M. P. SIBI,* L. M. STANLEY, T. SOETA (NORTH DAKOTA STATE UNIVERSITY, FARGO, USA)
Enantioselective 1,3-Dipolar Cycloadditions of Diazoacetates with Electron-Deficient Olefins
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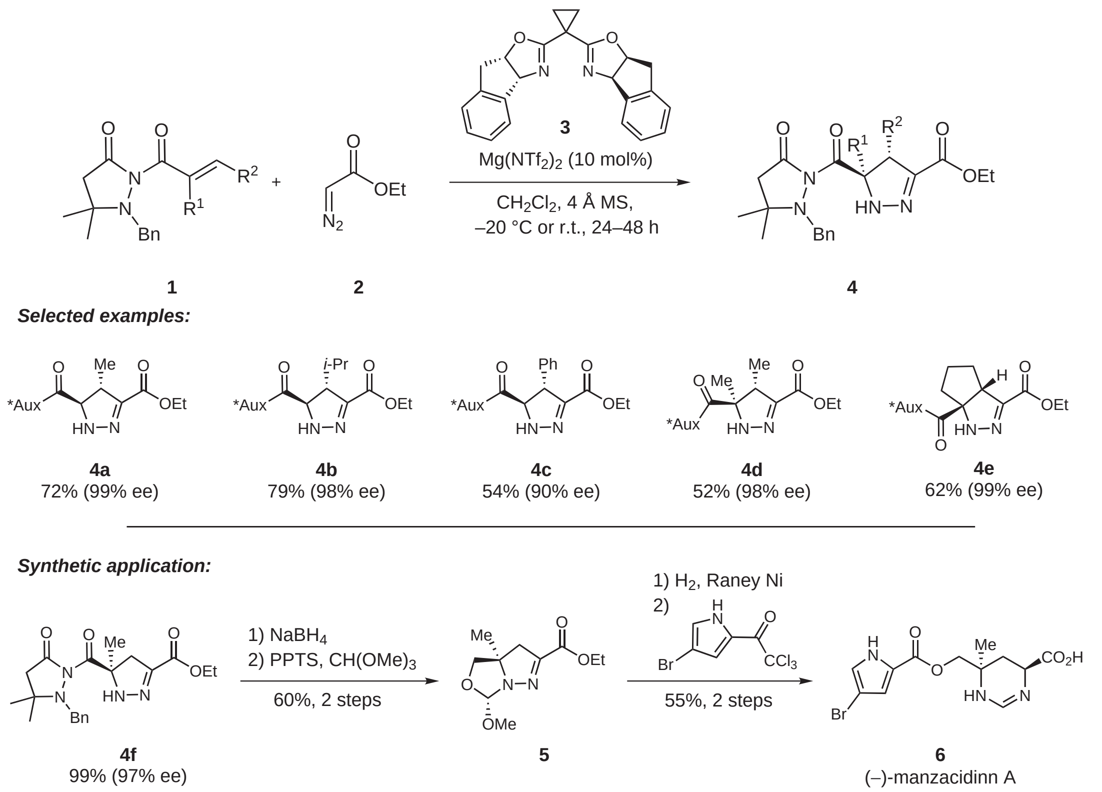
Category
Metal-Catalyzed Asymmetric Synthesis and Stereoselective Reactions

Key words
1,3-dipolar cycloaddition
chiral relay
magnesium
cp-Indabox ligand
diazoesters
pyrazolines

SYNFACT of the month

Synthesis of Pyrazolines via Enantioselective 1,3-Dipolar Cycloadditions



Significance: Cycloadditions are among the best ways to rapidly create complexity in heterocycle synthesis. Readily available diazoesters **2** can now be used in enantioselective dipolar cycloadditions with activated alkenes **1**. Previous methods were limited either to diazomethane derivatives, or did not tolerate β-substitution on the alkene (R^2 in **1**). The method was applied to a rapid total synthesis of (–)-manzacidin A (**6**), where the stereochemistry of the quaternary *tert*-alkyl amino stereocenter was fully controlled in the key step.

Comment: The method relies on pyramidalization of the cyclic hydrazine to act as chiral relay to obtain the pyrazoline cycloadducts **4** in excellent enantioselectivity. An intriguing observation was made by the authors who point out that, in multiple instances, the reaction gives better enantioselectivity at higher temperatures. Although no explanation is given, it is still fortunate as some substrates needed higher temperatures to achieve reasonable yields.

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