

Hantzsch-type Reaction of β -Formyl- β -nitroenamine: Multi-component Synthesis of 4-Substituted-3,5-dinitro-1,4-dihydropyridine

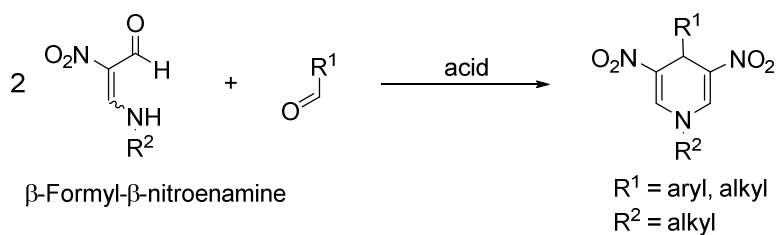
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1,4-Dihydropyridine (DHP) derivatives have attracted a considerable attention in medicinal chemistry and pharmacology due to the wide range of bioactivities, among which 4-arylated DHPs are also often found as the fundamental framework in drugs such as calcium antagonists and cardiovascular diseases.

On the other hand, we recently reported the novel method for construction of 4-arylated 3,5-dinitro-1,4-DHPs from β -formyl- β -nitroenamine as a reactive building block. Although this reaction serves as dinitro-DHPs that are not easily prepared by other method, the scope of the substrate is limited to highly electron-rich aromatics, and the theoretical maximum yield should be below 67%.

In this context, we have improved this reaction by using the strategy of Hantzsch-type multi-component reaction. Namely, a relevant multi-component reaction between two molecules of β -formyl- β -nitroenamine and an aldehyde is designed (Scheme), and we have succeeded to prepare various kinds of 4-aryl and 4-alkyl-3,5-dinitro-1,4-DHPs in high yields.



Scheme. Multi-component Synthesis of Dinitro-dihydropyridine