Chemistry of alpha-Amino Acids: A Multi-Step Synthesis of Hippuric Acid and Derivatives

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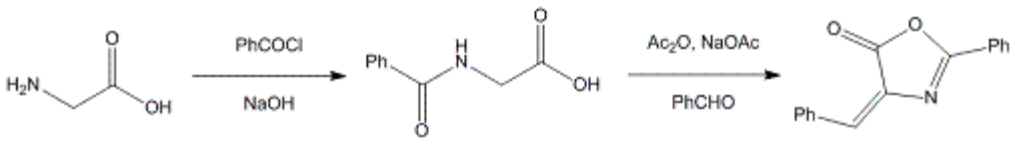
Experiment Overview

In this experiment, you will synthesise hippuric acid starting from glycine, an amino acid that is commonly found in proteins, and benzoyl chloride. The reaction of glycine with benzoyl chloride in the presence of an alkaline catalyst yields the amide, benzoylglycine (hippuric acid). The name comes from the Greek work for horse, *hippos*, because hippuric acid was first isolated from the urine of horses. With hippuric acid in hand, you will prepare a heterocycle, 4-benzylidene-2-phenyloxazol-5-one - the overall scheme is illustrated below. This heterocyclic system is activated towards new carbon-carbon bond formation and can be utilised for the synthesis of new α-amino acids.



The *in vitro* synthesis of hippuric acid in this experiment is like the *in vivo* synthesis of hippuric acid from benzoic acid and glycine. Benzoic acid is present in many fruits and vegetables and is a common preservative in food products such as soft drinks and canned foods. Sodium benzoate, the sodium salt of benzoic acid, is also used as an anti-fungal agent to preserve bread.

An adult human being excretes about 0.7 g of hippuric acid daily. The enzyme-catalysed biosynthesis of hippuric acid in the liver proceeds by reaction of glycine with a thioester, benzoyl CoA. Hippuric acid is more water-soluble than benzoic acid; this property allows hippuric acid to be excreted more efficiently. The conversion of relatively water-insoluble substances to more soluble products is a general process for the elimination of foreign substances from our bodies. The metabolism of sodium benzoate is sometimes used in hospitals as a test of liver function.

Level of Experiment

The experiment can be run at different levels (with appropriate modification) ranging from first year through to third year. Currently this laboratory as it appears features as a third year preparative laboratory at the Australian National University; it could equally well serve as it appears as a second year laboratory.

The experiment could be adapted to a first year preparation by completing only part 1, involving the preparation of hippuric acid and eliminating the need for analysis of NMR spectroscopic data.

Keyword Descriptions of the Experiment

Domain
organic chemistry

Specific Descriptors
acylaction, condensation, amino acid chemistry

Course Context and Prerequisite Knowledge and Skills

For the experiment as presented, students are expected to have completed a first year course in chemistry. They should be familiar, through lectures, with concepts involving nucleophilic substitution at carbonyl centres. Mechanistic detail can be as detailed as the laboratory supervisor would like to take it. At third year level we routinely ask for full mechanistic detail as an aid to understanding.

Time Required to Complete

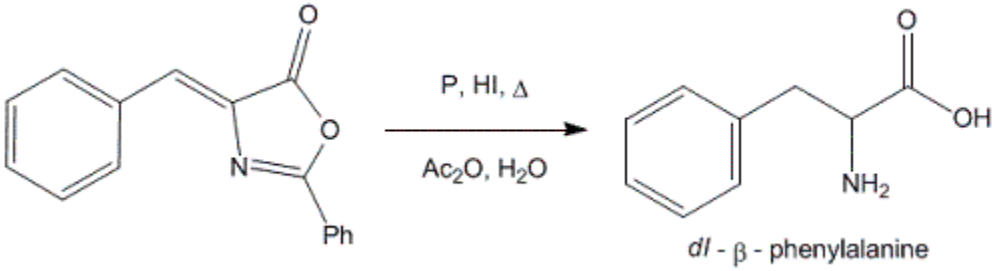
Prior to Lab: 30 min
In Laboratory: 3-5 h (an overnight wiat is required; such steps can be included in experiments to encourage students to plan their experimental work and to work efficiently.)
After Laboratory: 2 h

Experiment History

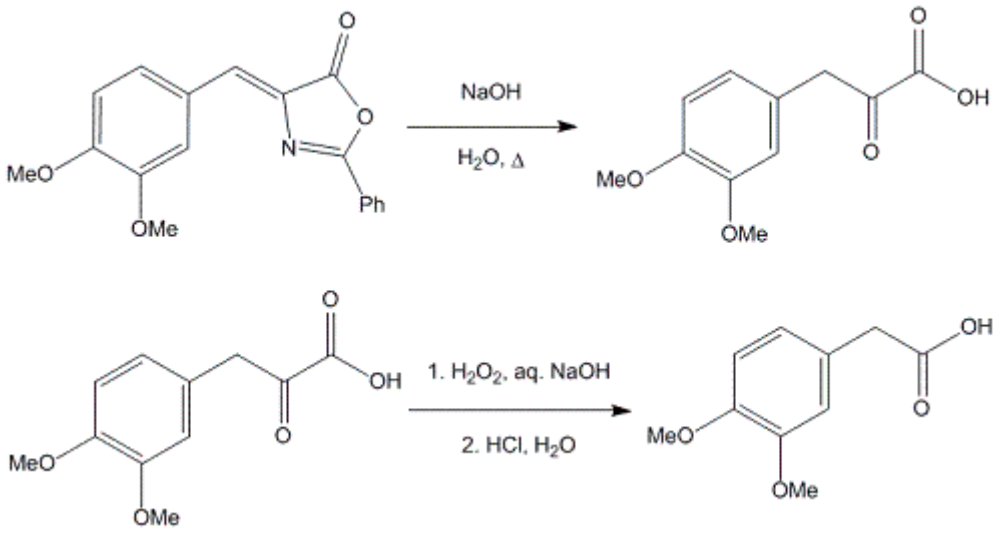
The experiment is adapted from an Organic Synthesis preparation dating from the 1930s - see references for details.

Comments

Students should be encouraged to determine what types of compounds can be prepared from the oxazolone. For example, *dl*-β-phenylalanine can be prepared as follows:



Similar oxazolones can be used to prepare a-ketocarboxylic acids and phenylacetic acid derivatives:



References

Organic Syntheses, Coll. Vol. 2, p.55 (1943); Vol. 13, p.8 (1933).

Organic Syntheses, Coll. Vol. 2, p.333 (1943); Vol. 15, p.31 (1935).

Organic Syntheses, Coll. Vol. 2, p.489 (1943); Vol. 19, p.67 (1939).