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An Efficient C–H Arylation of a 5-Phenyl-1H-tetrazole Derivative: A Practical Synthesis of an Angiotensin II Receptor Blocker

**Synthesis of Candesartan Cilexetil**

\[
\text{N} \quad \text{N} \quad \text{N} \quad \text{N} \quad \text{Bn} \quad + \quad \text{N} \quad \text{N} \quad \text{Bn} \quad + \quad \text{NO}_2 \quad \text{HCl} \quad \text{MeOH}, \text{r.t., o/n} \\
\text{mp 115 °C} \quad \text{mp 73 °C} \\
\text{SnCl}_2 \cdot 2\text{H}_2\text{O} \quad \text{K}_2\text{CO}_3 \quad \text{1.03 equiv} \quad \text{1.5 equiv} \quad \text{86%} \quad \text{81%} \quad \text{19.2 mmol scale} \quad \text{24 mmol scale} \\
\text{mp 71 °C} \quad \text{mp 77 °C} \\
\]

**Significance:** Candesartan cilexetil (Atacand®) is an angiotensin II receptor antagonist that is prescribed for the treatment of hypertension. It is a prodrug that is hydrolyzed to candesartan in the gut. The synthesis depicted, features an efficient protocol for ruthenium-catalyzed C–H arylation of the tetrazole A.

**Comment:** A significant challenge in this small-scale synthesis was the final removal of the benzyl protecting group from the tetrazole unit using transfer hydrogenation. Best results were obtained using a ‘thickshell’ Pd/C catalyst from Evonik.

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