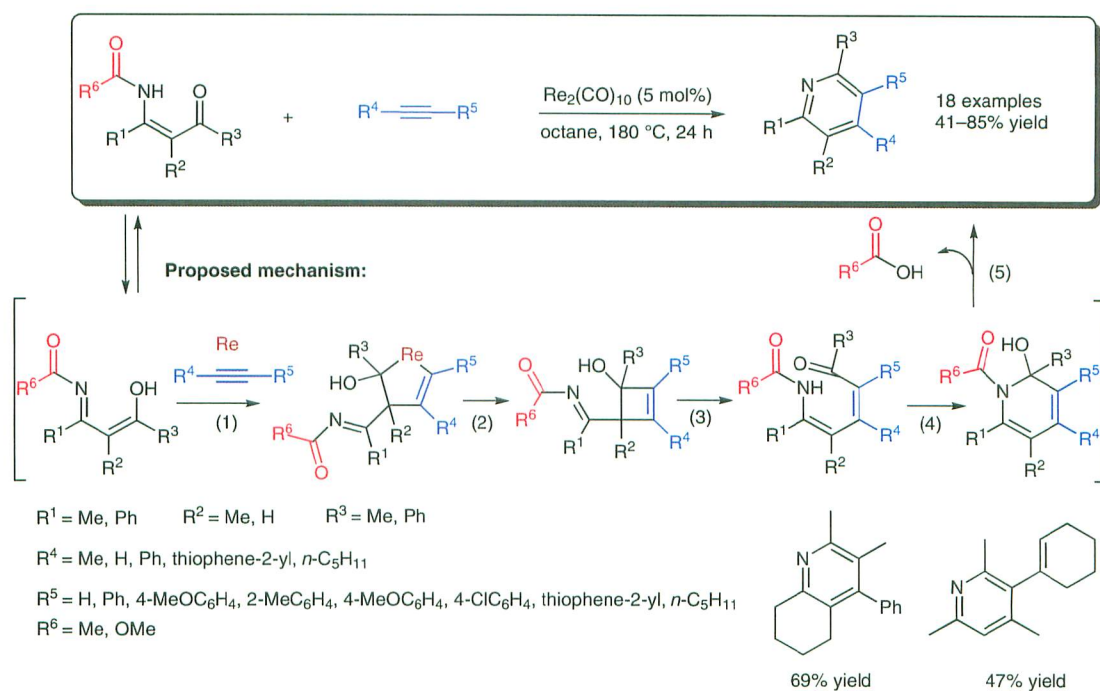


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Rhenium-Catalyzed Regioselective Synthesis of Multisubstituted Pyridines from  $\beta$ -Enamino Ketones and Alkynes via C–C Bond Cleavage

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## Polysubstituted Pyridines via Re-Catalyzed Alkyne Insertion



**Significance:** Reported is a de novo synthesis of multisubstituted pyridines via a regioselective reaction of terminal or internal alkynes with *N*-acetyl  $\beta$ -enamino ketones catalyzed by  $\text{Re}_2(\text{CO})_{10}$ . In this reaction, substituents ( $R^4$  and  $R^5$ ) appear at the 3- and 4-positions of the pyridine products with regioselectivity. The proposed mechanism involves a cyclobutene intermediate generated from oxidative cyclization (1) followed by reductive elimination (2). After C–C bond cleavage by a retro-aldol-type reaction (3), intramolecular cyclization (4), and elimination of acetic acid (5) leads to the pyridine product. A reasonable scope of substrates was investigated. For terminal alkynes, improved regioselectivity was observed when starting *N*-methoxy carbonyl  $\beta$ -enamino ketones ( $R^6 = \text{OMe}$ ) were employed.

**Comment:** Aside from the widely used classical Hantzsch synthesis of pyridine derivatives, many recent methods for highly substituted pyridine synthesis have been developed which involve reactions of transition-metal-catalyzed C–H activation followed by C–C bond formation (R. M. Martin, R. G. Bergman, J. A. Ellman *J. Org. Chem.* **2012**, *77*, 2501). In these reactions, use of unsymmetrical alkynes as starting material often leads to a mixture of regioisomers. The present method is based on a previously reported Re-catalyzed terminal alkyne insertion into 1,3-dicarbonyl compounds developed in the same group (Y. Kuninobu, A. Kawata, K. Takai *J. Am. Chem. Soc.* **2006**, *128*, 11368) and provides a new regioselective synthesis of polysubstituted pyridines. The catalyst  $\text{Re}_2(\text{CO})_{10}$  is commercially available from Strem Chemicals Inc. at \$248.00/5 g.

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