Heteropolyacid-Catalyzed Synthesis of Aspirin

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Abstract: Aspirin was synthesized from salicylic acid and acetic anhydride in the presence of noncorrosive 12-tungstophosphoric acid as an alternative catalyst to liquid acids, e.g., sulfuric acid. This process can be carried out at room temperature and gives a reasonable yield of isolated product.

The synthesis of aspirin from salicylic acid and acetic anhydride, a rapid *O*-acetylation reaction carried out with simple equipment, is one of the most common experiments in undergraduate laboratories [1]. The most widely employed catalysts for this reaction are concentrated sulfuric [2] and phosphoric acid [3]. Unfortunately, both of these acids are strongly corrosive and must be handled with care. Recently, an alternative method was reported by which aspirin could be prepared using acetyl chloride—pyridine as the acetylating agent at lower temperatures [4]. However the obnoxious and irritating odors of these reagents make them unsuitable for undergraduate experiments.

In this paper we introduce a convenient and noncorrosive strong-acid catalyst, 12-tungstophosphoric acid ($H_3[PW_{12}O_{40}]$•24 H_2O), which is an efficient homogeneous catalyst in organic synthesis [5, 6]. Heteropolyacids are commercially available and are easy to prepare from readily available tungstates, molybdates, and phosphates [7]. The preparation of aspirin using heteropolyacid as a catalyst can be conducted at room temperature and gives reasonable yields.

Experimental

Salicylic acid (2.0 g, 15 mmol) was placed in a 125-mL Erlenmeyer flask, followed by 5 mL acetic anhydride and 0.2 g 12-tungstophosphoric acid. The solid dissolved in the acetic anhydride to form a dark red–brown solution. The reaction was maintained at room temperature for 15 min with occasionally swirling. On completion of the reaction, the mixture was diluted with 50 mL water. The flask was placed in an ice bath and the flask wall was scratched with a glass rod to hasten crystallization. The crude product was collected by vacuum filtration, removed, and treated with saturated sodium bicarbonate solution until no further bubbles were released. A gumlike polymeric byproduct was removed by suction filtration, and the resulting filtrate was treated by dropwise addition of 2 M HCl until the solution was adjusted to pH 2. After cooling in an ice bath, the mixture was subjected to vacuum filtration. The resulting solid was washed with cold water and air dried. Recrystallization from ethyl acetate gave 1.5 g (57% yield) of product, mp 135–136 °C (literature value 135 °C) [3]. Testing with a methanol–water solution of ferric chloride gave a negative result. If the reaction time was prolonged to 30 min, a higher yield (71%) was obtained.

Handling and Disposal

The filtrate containing acetic acid, 12-tungstophosphoric acid, and unreacted salicylic acid should be poured into an appropriate liquid-waste container.

References and Notes

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