Organocatalytic Route to 2,3,4,6-Tetra- and 2,3,4,5,6-Pentasubstituted Pyridines

**Significance:** Reported is the synthesis of 2,3,4,6-tetra- and 2,3,4,5,6-pentasubstituted pyridines 3 and 4 from the reaction of allenoates 1 with 1-aza-1,3-dienes 2 via an aza-Rauhut–Currier/cyclization/desulfonation reaction sequence. The starting materials 1 and 2 were obtained by following reported protocols as cited in the supporting information. Although 20% TMEDA in toluene was found to be optimum for the reaction, it also proceeds with other catalysts (alkyl amines) or solvents (MeCN, CH₂Cl₂, CHCl₃, THF), albeit in lower yields. A variety of highly functionalized pyridines were obtained in moderate to good yields under optimum conditions (eq. 1). Both electron-donating and -withdrawing groups containing aryls, as well as heteroaryl (R₃) may be used. Highly unstable 1 (R¹ = Ph, R² = H) was tolerated under the reported conditions. One example of a one-pot three-component reaction was reported to further simplify this protocol (eq. 2). A reaction mechanism starting with nucleophilic addition of TMEDA to 1 was provided without any experimental evidence.

**Comment:** While the Morita–Baylis–Hillman (MBH) reaction has emerged as a popular synthetic methodology for providing highly functionalized compounds, its analogous variant, i.e., vinyllogous MBH (Rauhut–Currier (RC)) reaction is lesser known because of the low reactivity of substrates and the difficulty in controlling the selectivity of the cross-coupling reaction (see Review below). A majority of RC reactions utilize air-sensitive phosphine catalysts, and stable amine-catalyzed RC reactions are uncommon. The current work is an improvement on previous work as it provides valuable highly functionalized pyridines by using an inexpensive and air-stable catalyst at ambient temperature. However, lack of easily available starting materials is a limitation of this method.