

VCL₃ CATALYZED EFFICIENT ONE-POT SYNTHESIS OF α -AMINO PHOSPHONATES

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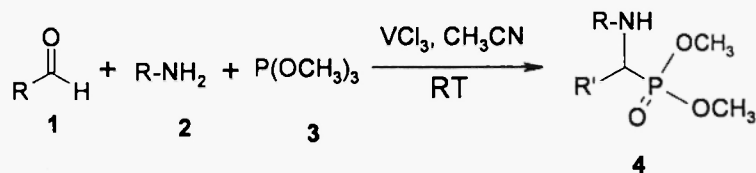
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Abstract : α -Aminophosphonates are synthesized by three component condensation of aldehydes, amines and trimethylphosphite in acetonitrile by using VCl₃ as catalyst. Compared to the conventional methods, this new method consistently has the advantages including excellent yields, short reaction times and mild reaction conditions.

Introduction

α -Aminophosphonates continue to attract increased interest as synthetic targets, because of their structural analogy to α -Aminoacids. Aminophosphates are the important class of biologically active compounds¹, They act as peptide mimics², enzyme inhibitors³, antibiotics⁴, crop protection agents⁵ and catalytic antibodies⁶. As a result, a variety of synthetic approaches⁷ have been developed for the synthesis of α -Aminophosphonates. Of these methods, the nucleophilic addition of phosphates with imines, catalyzed by an acid or a base is one of the most convenient methods. It is interesting to note that the Lewis acids catalyze the reaction in much milder conditions⁸. Among these Lewis acids such as SnCl₂, SnCl₄, BF₃.OEt₂, ZnCl₂ / MgBr₂ have been used for this transformation^{9,10}. However, these reactions cannot be carried out in a one-pot operation starting from aldehydes¹⁰. Recent reagent include ZrCl₄¹¹, lanthanide triflates¹², InCl₃¹³, LiClO₄-TMSCl¹⁴ and Montmorillonite-KSF¹⁵ were used for this transformation. Very recently a solvent free reaction between aldehydes, ammonium formate and dialkyl phosphite catalyzed by alumina under microwave conditions is also reported¹⁶. Most of the above mentioned procedures employ dimethylphosphite as the reagent, with a view to see the migration of methyl carbonium ion to that of using dimethyl (trimethyl silyl) phosphite¹⁷, was the primary aim of the present investigation. The present study also aims at development of cheaper alternative reagent. Herein we report an efficient and inexpensive protocol for the synthesis of α -Aminophosphonates using catalytic amount of VCl₃ under mild reaction conditions **Scheme 1**.

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Results and Discussion

Experimental

In summary, we have demonstrated a novel and efficient protocol for the synthesis of α -Aminophosphonates using catalytic amount of VCl_3 . The method offers several advantages including high yields of product, very short reaction times, inexpensive catalyst, does not involve any additives to promote the reaction.

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Table –1: VCl₃ catalyzed efficient synthesis of α-Aminophosphonates^a

Entry	Aldehyde	Amine	Reaction Time (min)	Yield (%) ^b
4a	C ₆ H ₅ CHO	C ₆ H ₅ NH ₂	5	95
4b	2-(OH) C ₆ H ₄ CHO	C ₆ H ₅ NH ₂	10	90
4c	4-(CH ₃) C ₆ H ₄ CHO	C ₆ H ₅ NH ₂	5	94
4d	4-(OCH ₃)	C ₆ H ₅ NH ₂	10	92
4e	2-(Cl) C ₆ H ₄ CHO	C ₆ H ₅ NH ₂	10	90
4f	4-(CHO) C ₅ H ₄ N	C ₆ H ₅ NH ₂	5	93
4g	C ₆ H ₅ CHO	2-(CH ₃) C ₆ H ₄ NH ₂	10	94
4h	C ₆ H ₅ CHO	4-(CH ₃) C ₆ H ₄ NH ₂	10	90
4i	C ₆ H ₅ CHO	4-(Cl) C ₆ H ₄ NH ₂	10	94
4j	C ₆ H ₅ CHO	C ₆ H ₅ CH ₂ NH ₂	10	95
4k	C ₆ H ₅ CHO	2-(Br) C ₆ H ₄ NH ₂	15	93
4l	2-(CHO) C ₄ H ₃ O	C ₆ H ₅ NH ₂	15	94
4m	2-(CHO) C ₄ H ₃ O	C ₆ H ₅ CH ₂ NH ₂	15	93

^aAll products were characterized by ¹H NMR, IR, and Mass spectra^bIsolated and unoptimized yield

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