

CeCl₃ catalyzed imino Diels-Alder reactions: hydrated vs anhydrous

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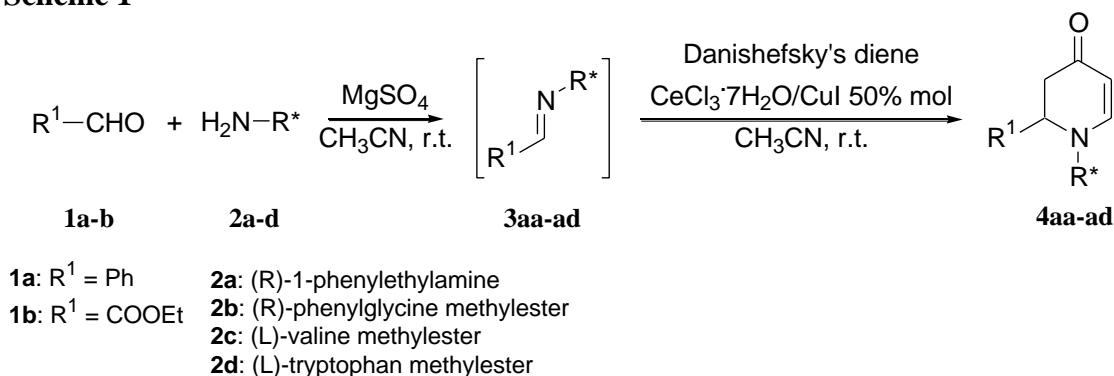
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Aza-Diels-Alder reaction is a straightforward way to synthesize useful nitrogen containing heterocyclic structures.¹ In particular, the known reaction between imines and Danishefsky's diene has proved to be an excellent way to obtain the 1,2-substituted-2,3-dihydropyridinone scaffold, widely present in bioactive small molecules and versatile building block for the synthesis of more complex structures.²

The reaction of Danishefsky's diene with aromatic imines has been widely studied in last years, anyway less examples of the same reaction involving imines derived from aliphatic amines or aldehydes are present. For this reason the possibility to extend the potentiality of this reaction performing it on a large variety of imines was studied, under the Lewis acid promoting system CeCl₃·7H₂O/CuI, previously applied with success³ in many other synthetic methodologies.

Imines **3** were prepared by direct condensation of aliphatic or aromatic amines and aldehydes and then the diene was added together with the catalyst, obtaining dihydropyridinones **4** with good to excellent yields in short reaction times. To extend the scope of this work, also imines derived from aminoacids were tested as dienophiles.

Scheme 1



The only moderate diastereoselectivity and the long time needed with some homochiral dienophiles prompted us to have a deeper insight into the mechanism, with the conclusion that the reaction proceed also through a slower competitive Mannich-Michael pathway, favoured by the presence of water in the catalyst.

1) Buonora, P.; Olsen, J.-C.; Oh, T. *Tetrahedron* **2001**, *57*, 6099-6138.

2) Cant, A. A.; Sutherland, A. *Synthesis* **2012**, *44*, 1935-1950.

3) Bartoli, G.; Marcantoni, E.; Marcolini, M.; Sambri, L. *Chem. Rev.* **2010**, *110*, 6104-6143.