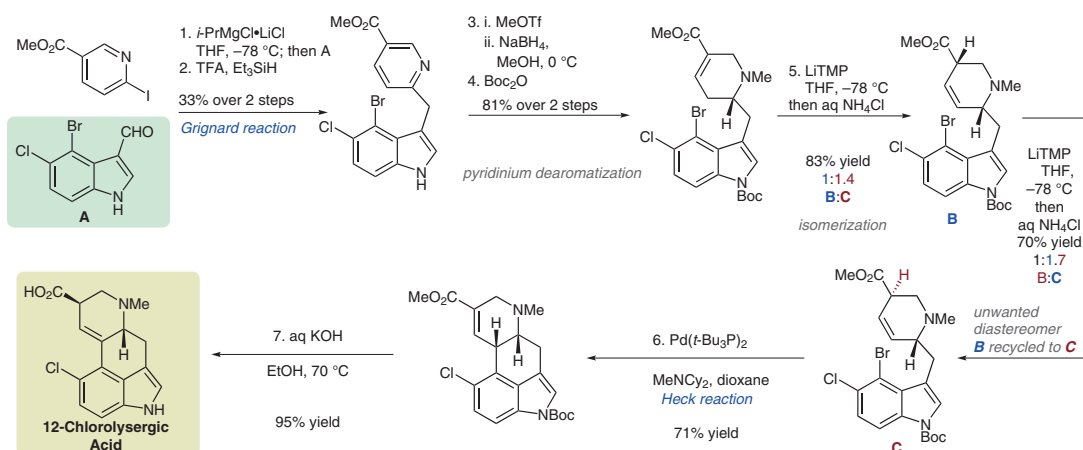


Synthesis of Novel (±)-Lysergic Acid Derivative 12-Chlorolysergic Acid



Significance: Lysergic acid remains a classic target in total synthesis and an intriguing scaffold for the development of novel bioactive compounds. Benzenoid substitutions on lysergic acid remain largely unexplored towards the understanding of the neuropharmacology of lysergic acid diethylamide. A swift synthesis of a chloro-lysergic acid derivative (12-chlorolysergic acid) can allow for different substitutions at the benzene ring to create analogues for the use of psychedelics in the treatment of neurological disorders.

Comment: The application of pyridinium chemistry towards accessing piperidine heterocycles in a streamlined manner remains a very exciting avenue in the synthesis of natural products and pharmaceutical drugs. A facile approach to the synthesis of lysergic acid demonstrated the utility of pyridines as valuable building blocks in accessing an exciting natural product. The synthesis of analogues such as 12-chlorolysergic acid may facilitate a new structure activity relationship model guiding the way for the next generation of pharmaceuticals.