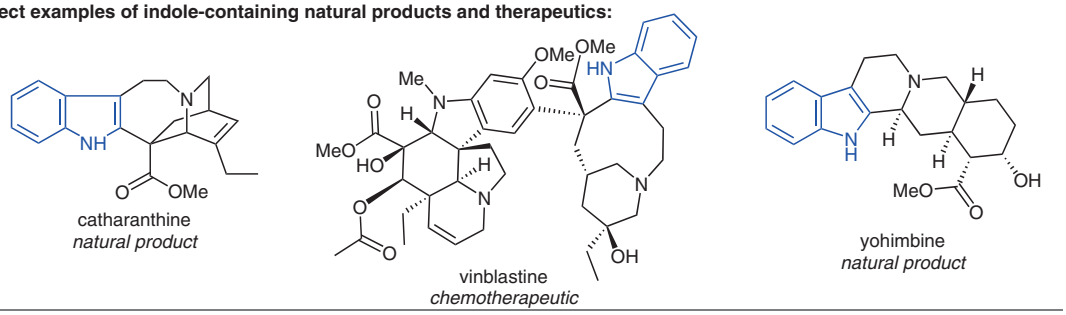
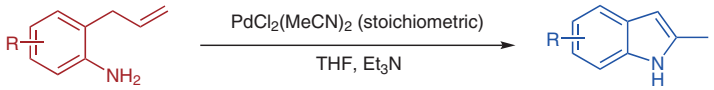
L. S. HEGEDUS*, G. F. ALLEN, E. L. WATERMAN (COLORADO STATE UNIVERSITY, USA)
Palladium Assisted Intramolecular Amination of Olefins. A New Synthesis of Indoles
J. Am. Chem. Soc. **1976**, *98*, 2674–2676, DOI: 10.1021/ja00425a051.

Hegedus Indole Synthesis: Intramolecular Nucleopalladation of *ortho*-Allyl Aryl Nucleophiles

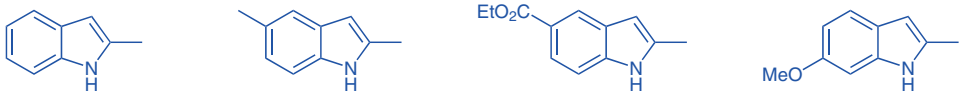
Select examples of indole-containing natural products and therapeutics:



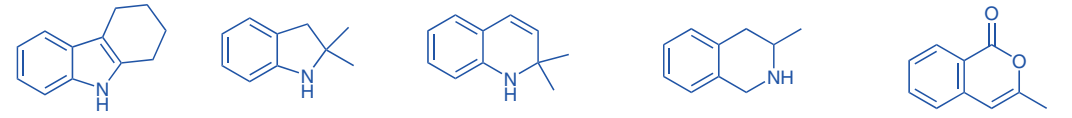
Synthesis of heterocycles using Pd(II) salts – Hegedus and co-workers, 1976:



Selected examples:

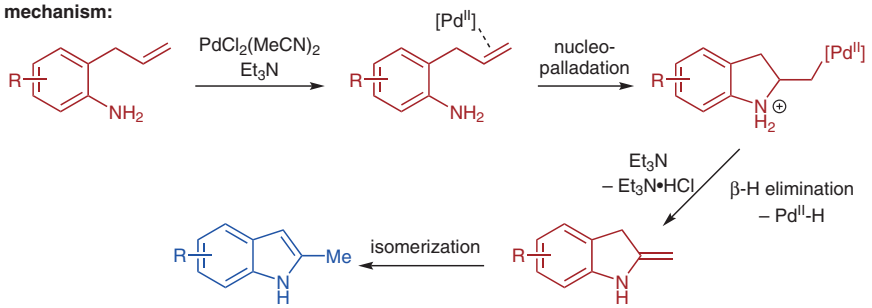


Additional heterocycle derivatives accessible:



[a] The authors note the reactions proceed with yields between 45% and 65% and were not optimized.
[b] The authors note the cyclization of *o*-allylbenzoic acid towards the isocoumarin derivative proceeds in good yield.

Proposed mechanism:



Significance: Indoles are widely found within natural products, derivatives of which are commonly used as therapeutic agents for a broad range of indications. Hegedus and co-workers report an efficient synthesis of indoles (and other) heterocycles from the cyclization of aryl nucleophiles bearing an *ortho*-allyl group. The aminopalladation chemistry of Hegedus has been employed in the synthesis of ergot alkaloids and has inspired additional nucleopalladation methodologies to be developed.

Comment: Although the yields are not documented in detail, the scope of this aminopalladation was established towards heterocycles including to carbazole, indoline, dihydroquinoline, tetrahydroisoquinoline, and isocoumarin derivatives. Hegedus and co-workers published a follow-up report in 1978, outlining a catalytic methodology to perform the same reaction, employing benzoquinone as an oxidant to regenerate the necessary Pd(II) catalyst.

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