

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 (Ac₂O)

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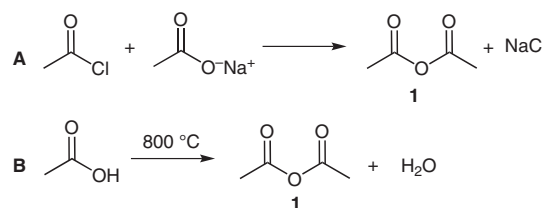


Introduction

Acetic anhydride (Ac₂O) 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 thiohydantoin,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 nitropryroles.¹²

Preparation

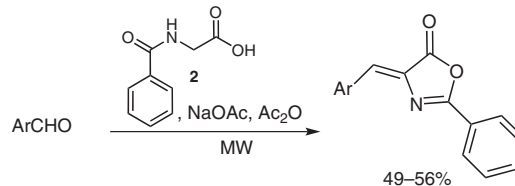
Ac₂O (**1**) was formerly produced starting from sodium acetate and acetyl chloride (**A**). However, nowadays it is usually prepared from acetic acid dehydration (**B**, Scheme 1).¹³



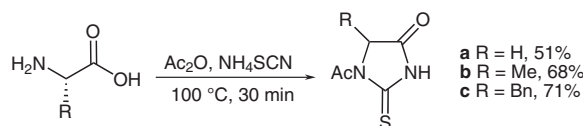
Scheme 1

Abstracts

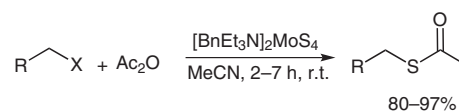
(A) Sun and Cui described the synthesis of oxazolones from a mixture of aryl or heteroaryl aldehydes, hippuric acid (**2**) and anhydrous sodium acetate in Ac₂O under microwave irradiation. All reactions were carried out in a few seconds and provided good yields (49–56%).²



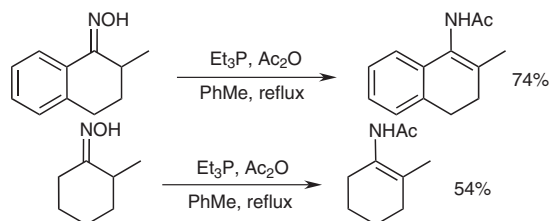
(B) According to Reyes and Burgess, the reaction of some amino acids (e.g., glycine, alanine, and phenylalanine) with Ac₂O and ammonium thiocyanate gave the 1-acetyl-2-thiohydantoin in good yields (51–71%), respectively.³



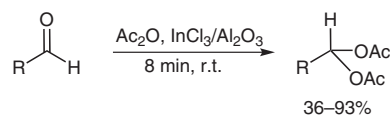
(C) Nasir Baig and co-workers reported a simple and efficient methodology to synthesize thioacetates from alkyl halides in good yields (80–97%). [BnEt₃N]₂MoS₄ and Ac₂O are key reagents in this multi-step tandem reaction process.⁴



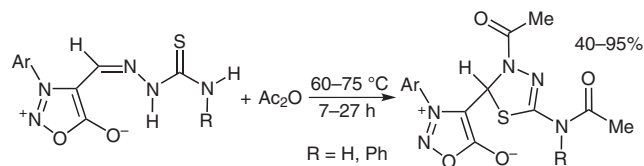
(D) Benzylic and non-benzylic ketoximes can be successfully converted into enamides using a mixture of Ac₂O and Et₃P in toluene.⁵



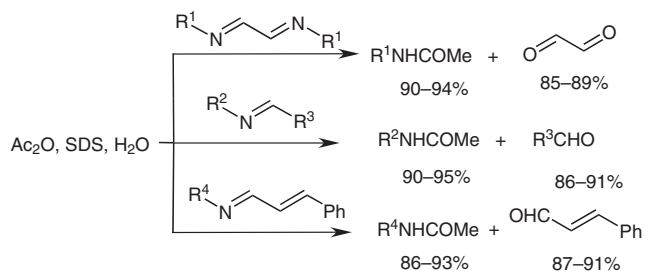
(E) Geminal diacetates can be prepared from aliphatic and aromatic aldehydes in moderate to excellent yields (36–93%) by a simple treatment with Ac_2O in the presence of $\text{InCl}_3/\text{Al}_2\text{O}_3$.⁶



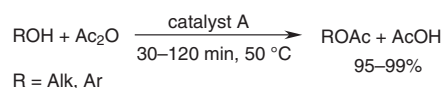
(F) Thiosemicarbazones react with Ac_2O under mild conditions to give thiadiazole compounds in moderate to high yields (40–95%).⁷



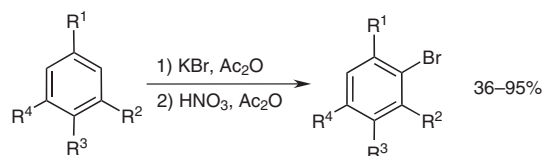
(G) The SDS (sodium dodecyl sulphate) surfactant mediated cleavage of imines to the corresponding carbonyls (aldehydes and ketones) and acetanilides can be achieved with Ac_2O in water in very good to excellent yields (85–91%).⁸



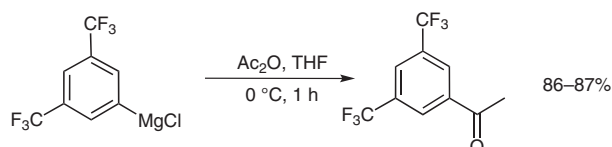
(H) Various alcohols and phenols can be acetylated under solvent-free conditions using Ac_2O as acylating agent and a catalytic amount of heterogeneous cobalt(II) Salen complex (catalyst A). The products were prepared under mild conditions, short reaction times, and in high yields (95–99%).⁹



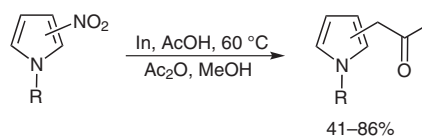
(I) An efficient procedure for the monobromination of activated aromatic compounds can be achieved by treatment with KBr in Ac_2O followed by a dropwise addition of nitric acid in Ac_2O .¹⁰



(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



References

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