Synthesis and Recrystallization of Acetanilide

Purpose:

Aniline and acetic anhydride were reacted to form solid acetanilide. Small amounts of crude crystals were used to determine a suitable recrystallization solvent. The crude product was purified using recrystallization in water. Following the purification with recrystallization, the purified product was characterized by ^{1}H NMR and IR spectral analyses. Recrystallization is a simple and straightforward technique used to purify a crude solid with small amounts of impurities. It was applicable to this reaction because the product acetanilide was a solid and neither of the reactants were solids, so the crude product had little impurities with different polarities.

Results, Discussion, and Conclusions:

The reaction between aniline and acetic anhydride is characterized by a nucleophilic acyl substitution. The mechanism involves the nucleophilic attack on the carbonyl carbon of acetic anhydride by the nitrogen on aniline. The tetrahedral intermediate that forms then collapses to form acetanilide and acetic acid (2). The acetanilide product precipitates out of the solution as the reaction progresses. It can then be isolated and prepared for recrystallization. The crude crystals, however, contain trace impurities such as unreacted starting material and secondary product. Recrystallization allows for the purification of the crude product by choosing a solvent, that, when heated, brings all of the solid product and its impurities into solution and, when cooled slowly, allows the pure product to crystallize while the impurities remain in solution. It is a very simple, cheap, and effective way to purify a crude solid product (1).

Following the isolation of crude acetanilide, a suitable recrystallization solvent needed to be chosen. A suitable recrystallization solvent is slightly more polar or slightly less polar than the solute so that the solute is insoluble at low temperatures but soluble at high temperatures. Several different solvents were experimented with to determine which was most suitable. First, roughly 50 mg of crude product was dissolved in 0.5 mL of a solvent. If the product was soluble at room temperature, the solvent was deemed unsuitable for recrystallization. If the product was insoluble after heating the solvent, the solvent was also deemed unsuitable. If the product was soluble after being cooled down in an ice bath, the solvent was also deemed unsuitable. Therefore, the recrystallization solvent is suitable is the solute is insoluble or partially soluble at room temperature, soluble when heated, and insoluble when cooled. The two solvents that fit this character were water and 20% ethanol. Water was chosen as the recrystallization solvent for this particular recrystallization. Water is slightly more polar than acetanilide. Both have sights for hydrogen bonding, but the geometry of the water molecule causes it to be slightly more polar than the amide group on acetanilide.

After a recrystallization solvent was found, the recrystallization of the entire product was performed. As hot solvent was added, the crude product did not seem to dissolve, even after all of the solvent prepared was added. Therefore, another 10 mL of ethanol was added to facilitate the dissolving of the product. After the recrystallization and isolation of the purified product, melting point analysis was performed. The experimental melting point was 120.9 - 123.4 ℃, which is higher than the actual melting point of acetanilide, 113 - 115 ℃. Generally, the presence of impurities results in a melting point that is less than the actual melting point (3). The higher than expected melting point could have been due to the presence of impurities, or could also have been due to faster than suitable heating of the solid. Acetanilide was certainly made in this reaction, since the IR spectrum shows a characteristic amide peak at 1661.50 cm^{-1} while the ^1H NMR spectrum shows an aromatic multiplet with an integral value of 5.92. This multiplet therefore must account for the 5 aromatic hydrogens as well as the secondary amine hydrogen (1). However, acetanilide was not recrystallized with good recovery, with just 36.89 % of the crude product being obtained after recrystallization, meaning much of the acetanilide in the crude product was lost during the recrystallization, most likely remaining dissolved after cooling down because too much solvent was added. The purity of the product was also questionable because of a notable 0.25 integral value impurity peak in the ^1H NMR. This was likely a starting material impurity, as the downfield shift indicates the presence of an amine group, which is contained in the reactant aniline.

The reaction to form acetanilide had a high yield of 84.05%. The relatively small amount of product that was lost was most likely simply left over in the round bottom flask while pouring into the vacuum filtration apparatus or on the filter paper and funnel. ^1H NMR spectral analysis showed two major peaks. One was a sharp singlet at a chemical shift of 2.2 ppm and an integral value of 3, which was indicative of an amide methyl functional group present on the expected product acetanilide. The other was a large multiplet at a chemical shift of 7.4 ppm and an integral value of 5.92, which is indicative of the 5 aromatic protons in acetanilide. Upon further inspection, a sharp singlet could also be seen within this multiplet, which represents the single secondary amide proton that overlaps the aromatic protons. The presence of the secondary amide proton overlapping the aromatic multiplet also explains why the integration value for the multiplet is closer to 6 rather than the expected integration value of 5. Two impurity peaks were present, one at a chemical shift of 3.6 ppm, which is likely from the water or ethanol from the recrystallization solvent and another at a chemical shift of 5.7 ppm, which is likely from the starting material aniline. IR spectral analysis also showed that acetanilide was present. Characteristic aromatic absorption was present between 3000 and 3291.94 cm^{-1} and an amide carbonyl absorption at 1661.50 cm^{-1}. The IR spectrum did not seem to include an amine peak, which would have had a high absorption around 3300-3400 cm^{-1}, indicating the deprotonation of the amine hydrogen.

In this experiment, aniline was reacted with acetic anhydride to form acetanilide in a nucleophilic acyl substitution reaction. The reaction performed for this experiment ran extremely well with 84.05% yield, but the recrystallization procedure was hampered by the use of water rather than 20% ethanol as the recrystallization solvent, as the percent recovery was just 36.89%. Excess addition of recrystallization solvent resulted in a poor percent recovery of the purified product following the cool down process. Other factors that may have decreased the percent yield or percent recovery could have been from solid product left behind in the reaction vessel or on the vacuum filtration apparatus.

Experimental:

Distilled water (15 mL), aniline (2.06 g), and acetic anhydride (3 mL) were stirred together for 30 minutes. The crude acetanilide precipitate was isolated with vacuum filtration. A suitable recrystallization solvent was determined by adding a small amount of dry crude product (50 mg) to 6 test tubes containing a small amount (0.5 mL) of water, ethanol, 20% ethanol in water, ethyl acetate, dichloromethane, and hexanes. The tubes were agitated vigorously for 30 seconds and solubility was observed. If the product was insoluble, the product was heated in a sand bath until it began to boil. If the solid dissolved, the tube was transferred to an ice water bath for 2 minutes. If solid crystals were observed coming out of solution, the solvent was determined to be suitable for recrystallization. Recrystallization of the remaining crude product was performed using water. Hot water (20 mL) was added to the crude crystals and the mixture was gently heated and stirred. Additional water (5 mL increments) was added until all of the crystals were dissolved. Once all solid was dissolved, the solution was cooled to room temperature, then cooled on ice for 10 minutes. Scratching was used to help facilitate the start of recrystallization. The purified crystals were isolated by vacuum filtration and allowed to dry. ^{1}H NMR (60 MHz, deuterated chloroform) δ (ppm): 2.1-2.2 (s, 3H), 5.7-5.8 (s, 1H). 7.1-7.6 (m, 6H). IR ν_{max} (cm^{-1}) 3291.94, 2801.75, 1661.50, 1596.35, 1538.15, 1366.32.

References

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