SELECTIVE OXIDATION OF ERGOT ALKALOIDS

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Ergot alkaloids, isolated from the fungi of genus Claviceps (C. purpurea, C. paspali, C. fusiformis) and some plants, belong among very important drugs, widely used in medicine. Lysergic acid and its derivatives form majority of clinically used ergot alkaloid preparations. Production of lysergic acid from peptide ergot alkaloids requires rather harsh conditions (NaOH/EtOH/H2O) that result in considerable losses of substrates. Respective alcoholic precursors of lysergic acids, e.g., lysergol, dihydrolysergol and elymoclavine can be obtained easily and in sufficient amounts e.g., from plants of the genus Ipomoea or by submerged fermentation of Claviceps strains. However, oxidation of their primary alcoholic group to the corresponding aldehydes or carboxylic acids – despite its apparent simplicity - remained a challenge to the chemists for last 50 years.

Numerous attempts of the oxidations did not yield any products or led to partial or total decomposition of the ergoline skeleton. Poor solubility of these compounds in aprotic organic solvents (e.g. CH2Cl2) is another reason of these failures because it notably limits the spectrum of applicable oxidation methods.

A large series of modern oxidizing methods was tested on the derivatives of these alkaloids with improved solubility. Reagents based on the chromium (VI) oxide or Dess-Martin periodinane are not suitable for this task, but modified Swern oxidation (DMSO/TFAA) proved to be very useful method for the preparation ergot alkaloid aldehydes from the relevant alcohols.

These aldehydes represent convenient intermediates for the subsequent chemical modifications including oxidation to corresponding carboxylic acids.

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