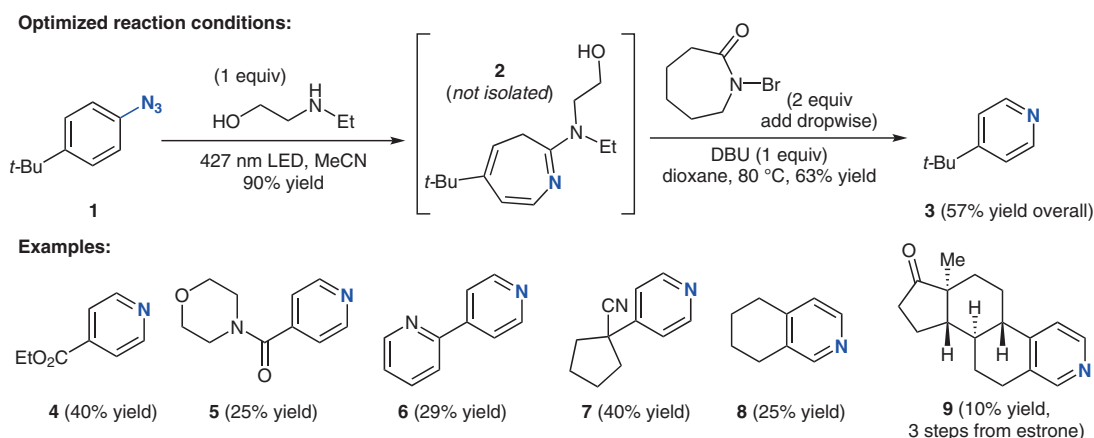


## Direct Carbon for Nitrogen Replacement Reaction to Access Functionalized Pyridines



**Significance:** Substitution of an aromatic carbon for a nitrogen to afford a pyridine system is a common strategy within medicinal chemistry to both modulate physicochemical properties and improve binding affinities through introduction of an H-bond acceptor. However, positioning of the specific nitrogen is critical given the various isomeric permutations involved leading often to laborious synthesis campaigns to evaluate each possibility. The current report details the development of a direct carbon to nitrogen replacement reaction through a two-step, one-pot procedure starting from aryl azides. The nitrogen in the final product is incorporated at the original site of azide substitution on the ring.

**Comment:** Aryl nitrene insertion into an aromatic nucleus has been known since 1966 (W. von E. Doering, R. A. Odum *Tetrahedron* **1966**, *22*, 81), though previous studies on oxidative carbon extrusion reactions have led to isomeric mixtures. Model studies on the current system highlighted not only the essential need for a pendant alcohol on the amine nucleophile to enable spirocycle formation prior to pyridine extrusion but also the critical selection of *N*-bromocaprolactam as the oxidizing reagent. A range of aryl azides were successfully converted into the corresponding pyridines with the *ipso* selectivity confirmed by  $^1\text{H}$  NMR spectroscopy. The overall functional group tolerance of the transformation was good, though free amines and alcohols require protection to avoid oxidation. The value of the protocol is showcased through the late-stage functionalization of estrone derivative **9**.