SYNLETT Spotlight 200

Ammonium Acetate

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This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

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Introduction

Ammonium acetate (NH_4OAc) is an easily biodegradable chemical, which displays its versatility in almost all arrays of chemical science. It is a white crystalline solid with a melting range of 110–114 °C and is generally stored at low temperature under vacuum because it is hygroscopic and decomposes at elevated temperatures. Pure ammonium acetate can be prepared by saturating glacial acetic acid with dry ammonia.¹ Qualities like cheap and wide commercial availability, safe and easy handling, fair solubility in water and organic solvents and, above all, its non-toxic and eco-friendly nature make ammonium acetate a popular reagent and effective alternative to gaseous ammonia.

From the budding stage of chemistry it has been used in textile and rubber industries, agro and food technology, for analytical purposes as buffer,² and in many organic reactions (Knoevenagel condensation,^{3a} Hantzsch pyridine synthesis,^{3b} Krohnke pyridine synthesis,^{3c} reactions involving $\text{NH}_4\text{OAc}/\text{HOAc}$ combination^{3d}).

In 1957, Hasselstrom et al. reported an amazing synthesis of amino acids by β -radiation of NH_4OAc .⁴ In some cases ammonium acetate shows excellent catalytic activity.⁵

Literature reveals that it has been extensively used in the synthesis of N-heterocyclic compounds (pyridines,^{6–8} pyridopyrimidines,⁹ aziridines,¹⁰ imidazoles,¹¹ benzoxazines¹²), many of which exhibit pharmacological activity or act as drug precursors. Moreover, it finds application in modern techniques of analytical chemistry^{13a} and molecular biology (purification and precipitation of DNA,^{13b} protein crystallization^{13c}). Recently, a valuable regioselective synthesis of synthetically important α -iodo acetates from alkenes, NH_4OAc , and I_2 was reported.^{14a}

Ammonium acetate is an efficient reagent in low- and high-boiling organic solvents at room temperature^{14b} as well as under reflux conditions.^{6–9} Its high efficacy as reagent in water,^{7a} ionic liquids,^{7b} microwave-promoted solvent-less synthesis,¹² and supercritical water¹⁵ gives it a unique position in the present scenario of green chemistry.

Abstracts

(A) Raston and Cave^{6a} reported a practical synthesis of Krohnke-type pyridines, both symmetrical and unsymmetrical 2,6-bisaryl-substituted, in high yield (75%) by cyclocondensation of a pre-formed 1,5-diketo compound with NH_4OAc in acetic acid. Krohnke pyridines and related terpyridines^{6b} are building blocks in supramolecular chemistry and used as therapeutic agents.

(B) 1,4-Dihydropyridines (1,4-DHP's) and Hantzsch esters are calcium-channel blockers and drugs against cardiovascular diseases.⁷ In a green approach 1,4-DHP derivatives were prepared by a multicomponent reaction of an aromatic aldehyde, a cyclic or acyclic 1,3-dicarbonyl compound, Meldrum's acid and NH_4OAc in ionic liquid.^{7b}

(C) Bagley and co-workers⁸ provided a route to polysubstituted pyridines with total regiocontrol via a one-pot reaction of an alkynone, a 1,3-diketo compound, and NH_4OAc without using acid catalysts and applied this strategy in the total synthesis of the acid-sensitive target dimethyl sulfomycinamate, which is a member of the sulfomycin family of thiopeptide antibiotics.

(D) A 1,3-diazabicyclo[3,1,0]hex-3-ene system was obtained in high yield and excellent diastereocontrol via a three-component one-pot synthesis involving phenacyl chloride, aldehyde, and NH_4OAc . The method provides an easy route to bridgehead aziridines, which are potential drug precursors.¹⁰

(E) Ammonium acetate has been utilized to prepare medicinally important enantiopure substituted imidazoles through a cyclocondensation reaction of 1,2-aminoalcohol with an aldehyde, a 1,2-dicarbonyl compound, and NH_4OAc . A study using different ammonia sources in this method established that NH_4OAc is superior to other sources like aqueous NH_3 and NH_4Cl in its efficiency and in the stereoselectivity of the reaction.^{11a}

(F) A reinvestigation reaction of NH_4OAc with acetyl derivatives of Baylis–Hillman adducts in dry methanol at room temperature resulted in the formation of 2° and 3° allylamines (in the case of acrylonitrile and acrylates, respectively) instead of 1° allylamines. This method provides a route to 2° and 3° allylamines and points out the role of ammonium acetate in product selectivity.^{14a}

(G) Ammonium acetate is employed to prepare synthetically important α -iodo acetates in a regioselective synthesis via the reaction of cyclic or acyclic alkenes with NH_4OAc and I_2 in acetic acid.^{14b}

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