**Acetic Anhydride (Ac₂O)**

Compiled by Lucas Villas Bôas Hoelz

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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 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 nitropyroles.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](image)

**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-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%). [BnEt₃N]₂MoS₄ and Ac₂O 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 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 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 acetanilides 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.


