Synthesis of oxazolones under Dakin-West conditions

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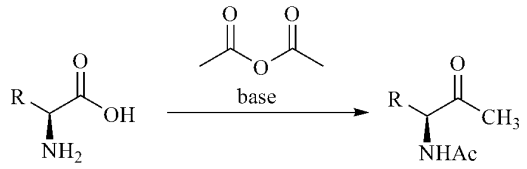
INTRODUCTION

The Dakin-West reaction is a known route for the synthesis of β-acetamido ketones from α-aminoacids. The reaction takes place in the presence of carboxylic anhydrides and a base such as pyridine (Scheme 1).[1]



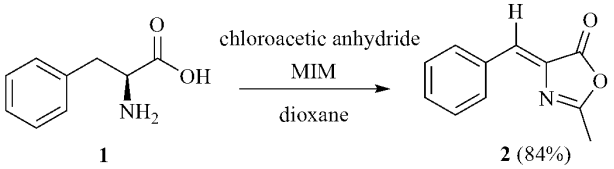
Scheme 1. Dakin-West reaction.

In the current work we report the use of chloroacetic anhydride in the Dakin-West reaction.

RESULTS AND DISCUSSION

We proceeded the reaction using phenylalanine (520 mg; 3 mmol), chloroacetic anhydride (1,5 g; 9 mmol; 3 eq), methylimidazole (0,105 ml, 1,2 mmol; 0,5 eq) as the catalyst and dioxane as the solvent (5 ml).[2] The reaction was kept under reflux during 2 hours. Afterwards, water was added to hydrolyze the remaining anhydride. The organic layer was washed with saturated solution of potassium bicarbonate and water and then dried with anhydrous Na_2SO_4. After evaporation of the solvent, the product was recrystalized in a mixture of ethyl acetate and hexane (468 mg; 84% yield).

Surprisingly, the espectroscopical data for the isolated product indicated the absence of methylene as well as the chlorine atom. A methyl group was observed in these analysis. These data correspond with the data reported for oxazolone **2** as the sole product of the reaction**.**



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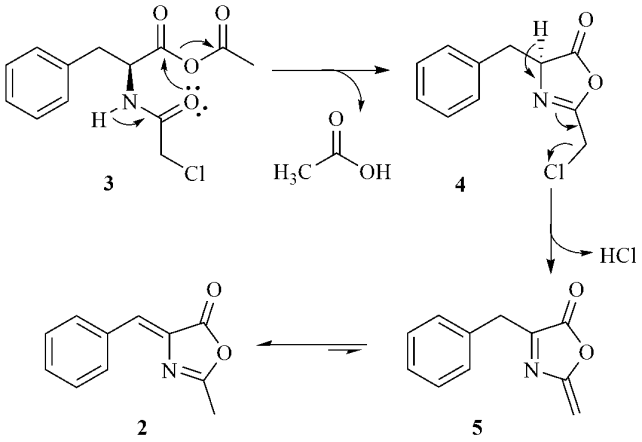
Scheme 2. Synthesis of oxazolones under Dakin-West conditions.

The formation of compound **2** can be explained by an overview of the reaction mechanism. The mechanism dictates that the acetyl-aminoacid 3 cyclizes to form the oxazolinone **4** through the intermediate of a mixed anhydride. In this case, further elimination of chloridric acid happens and a thermodynamic equilibrium between both tautomer takes place. Because tautomer **6** is thermodynamically more stable its formation is favoured, and this is the only product observed.



Scheme 3. Reaction mechanism overview and formation of oxazolone **2**.

CONCLUSION

In summary, we synthesized oxazolone **2** in excellent yield (84%) from phenylalanine, chloroacetic anhydride. To the best of our knowledge this is the first report of the synthesis of oxazolones under Dakin-West reaction conditions.

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