7,9-penta(4carboxyphenyl)corannulene, 3, in 86% yield. Reduction of 2 with DIBAL-H in THF at room temperature afforded 1,3,5,7,9-penta(4-hydroxymethylphenyl)corannulene, 4, in 65%. Avoiding filtration/chromatography workup in all other reactions afforded numerous penta-arylcorannulenes, 2-14, in good yields. All products exhibited low solubility in common organic solvents, such as toluene, chloroform, and ethyl acetate.

For example, 1,3,5,7,9-penta(4-methoxyphenyl)corannulene, 5,14,22 and 1,3,5,7,9-penta(4-tert-butylthiophenyl)corannulene, 8, were obtained in 83% and 59% yields, respectively. While the pentaether 5 and pentathioether 8 exhibited

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Scheme 1. Preparation of Penta-arylcorannulenes 2–14



partial solubility in organic solvents, such as tetrachloroethane, their correponding pentaphenol, **6**, and pentathiophenol, **9**, were found to be insoluble for characterization by solution NMR. Compound **6** was obtained in 87% yield by treatment of **5** with BBr<sub>3</sub> in CH<sub>2</sub>Cl<sub>2</sub> at room temperature for 18 h. Similarly, **8** was converted to **9** in 90% yield by treatment with triflic acid and TFA in toluene at 80 °C for 16 h. In order to determine their structures, **6** and **9** were allylated by treatment with allylbromide and NaH in DMF at room temperature for 24 h. The allylated products, 1,3,5,7,9penta(4-allyloxy-phenyl)corannulene, **7**, and 1,3,5,7,9-penta(4allylthio-phenyl)corannulene, **10**, were obtained as yellow solids in 65% and 82% yield, respectively, sufficiently soluble for characterization by NMR.<sup>23</sup>

1,3,5,7,9-Penta(4-formyl)phenylcorannulene, **12**, was prepared in two steps. First, coupling of 4-(1,3-dioxan-2yl)phenylboronic acid with **1** afforded 1,3,5,7,9-penta(4-(1,3diox-an-2-yl)phenyl)corannulene, **11**, in 61%. Acid-catalyzed hydrolysis (TFA, CH<sub>2</sub>Cl<sub>2</sub>-H<sub>2</sub>O, 85% yield) afforded the corresponding penta-aldehyde, **12**. The latter derivative represents a potential candidate for the synthesis of a chemical capsid using imine chemistry according to the concept of dynamic covalent chemistry.<sup>24,25</sup>

For the cross-coupling of heteroaryl boronic acids with **1** we used slightly modified conditions.<sup>19d</sup> 1,3,5,7,9-Penta(6-

methoxypyridin-3-yl)corannulene, **13**, was obtained in 51% yield using catalytic  $Pd[P(t-Bu)_3]_2$  and  $K_3PO_4$  in dioxane– $H_2O$  at 80 °C for 72 h. Similarly, 1,3,5,9-penta(pyridin-4-yl)corannulene, **14**, was prepared in 24% yield using catalytic  $Pd[P(t-Bu)_3]_2$  and  $K_3PO_4$  in DMF– $H_2O$  at 100 °C for 72 h. The latter two derivatives represent the first example of corannulene substituted with heteroaromatic groups, which may lead to icosahedral capsids by metal-mediated self-assembly. The metal coordination strategy has been successfully used by Stang and others for the construction of large supramolecular architectures.<sup>26</sup>

The above-described functionalized corannulene derivatives represent attractive building blocks for the synthesis of new dendrimers that have 5-fold symmetry.<sup>27</sup> Such monodispersed macromolecules could have interesting applications, including medicinally relevant compounds,<sup>28</sup> sensors,<sup>29</sup> catalysts,<sup>30</sup> and molecular encapsulators.<sup>31</sup>

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<sup>(23)</sup> Whereas compound **7** has sufficient solubility in  $C_2D_2Cl_4$  for performing both <sup>1</sup>H and <sup>13</sup>C NMR experiments, compound **10** has poor solubility and its carbon chemical shifts could not be measured.

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Scheme 2. Preparation of Third Generation Fréchet-Type Dendrimer 17



Thus, applying the divergent growth approach, a third generation Fréchet-type dendrimer, 17 (Scheme 2), was prepared from 6 in three steps, utilizing "click" chemistry.  $^{32,33}$  The penta-phenol, **6**, was reacted with the substituted benzylic bromide, 18,<sup>34</sup> to produce the corresponding penta ether, 15, in nearly quantitative yield. The 10 terminal acetylene groups of compound 15 underwent high-yield, copper-catalyzed 1,3-dipolar cycloaddition with excess azide 19 to produce the icosaphenol, 16. Without any purification of either 15 or 16, the latter underwent another etherification with **18** to produce dendrimer **17** in 75% overall yield for the three steps from 6. Whereas compounds 15 and 16 still suffered from low solubility that characterizes many other penta-arylcorannulene derivatives, the third generation dendrimer, 17, having 40 terminal acetylene groups, exhibited excellent solubility in common organic solvents, including CH<sub>2</sub>Cl<sub>2</sub> and ethyl acetate. Its structure was confirmed by both <sup>1</sup>H and <sup>13</sup>C NMR and MS (MALDI-TOF; m/z 7316.7 M<sup>+</sup>, calcd 7317.6).

In conclusion, the palladium-catalyzed cross-coupling reaction of 1 with a broad variety of substituted arylboronic

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acids provides a general entry to penta-substituted corannulene derivatives with high yields and high chemoselectivity. The reaction works equally well with arylboronic acids bearing variety of useful functional groups, including electron-rich (OMe, S-t-Bu, 1,3-dioxan-2-yl) and electrondeficient (CO<sub>2</sub>Me) substituents to produce the pentasubstituted derivatives in 50-83% yield (87-96% per site). For the cross-coupling of *sym*-pentachlorocorannulene with aryls, Fu's catalyst was found to be more efficient and more general than Nolan's catalyst with a carbene ligand. The high reactivity of Fu's catalyst allows for low catalyst loading (20%, 4% per site) and only a small excess of the coupled boronic acid (1.6 equiv per site). Considering the low solubility of the corannulene derivatives, the recommended workup procedure avoids chromatographic purification. It simply involves treatment of the crude product with toluene, collecting the precipitate and washing it with other organic solvents.

This work demonstrates that functionalized penta-arylcorannulenes are useful building blocks for various structures of high complexity, such as pentagonal dendrimers. Further efforts toward other molecular and supramolecular architectures, including synthetic capsids<sup>3</sup> and discotic liquid crystals, are currently underway in our laboratories.

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**Supporting Information Available:** Experimental procedures and spectral characterization of all compounds. <sup>1</sup>H and <sup>13</sup>C NMR spectra for selected compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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