Abstract

The potato plant belongs to one of the most appreciated crops providing food for humans. Since the last two centuries the production in The Netherlands has almost increased a five fold due to improved production techniques (e.g. crop rotation, trap crops, use of nematicides, and nematode resistant plants). However, facing the continually increasing world population, significant harvest loss can result in serious problems.

The potato cyst nematode (PCN) is a small roundworm that parasitizes the potato root, causing severe damage to the plant (potato sickness). A heavily infested potato field can suffer from major losses up to 90%. The juvenile nematodes are triggered to hatch by root exudates of the potato plant during the spring season. The key hatching agent is one of the most active hatching agents known, and already displays activity at the nanogram/L range. It was isolated in 1986 form potato root extracts and the absolute structure was determined in 1992 by means of X-ray analysis by Dutch scientists. This hatching agent was called solanoclepin A.

This group aims for a convergent approach towards the synthesis of solanoclepin A, in which the aldol coupling of the two fragments is applied as one of the key-steps. During this internship the aldol coupling using easier to prepare model components (depicted below) was evaluated.

The very strained tricyclic right-hand system, containing three quaternary stereogenic carbon atoms, can be prepared by a [2+2] photocycloaddition from a relatively simple precursor. For the first time, the second isomer that is formed during uv irradiation was isolated and subjected to X-ray analysis. The obtained structure provided additional support for our notion regarding the explanation for the observed diastereoselectivity in the [2+2] photocycloaddition.
The aldol product could be obtained in moderate yield, as the maximal conversion of the reaction obtained was only 50%. Fortunately, this reaction was clean and the starting materials could be recovered resulting in a yield of 81% b.r.s.m. To our delight, this aldol product was formed as a single isomer containing the correct stereochemistry as in the natural product. The protection of the aldol product proved to be very troublesome, because it decomposed under acidic conditions and resulted in the E1cB-elimination under basic conditions.

Therefore, the addition of vinylmagnesium bromide was performed directly on unprotected aldol product, yielding the product in a diastereomeric ratio of 5:1. Unfortunately, enolization of the aldol product by the Grignard reagent prohibited a full conversion, and addition of CeCl₃ to the Grignard reagent did not result in satisfactory results. The addition of an acetylide anion also suffered from this competing side reaction, and yielded the product in comparable yield and dr. Various attempts to dehydrate the vinyl and acetylene adducts resulted in surprising side products, but synthesis of the desired diene was not achieved. It has been shown that selective protection of the secondary alcohol can be achieved directly after the addition of the organometallic species on the aldol product. Most likely, this alcohol needs to be protected at this stage in the total synthesis.