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Highly selective Ir-catalyzed direct sixfold borylation of peripheral aromatic substituents on hexakisaryl-substituted [28]hexaphyrin(1.1.1.1.1.1)

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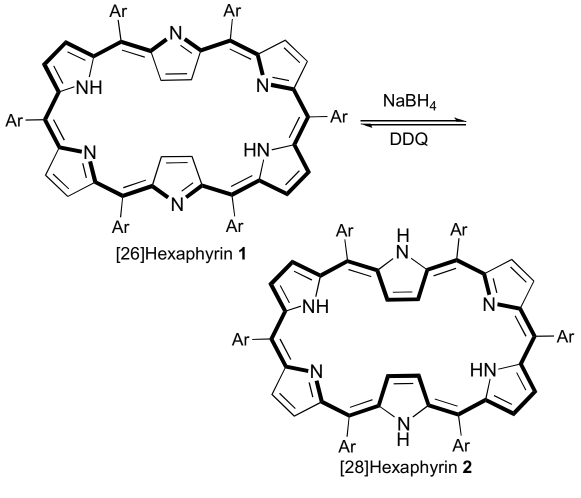
Abstract

Direct functionalization of aromatic substituents on [28]hexaphyrin was achieved by Ir-catalyzed borylation with the Smith–Miyaura–Hartwig protocol. High para selectivity was observed in the reaction on 2,6-dichlorophenyl and 2,6-dimethoxyphenyl substituents of [28]hexaphyrin. The reaction with [26]hexaphyrin resulted only in reduction of the substrate to provide [28]hexaphyrin without borylation, thus highlighting the importance of the oxidation state of substrates in this catalytic transformation. The borylated hexaphyrin can be used for Suzuki–Miyaura cross-coupling reaction.

In recent years, much attention has been paid for expanded porphyrins, which are porphyrin analogues with more than five pyrrolic subunits, because of unique properties, such as their structural features, multiple redox behavior, and unique metal-coordination.[1] Due to their largely extended π-conjugation, expanded porphyrins often possess multiple stable redox states, while porphyrins seldom show such behaviors. As a representative case, meso-aryl hexaphyrin(1.1.1.1.1.1) consists of two compounds [26]hexaphyrin **1** and [28]hexaphyrin **2**, which have different oxidation states with 26π and 28π conjugation, respectively.[2] They are easily interconvertible upon reduction with $NaBH_4$ and oxidation with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) (Scheme 1).



Scheme 1. Interconversion of [26]- and [28]hexaphyrins.

We have been interested in the reactivity of this intriguing π-system, as well as their unique properties.[3] Here, we wish to report the direct functionalization of aromatic substituents of hexaphyrins. Recently, we have achieved efficient and selective introduction of boryl substituents onto porphyrins and other related molecules through C–H bond activation with Smith–Miyaura–Hartwig protocol.[4,5] This method has proved to be very powerful to create novel porphyrins and related fascinating π-systems.[6] We anticipated that this method would also be applicable

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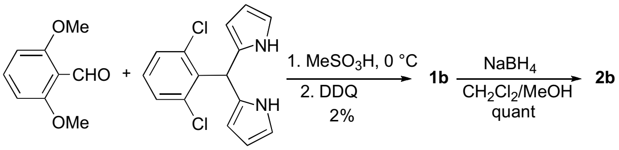
to expanded porphyrins for the selective functionalization and construction of novel hexaphyrin-based molecules.

We first attempted the borylation reaction of hexakis(2,6-dichlorophenyl) [26]hexaphyrin(1.1.1.1.1.1) **1a** with bis(pinacolato)diborane (pin$_2$B$_2$, 24 equiv) in the presence of [Ir(OMe)(cod)]$_2$ catalyst (10 mol %) and 4,4′-di-*tert*-butyl-2,2′-bipyridyl (dtbpy, 20 mol %) as a ligand in refluxing 1,4-dioxane. However, the reduced product, namely the corresponding [28]hexaphyrin **2a**, was obtained in almost quantitative yield. It is most likely that the iridium catalytic active species, which is known to be tris(boryl)iridium(III),[7] is killed via reduction with [26]hexaphyrin **1**. To our delight, however, hexakis (2,6-dichlorophenyl) [28]hexaphyrin(1.1.1.1.1.1) **2a** was efficiently borylated under the standard conditions (Scheme 2). Product **3a** was stable enough to be separated by silica gel column chromatography, and characterized by ^{1}H NMR and mass spectra.[8] Its parent mass ion peak was observed at $m/z = 2092.4249$ (calcd for $(C_{102}H_{101}B_6Cl_{12}N_6O_{12})^+ = 2092.4297$ $[(M+H)^+]$) in its high resolution electrospray-ionization time-of-flight (HR ESI-TOF) mass spectrum, demonstrating that sixfold borylation occurred on hexaphyrin. The yield of the product was 72%, and the borylation process is quite efficient considering that six consecutive C–H activation reactions should take place. ^{1}H NMR spectrum elucidated that the product contained a single isomer and the boryl groups were introduced to each 2,6-dichlorophenyl group at the para position. Such regioselectivity should result from the steric effect of the 2,6-disubstituted phenyl group. Then, tris(2,6-dichlorophenyl)-tris(2,6-dimethoxyphenyl) [28]hexaphyrin(1.1.1.1.1.1) **2b** was prepared from the quantitative reduction of the corresponding [26]hexaphyrin **1b**, which was obtained from acid-catalyzed condensation of 2,6-dimethoxybenzaldehyde and 2,6-dichlorophenyldipyrromethane followed by DDQ oxidation (Scheme 3).[2c] Borylation of **2b** also afforded the desired hexaborylated hexaphyrin **3b**[9] in 81% yield as a single isomer.



Scheme 3. Synthesis of [28]hexaphyrin **2b**.

Hexaborylated [28]hexaphyrin can be converted to the corresponding [26]hexaphyrin without loss of boryl groups via oxidation with MnO$_2$, but the isolation of the product was difficult due to decomposition under atmospheric conditions.

In the UV/vis absorption spectra, the Soret-like band of **3a** as well as the Q-like bands are slightly red-shifted compared to **2a** along with the broadening of the Soret band (Fig. 1).

The borylated hexaphyrin can be applied to Suzuki–Miyaura cross-coupling. The reaction of **3a** with iodobenzene under the standard conditions furnished hexaphenylated [28]hexaphyrin in good yield, which was oxidized to [26]hexaphyrin **4a**[10] with MnO$_2$ for easy separation (Scheme 4).

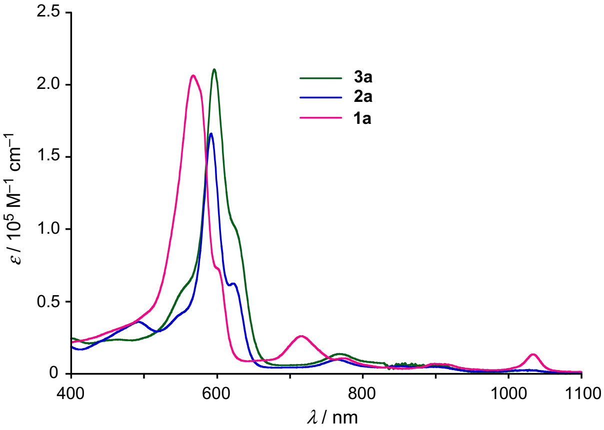
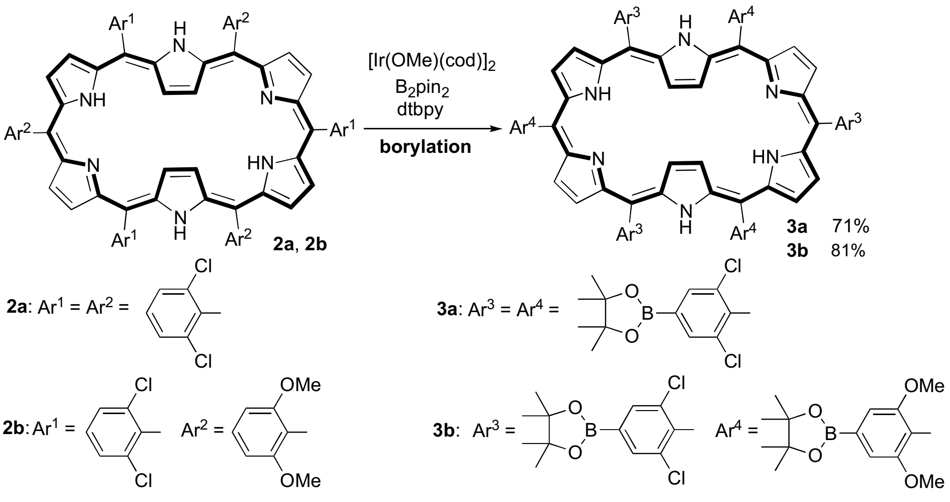
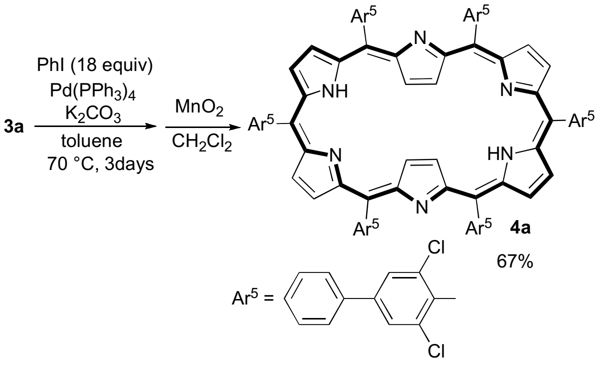


Fig. 1. UV/vis absorption spectra of **1a**, **2a**, and **3a** in dichloromethane.



Scheme 2. Ir-catalyzed direct borylation of hexaphyrins.



Scheme 4. Suzuki–Miyaura coupling of borylated hexaphyrin.

In conclusion, we have achieved regioselective direct six-fold borylation of [28]hexaphyrin(1.1.1.1.1.1). The oxidation state of the hexaphyrin substrates is essential for the successful reaction. Borylated hexaphyrin thus prepared will be useful platforms to construct hexaphyrin-based molecules by taking advantage of organoborane chemistry.

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8. The mixture of hexaphyrin **2a** (90 mg, 67.2 μmol), $[Ir(cod)OMe]_2$ (9.0 mg, 4.0 μmol), 4,4′-di-*tert*-butyl-2,2′-bipyridyl (8.4 mg, 8.0 μmol), and bis(pinacolate)diborane (414 mg, 1.63 mmol) in 1,4-dioxane (6.0 mL) was stirred at 100 °C for 2 days. After cooling, the reaction mixture was passed through a short silica gel column with ethyl acetate. Purification by size-exclusion chromatography and recrystallization from CH_2Cl_2/MeOH gave **3a** (101 mg, 48.2 μmol) in 72% yield. ^{1}H NMR (CD_2Cl_2): δ 7.99 (s, 4H, Ar), 7.58 (s, 8H, Ar), 7.51 (d, $J = 4.6$ Hz, 4H, outer β), 7.31 (d, $J = 4.6$ Hz, 4H, outer β), 3.80 (br, 2h, NH) 2.53 (s, 4H, inner β), 1.40 (s, 48H, pinacol), 1.30 (s, 24H, pinacol); UV/vis (CH_2Cl_2): λ_{max} (ε [M^{-1} cm^{-1}]) = 597 (219,000), 770 (17,300), 867 (8800); HR-MS (ESI-MS): *m/z* calcd for $C_{102}H_{101}B_6Cl_{12}N_6O_{12}$: 2092.4297 $[M+H]^+$, found: 2092.4249.
9. Compound **3b**: ^{1}H NMR ($CDCl_3$): δ 8.02 (s, 2H, Ar), 7.77 (s, 4H, Ar), 7.68 (d, $J = 4.6$ Hz, 2H, outer β), 7.45 (d, $J = 4.6$ Hz, 2H, outer β), 7.39 (d, $J = 4.6$ Hz, 4H, outer β), 7.26 (s, 2H, Ar), 6.71 (s, 4H, Ar), 3.70 (s, 6H, OCH_3), 3.53 (s, 2H, inner β), 3.39 (s, 2H, inner β), 2.78 (s, 12H, OCH_3), 1.45 (s, 12H, pinacol), 1.43 (s, 12H, pinacol), 1.35 (s, 24H, pinacol), 1.25 (s, 24H, pinacol); UV/vis (CH_2Cl_2): λ_{max} (ε [M^{-1} cm^{-1}]) = 598 (261,000), 768 (17,400), 869 (7000); HR-MS (ESI-MS): *m/z* calcd for $C_{108}H_{118}B_6Cl_6N_6O_{18}$: 2064.7166 $[M]^+$, found: 2064.7238.
10. Compound **4a**: ^{1}H NMR ($CDCl_3$): δ 9.28 (d, 4H, $J = 4.6$ Hz, outer β), 8.97 (d, 4H, $J = 4.6$ Hz, outer β), 8.11 (s, 4H, Ar), 7.85–7.95 (m, 12H, Ar), 7.62–7.70 (m, 12H, Ar), 7.55 (t, 2H, $J = 7.3$ Hz, Ar), 7.38–7.47 (m, 12H, Ar), –1.97 (br, 2H, NH), –2.37 (s, 4H, inner β); UV/vis (CH_2Cl_2): λ_{max} (ε [M^{-1} cm^{-1}]) = 574 (226,000), 718 (25,700), 897 (5800), 1036 (11,800); HR-MS (ESI-MS): *m/z* calcd for $C_{102}H_{57}Cl_{12}N_6$: 1791.0852; $[M+H]^+$, found: 1791.0824.