Towards the Photolabile Opening of Quasi[1]catenane Model Systems
A.M. Bond

Abstract

Lasso peptides are very promising as new field of medicine, as they exhibit a wide range of biologically active properties. In order to eventually synthesize these peptides from their linear precursors, the chemistry around other similar structures needs to be fully understood and mastered. An example of such a structure is the [2]catenane: two interlocked rings.

Our group developed a templated backfolding strategy for the synthesis of quasi[1]catenanes: bicyclic compounds connected by a fluorene-centered tetrahedral carbon atom. To carry out the cleavage to yield a [2]catenane, a quasi[1]catenane was made in which the central part is a cyclic ketal. Many attempts were done, but cleavage by using reagents remained impossible due to severe steric hindrance.

In a recent paper from 2016 was found that acetals based on 3-amino benzaldehydes are photolabile. We wanted to investigate if the cyclic ketal of a quasi[1]catenane can be made photolabile by building 3-amino groups in the central fluorene moiety, and could thus be cleaved by irradiation. Therefore, we synthesized a model system, which is a ketal of 9-fluorenone with heterocyclic amines at the meta position. 9-Fluorenone was brominated to 2, followed by a ketalization to 5. This ketalization took a lot of effort since the reaction is very slow, and stops perhaps almost in the hemiketal stage. This compound was then aminated by a Buchwald-Hartwig cross-coupling mechanism with four different heterocyclic amines to compounds 6a-d. By irradiation with 360 nm UV of a solution of the ketals in CDCl3 and CD3OD it was then investigated if it is susceptible to this radiation. All four aminated ketals, 6a-d, were found to be photolabile upon irradiation. Only one ketal, 6c, was fully analyzed and it was found it did not hydrolyze to its ketone. However, other decomposition reactions take place upon irradiation. Ketal 5 was found to be not photolabile at this wavelength. Cleavage of the ketal by irradiation at this wavelength does not yet seem as an accessible route, but perhaps further investigations at slightly different wavelengths and conditions could be done.

A side project was done but no relevant information was obtained for the investigation of the photolabile opening of cyclic ketals in quasi[1]catenane model systems.