SYNLETT
Spotlight 291

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

Acetic Anhydride (Ac_2O)

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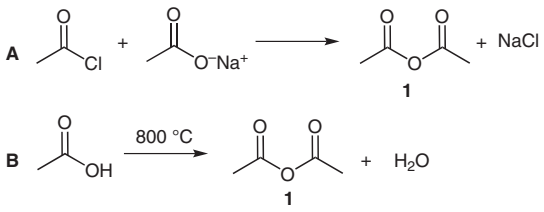
Introduction

Acetic anhydride (Ac_2O) is a very refractive liquid smelling strongly of acetic acid with a boiling point at 139 °C.[1] It is a cheap and commercialized reagent widely used in the synthesis of oxazolones,[2] thiohydantoins,[3] thioacetates,[4] enamides,[5] geminal diacetates,[6] thiadiazoles,[7] as well as in the preparation of carbonyl compounds from imines.[8] Further, it is used in acetylations,[9] brominations,[10] Grignard reactions,[11] and reductive acylations of nitropyrroles.[12]

Preparation

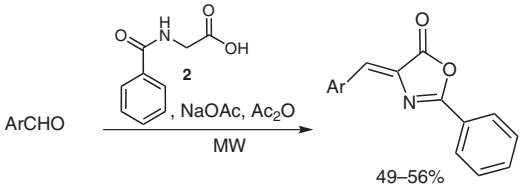
Ac_2O (**1**) was formerly produced starting from sodium acetate and acetyl chloride (**A**). However, nowadays it is usually prepared from acetic acid dehydration (**B**, Scheme 1).[13]



Scheme 1

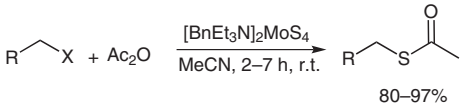
Abstracts

(A) Sun and Cui described the synthesis of oxazolones from a mixture of aryl or heteroaryl aldehydes, hippuric acid (**2**) and anhydrous sodium acetate in Ac_2O under microwave irradiation. All reactions were carried out in a few seconds and provided good yields (49–56%).[2]

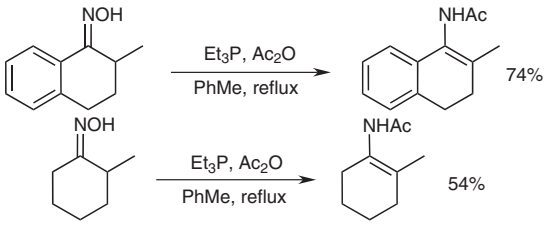


(B) According to Reyes and Burgess, the reaction of some amino acids (e.g., glycine, alanine, and phenylalanine) with Ac_2O and ammonium thiocyanate gave the 1-acetyl-2-thiohydantoins in good yields (51–71%), respectively.[3]

(C) Nasir Baig and co-workers reported a simple and efficient methodology to synthesize thioacetates from alkyl halides in good yields (80–97%). $[BnEt_3N]_2MoS_4$ and Ac_2O are key reagents in this multistep tandem reaction process.[4]



(D) Benzylic and non-benzylic ketoximes can be successfully converted into enamides using a mixture of Ac_2O and Et_3P in toluene.[5]



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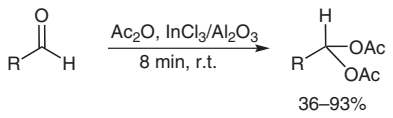
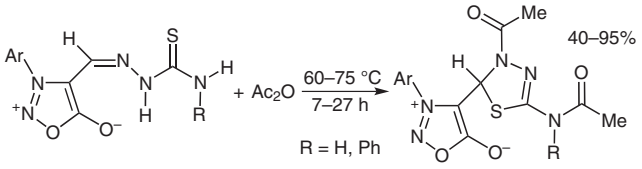
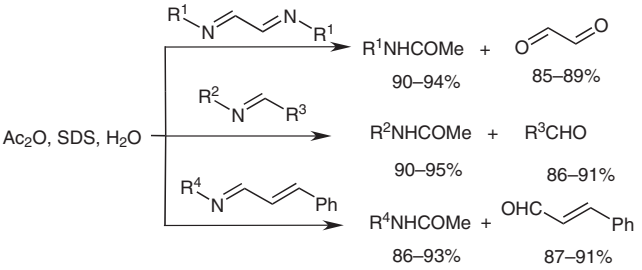
(E) Geminal diacetates can be prepared from aliphatic and aromatic aldehydes in moderate to excellent yields (36–93%) by a simple treatment with Ac_2O in the presence of $InCl_3/Al_2O_3$.[6]



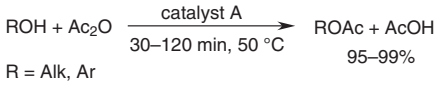
(F) Thiosemicarbazones react with Ac_2O under mild conditions to give thiadiazole compounds in moderate to high yields (40–95%).[7]



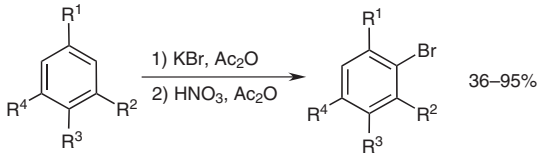
(G) The SDS (sodium dodecyl sulphate) surfactant mediated cleavage of imines to the corresponding carbonyls (aldehydes and ketones) and acetanilides can be achieved with Ac_2O in water in very good to excellent yields (85–91%).[8]



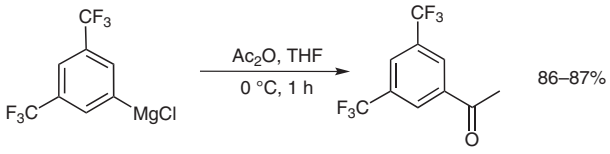
(H) Various alcohols and phenols can be acetylated under solvent-free conditions using Ac_2O as acylating agent and a catalytic amount of heterogeneous cobalt(II) Salen complex (catalyst A). The products were prepared under mild conditions, short reaction times, and in high yields (95–99%).[9]



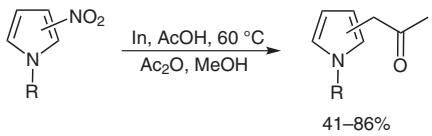
(I) An efficient procedure for the monobromination of activated aromatic compounds can be achieved by treatment with KBr in Ac_2O followed by a dropwise addition of nitric acid in Ac_2O.[10]



(J) 3,5-Bis(trifluoromethyl)phenylmagnesium chloride reacts with Ac_2O to produce 3,5-bis(trifluoromethyl)acetophenone. The product is formed within one hour in high yields (86–87%).[11]



(K) The reductive acylation of nitropyrroles using a mixture of Ac_2O, acetic acid, and indium powder provided pyrrolylamides in moderate to good yields (41–86%).[12]



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