

Synthesis of 3,5-dinitro-1,4,5,6-tetrahydropyridine-2-amine

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Abstract

Tetrahydropyridine derivatives possess antimicrobial, antioxidant, anti-inflammatory, analgesic effect. Therefore, the expansion of the range of these compounds and studying their properties is important. There are published data on various approaches to the formation of tetrahydropyridine structure: mild oxidation of piperidine and its derivatives, condensation of nitriles, primary amines, etc. Previously, we have implemented a selective dearomatization 6-tizanidine 3,5-dinitropyridine and 2-hydroxy-3,5-dinitropyridine under the action of tetrahydroborate sodium, followed by C-protonation of hydride adducts with the formation of tetrahydropyridine derivatives.

This article describes the two-step method of obtaining *N-R*-3,5-dinitro-1,4,5,6-tetrahydropyridine-2-amines based on *N*-substituted 3,5-dinitropyridine-2-amines. In the first stage under the action of a substrate, tetrahydroborate sodium as a result of dearomatization the selective joining of the hydride ion at the positions 4 and 6 of the pyridine ring with the formation of doubly charged intermediate σ -adduct. The target 3,5-dinitro-1,4,5,6-tetrahydropyridine-2-amines obtained by the action on σ -adducts diluted orthophosphoric acid. The transition to the soft conditions from the activated nitro groups by the pyridine system to anionic σ -adductum, and from them to the appropriate tetrahydropyridine allows obtaining products with high yields. The proposed method is applicable for obtaining new polyfunctional derivatives of Δ^2 -piperidine. In addition, further functionalization of amino-, nitro-, carboxyl groups opens up opportunities for a variety of compounds with presumably high biological activity.

The structure of the obtained compounds were proved by IR spectroscopy method, data of two-dimensional homo- (COSY) and heteronuclear (HMBC, HSQC) correlation NMR spectroscopy, and elemental analysis data. Final proof of the structure of the synthesized tetrahydropyridine was derived from RSA data of the crystal of the *N*-cycloheptyl-3,5-dinitro-1,4,5,6-tetrahydropyridine-2-amine. In the analyzed crystal tetrahydropyridine fragment is characterized by the conformation of the distorted elbow, with axial location of the nitro group in the 5-position. The oxygen atom of one of the nitro groups forms a strong intramolecular hydrogen bond with the proton of the amino group substituents, which leads to a reduction of the neighboring relations, in comparison with the average values from the Cambridge structural database.

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