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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

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.