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SYNTHETIC CONNECTIONS TO THE AROMATIC DIRECTED METALATION REACTION. ITERATIVE ORTHO METALATION-CROSS COUPLING TACTICS FOR THE CONSTRUCTION OF POLYPHENYLS

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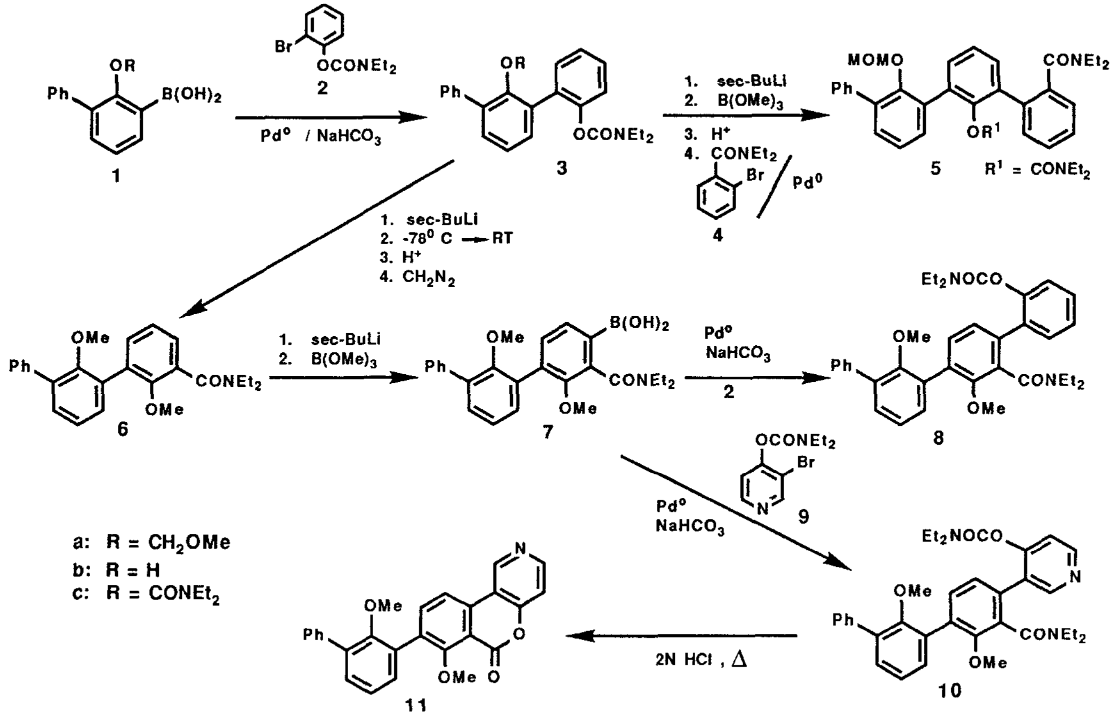
Abstract: An iterative ortho metalation transition metal catalyzed cross coupling strategy is delineated and illustrated for the construction of m-tetraphenyls **(5)**, mixed m- and p-tetraphenyls **(8)**, and heterotetraphenyls **(10)**.

In the accompanying Letter,[1] we have described an efficient new methodology for the synthesis of carbon- and heteroatom-functionalized biphenyls and m-terphenyls by Pd°-catalyzed cross coupling of aryl bromides with aryl boronic acids. The broad scope and the generality of this method is founded on a) the diversity and the regiospecificity of the directed ortho metalation process[2] and b) the facile synthesis of aryl boronic acids from aryl silanes by ipso borodesilylation. Herein we provide preliminary observations which indicate that this method is useful for the iterative assemblage or highly functionalized m-tetraphenyls **(5),** mixed m- and p-tetraphenyls **(8, 10)** (via anionic ortho-Fries rearrangement), and potentially higher order polyphenyls starting from simple m-terphenyl systems **(3).** This iterative tactic may have practical value for the systematic construction of polyaryls a propos to recent interest in enzyme models,[4] liquid crystals,[5] and organic conducting materials.[6]

Treatment of the biphenyl boronic acid **1a** [1] with N,N-diethyl o-bromophenyl carbamate **(2)** [7] under Suzuki or Gronowitz cross coupling conditions[1] gave a mixture of the m-terphenyls **3a** (31%) and **3b** (41%).[8] When **3a** was boronated and subjected to a second coupling reaction with **4,** the trifunctionalized m-tetraphenyl **5** was obtained (63%). In a second sequence, the m-terphenyl **3a** was metalated and allowed to warm to room temperature (s-BuLi/TMEDA/THF/-78°C → RT).[3] The crude product was hydrolyzed (5% aq HCl/THF/reflux) and methylated (CH_2N_2) to afford the m-terphenyl amide **6** in 62% overall yield. The aryl boronic acid **7,** obtained as before,[1] was once more coupled with **2** to give the tetraphenyl **8** (39%)[9] in which the final aryl ring is now para-related to the m-terphenyl unit. Both systems **5** and **8** are poised for further metalation-cross coupling processes. To illustrate the potential for heteropolyphenyl construction, **7** was coupled with the O-pyridyl-4-carbamate **9** [10] to give the pyridotetraphenyl **10** (10%).[9] Chemical corroboration of structure **10** was secured by conversion into the lactone **11**.

In view of the considerable scope of the directed ortho metalation strategy,[2] the iterative cross coupling protocol here derived offers advantage in regioselectivity, mildness of conditions, and tolerance in diversity of functionality over conventional methods[11] for the construction of carbon- and heteroatom-based polyphenyl systems.[12,13]



References and Footnotes

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8. The cleavage of the OMOM group could not be avoided. The corresponding aryl carbamate **1c** led, as expected under the basic conditions, even to greater amounts of phenol **3b**.
9. Variation of conditions to optimize these yields is in progress.
10. See ref. 3 in accompanying Letter.[1]
11. Prepared by metalation (s-BuLi/TMEDA/THF/-78°C) and bromination (Br_2) of the corresponding carbamate, see Miah, M.A.J.; Snieckus, V. J. Org. Chem. **1985**, 50, 5436.
12. All new compounds show analytical and spectral (IR, NMR, MS) data in full agreement with the depicted structures.
13. We acknowledge with gratitude the financial support of NSERC Canada, Imperial Oil, and Merck Frosst Canada.

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