Synthesis of diverse nitrogen heterocycles from N-vinyl nitrones

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Abstract: Synthesis of nitrogen heterocycles is one of the most important research fields in organic synthesis. Nitrones are appealing reagents to access various nitrogen heterocycles. N-Vinyl nitrones are unusual compounds that have rarely been utilized as synthetic intermediates. Most previous examples about N-vinyl nitrones were reported as side products or proposed intermediates. Recent studies of N-vinyl nitrones have shown that they were good precursors to prepare challenging heterocyclic scaffolds. During studies of N-vinyl nitrones in our group, we found that iron catalysts could control the selective cyclizations of N-vinyl-α,β-unsaturated ketonitrone 1. Polysubstituted pyridines 2 were obtained by a FeCl$_3$-catalysis while isoxazolines 3 were afforded in high yields by a combination of FeCl$_3$ and 1,10-phenanthroline. Treatment of the N-vinyl-α,β-unsaturated ketonitrone 1 with isocyanates furnished nine-membered ring compounds 4 in high diastereoselectivity. Similarly, when 1 reacted with benzyne precursors, nine-membered ring compounds 5 were formed in high yields. Cycloaddition of alkynes with 1 using FeCl$_3$ and Cu(OAc)$_2$ as cocatalysts afforded 2,3-dihydropyrrrolidines 6 in good yields. Treatment of 1 with acyl chloride under basic conditions resulted polysubstituted lactones 7 in high diastereoselectivity.

Keywords: N-Vinyl nitrones; Heterocycles; Cycloaddition; Rearrangement; Iron-catalysis