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 allenates 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 heteroaryls (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.