α-Azido Alcohols from Aldehydes by the Reaction with Hydrazoic acid

Christian Berndt and Klaus Banert*

Department of Chemistry, Chemnitz University of Technology
Straße der Nationen 62, D-09111 Chemnitz, Germany

Introduction

α-Azido alcohols derived from aldehydes are not known in literature but postulated to be unstable intermediates in solvolysis reactions. The synthesis starting from α-azidalkyl trimethylsilyl ethers,[1] geminal diazides[2] or α-azido ethers[3] only led to the corresponding aldehydes but not to α-azido alcohols (Figure 2). The aim of our work is to synthesize and characterize α-azido alcohols to examine their reaction behavior, to obtain their equilibrium constants, and finally to understand the kinetics of the reactions. After that, different reactions like substitution, esterification, dehydration, oxidation of the hydroxy-group and 1,3-dipolar Cycloaddition, photolysis, Staudinger reaction of the azido-group should be performed.

Motivation

Inspired by the azidomethanol (3), that was found after the reaction of tris(azidomethyl)amine (2) and hydrogen iodide containing traces of water, we were looking for an alternative synthesis of α-azido alcohols (Figure 1).

With the knowledge that azidomethanol (3) is not decomposing spontaneously in formic aldehyde and HN₃, we tried to figure out, whether α-azido alcohols can be generated in an analogous way to the cyanohydrin synthesis from aldehydes and hydrazoic acid instead of aldehydes and cyanohydrin acid (Figure 2).

Reaction of unsaturated aldehydes and hydrazoic acid

Lots of α,β-unsaturated aldehydes have been converted in literature with an excess of HN₃.[4] We thought, that the diazides 11 may have been formed but overseen in literature. Actually we found that only alcohols 9a lead to a diazide 11 (Figure 5).

Aldehydes with isolated C,C double or triple bond do not or only slowly add HN₃ at the carbon-carbon multiple bond. But intramolecular 1,3-dipolar cycloadditions of unsaturated azides can be very fast reactions, if bicyclic products with convenient ring sizes are generated.[5] Accordingly, unsaturated α-azido alcohols 13 resulting from the corresponding aldehydes 12 give heterocycles 14. Up to now, formation of monocycles 15 was not observed.

Equilibrium constants and kinetics of the formation of α-azido alcohols

Different aliphatic aldehydes were reacted with hydrazoic acid to see, whether a formation of α-azido alcohols is possible. If possible, the equilibrium constants were calculated from weighted aldehydes, titrated hydrazoic acid, and NMR study of the ³H NMR signals when the equilibration was reached.

Different α-azido alcohols are not decomposing

Summary and Outlook

We have been able to directly observe α-azido alcohols using low temperature NMR experiments for the very first time. To confirm our results more aldehydes and their behavior towards HN₃ should be investigated.

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Literature