SYNLETT
Spotlight 291

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

### Introduction

Acetic anhydride (Ac$_2$O) 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,$^3$ thioacettes,$^4$ 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 nitropyroles.$^{12}$

### Preparation

Ac$_2$O (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**

(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$_2$O 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$_2$O 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$_3$N]$_2$MoS$_4$ and Ac$_2$O are key reagents in this multi-step tandem reaction process.$^4$

(D) Benzylc and non-benzylc ketoximes can be successfully converted into enamides using a mixture of Ac$_2$O and Et$_3$P 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 Ac₂O in the presence of InCl₃/Al₂O₃.⁶

(F) Thiosemicarbazones react with Ac₂O 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 acetonilides can be achieved with Ac₂O in water in very good to excellent yields (85–91%).⁸

(H) Various alcohols and phenols can be acetylated under solvent-free conditions using Ac₂O 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 Ac₂O followed by a dropwise addition of nitric acid in Ac₂O.¹⁰

(J) 3,5-Bis(trifluoromethyl)phenylmagnesium chloride reacts with Ac₂O 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 nitropyroles using a mixture of Ac₂O, acetic acid, and indium powder provided pyrrolylamides in moderate to good yields (41–86%).¹²

References


(2) Sun, Y.-F.; Cui, Y.-P. Dyes Pigments 2009, 81, 27.


(4) Baig Nasir, R. B.; Sai Sudhir, V.; Chandrasekaran, S. Synlett 2008, 2684.


