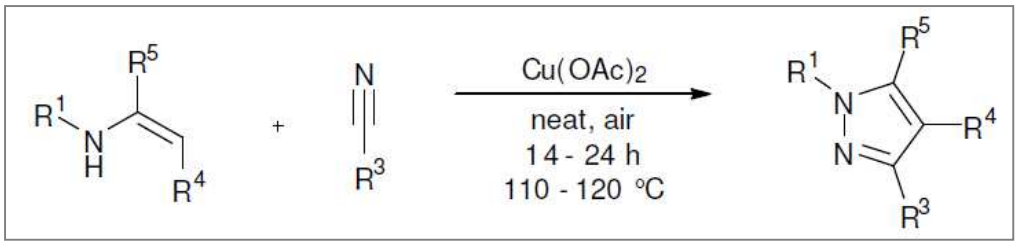
PEN

Efficient and catalytic formation of highly substituted Pyrazoles by Enamines and Nitriles

Invention

Scientist at the Westfälische Wilhelms University of Münster developed the efficient Cu-catalyzed **PEN** method for the formation of tetra-substituted pyrazoles. In this atomeconomic process, readily available enamines and nitriles are reacted by C-C and N-N bond formation. A broad scope of enamines and nitriles can be utilized in this process.



Commercial Opportunities

Pyrazoles are an intriguing class of important heterocycles, although rarely found in nature, many man-made biologically active compounds possessing agricultural and pharmaceutical activities contain pyrazole moieties. Surprisingly, the efficient and selective synthesis of highly substituted pyrazoles still represents a major challenge.

The most commonly used approaches to the synthesis of tetrasubstituted pyrazoles involve either the classical condensation of hydrazines with 1,3-dicarbonyl compounds (or their equivalents), the 1,3-dipolar [3+2] cycloadditions or the transition metal catalyzed C-N and/or C-C cross coupling on the preformed pyrazoles.

PEN is a novel synthetic approach to tetrasubstituted pyrazoles using equivalent amounts of nitriles with an efficient metal catalyst system employing molecular oxygen as the sole stoichiometric oxidant. The use of molecular oxygen as the terminal oxidant coupled with the catalytic metal system provides an attractive approach to the development of an oxidative process owing to its high abundance, low cost and reduction of toxic byproducts formation.

Current Status

PEN is laboratory tested with different substitutes. A European Patent Application and a granted US Patent are pending. On behalf of the University of Munster PROvendis GmbH offers companies license agreements.

Relevant Publications

M. Suri, T. Jousseaume, J. J. Neumann, F. Glorius, “An efficient copper-catalyzed formation of highly substituted pyrazoles using molecular oxygen as the oxidant”, Green Chem. 2012, 14, 2193-2196.

M. Suri, F. Glorius, “Synthesis of Tetrasubstituted 1H-Pyrazoles by Copper-mediated Coupling of Enaminones with Nitriles” Org. Synth. 2014, 91, 211-220.

J. J. Neumann, M. Suri, F. Glorius, „Effiziente Pyrazolsynthese durch oxidative C-C/N-N-Bindungsknüpfungskaskade“, Angew. Chem. 2010, 122, 7957-7961; Angew. Chem. Int. Ed. 2010, 49, 7790-7794.

An invention of the University of Münster (Uni Münster).

Competitive Advantages

- **atomeconomic process**
- **mild conditions**
- **no noble Catalyst needed**
- **molecular oxygen as the sole stoichiometric oxidant**
- **direct synthesis**
- **free choice of pyrazol-substitutes**
- **broad scope of enamines and nitriles can be utilized**
- **high abundance**
- **low cost**
- **reduction of toxic by products**

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