

# Synthesis of 3-Carbamoyl $\beta$ -Lactams via Manganese(III)-Promoted Cyclization of *N*-Alkenylmalonamides

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Manganese(III)-promoted cyclization of *N*-alkenylmalonamides (= *N*-alkenylpropanediamides) gave 3-(aryl/(alkylamino)carbonyl)  $\beta$ -lactams as well as 3-(aryl/(alkylamino)thiocarbonyl)  $\beta$ -lactams. The relative configuration of the obtained products was unambiguously determined by X-ray crystallography. The proposed method is very useful for the one-pot synthesis of a number of 3-(aryl/(alkylamino)carbonyl)  $\beta$ -lactams, especially those containing an amino(thiocarbonyl) moiety, which are not selectively accessible by other methods.

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**Introduction.** – For the period of almost seven decades, after the first documented use of penicillin had begun, the  $\beta$ -lactam system has been at the center of interest of organic chemistry. Of course, the main stream of research is related to the potential applications of  $\beta$ -lactams as effective antimicrobial chemotherapeutics. However, purely synthetic studies are also known, for example, the ‘*Ojima*  $\beta$ -Lactam Synthon Method’ for the preparation of peptides [1], amino acids [2], and hydroxy acids [3].

So far, several methods for the preparation of the azetidine-2-one system have been developed, *e.g.*, carbodiimide coupling of  $\beta$ -amino acids [4], condensation with  $\text{PPh}_3$  pyridine disulfide developed by *Ohno* and co-workers [5], *Grignard* reagent-mediated cyclization of silyl esters of amino acids [6], cyclizations using an epoxide system and anion-stabilizing group [7], intramolecular electrophilic addition to olefins [8], or radical cyclization of 3-oxoenamides [9]. However, it should be noted that the first method used for the preparation of  $\beta$ -lactams *via* the cycloaddition of ketenes to imines, proposed by *Staudinger* at the beginning of the 19th century [10], after several modification and improvements, is still one of the most popular methods for the preparation of these compounds.

Recently, we have reported a variation of the *Staudinger* method for the preparation of 3-carbamoyl  $\beta$ -lactams by addition of aldimines to carbamoyl ketenes, generated from 5-[hydroxy(arylamino)methylidene]-2,2-dimethyl-1,3-dioxane-4,6-dione [11]. Despite many advantages, mainly due to the simplicity of this method, we were not able to obtain models of 3-carbamoyl  $\beta$ -lactams with alkyl groups or S in the carbamoyl fragment.

As mentioned already, an alternative way of forming  $\beta$ -lactams may be the cyclization of enamides, which was demonstrated by *Trogolo* and co-workers [9] in the oxidative cyclization of 3-oxo enamides. On the other hand, we have recently developed a method for the preparation of *N*-alkenylmalonamides (= *N*-alkenylpropanediamides) and *N*-alkenylthiomalonamides **3** from carbamoyl and thiocarbamoyl *Meldrum*'s acids **1**, respectively [12].