

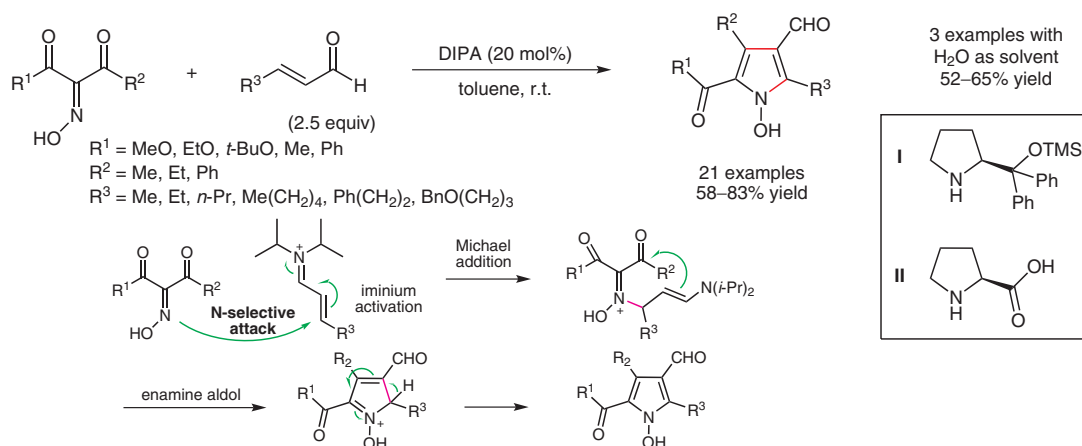
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Unusual Domino Michael/Aldol Condensation Reactions Employing Oximes as N-Selective Nucleophiles:

Synthesis of *N*-Hydroxypyrroles

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Synthesis of *N*-Hydroxypyrroles Using N-Selective Nucleophilicity of Oximes



Significance: Reported is the amine-catalyzed synthesis of tetrasubstituted *N*-hydroxypyrroles by reaction of α -carboxyoximes with α,β -unsaturated aldehydes through an iminium activation strategy. A mechanism involves an unusual *N*-selective nucleophilic Michael addition (K. Narasaka and co-workers *Eur. J. Org. Chem.* **2005**, 4505) followed by an intramolecular enamine aldol condensation and final aromatization. The use of diisopropylamine as catalyst affords tetrasubstituted *N*-hydroxypyrroles under mild conditions in moderate to good yields with several types of R^1 groups whereas the variation of R^2 is more limited. The reaction is successful with α,β -unsaturated aldehydes bearing $R^3 =$ nonaromatic but is completely inhibited if $R^3 =$ aromatic. When $R^1 = \text{Ph}$ and $R^2 = \text{Me}$, the proportion of the undesired regioisomer was reduced to traces by using amines **I** and **II** as catalyst.

Comment: Pyrrole derivatives form probably the most important class of π -excessive heterocycles. They are essential components of many natural products and drug intermediates (see Book below) and are used in materials application, for example batteries. The present paper demonstrates a one-step, mild and efficient preparation of tetrasubstituted pyrroles which are difficult to obtain by classical methods such as the Paal–Knorr synthesis which is often limited in terms of regioselectivity. The described method employs readily available starting materials and inexpensive catalysts and shows wide scope and good regioselectivity. The resulting *N*-hydroxypyrroles may be transformed into their corresponding 1*H*-pyrroles in good yield using Zn and AcOH. This reaction may also be performed in water affording pyrroles in moderate yields.

Book: In *Comprehensive Heterocyclic Chemistry II*, Vol. 2; A. R. Katritzky, C. W. Rees, E. F. V. Scriven, Eds.; Pergamon Press: Oxford, **1996**.

Review: P. Novák, K. Müller, K. S. V. Santhanam, O. Haas *Chem. Rev.* **1997**, *97*, 207-282.

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