Thematic Section: Preparative Research. **Full Paper**
Subsection: Organic Chemistry.
The Reference Object Identifier – ROI: jbc-01/19-57-3-83
The Digital Object Identifier – DOI: 10.37952/ROI-jbc-01/19-57-3-83
Submitted on March 11, 2019.

Synthesis and structure of new derivatives of 2-chloro-*N*-(3-*R*-1,5-dinitro-8-oxo-3-azabicyclo[3.3.1]non-6-en-7-yl)acetamides

© **Loik G. Mukhtorov**,[1]* **Evgenia V. Ivanova**,[1+] **Makhmadkul B. Karimov**,[2] **MariaB. Nikishina**,[1] **Irina V. Shahkeldyan**,[1] **Yury M. Atroshchenko**,[1] and **Konstantin I. Kobrakov**[3]

[1] *Department of Chemistry. Tula State Lev Tolstoy Pedagogical University. Lenina St., 125. Tula, 300026.Russia. Phone: +7 (4872) 35-78-08. E-mail: reaktiv@tspu.tula.ru*
[2] *Dushanbinsky Branch of the National Research Technological University. Nazarshoeva St., 7. Dushanbe, Republic of Tajikistan. Phone: +992 919-410-241. E-mail: karimovm.b@mail.ru*
[3] *Department of Organic Chemistry. Moscow State University of Design and Technology. Sadovnicheskaya St., 33. Moscow, 117997. Russia. Phone: +7 (495) 955-35-58. E-mail: kobrakovk@mail.ru*

*Supervising author; [+]Corresponding author

Keywords: hydride adducts, Mannich condensation, 2-chloro-*N*-(2-hydroxy-3,5-dinitrophenyl)acetamide, 2-chloro-*N*- (3-R-1,5-dinitro-8-oxo-3-azabicyclo[3.3.1]non-6-en-7-yl)acetamides, 3-azabicyclo[3.3.1]nonanes.

Abstract

The production of new 3-azabicyclononane derivatives is an important trend in the synthesis of organic compounds. It is known that 3-azabicyclononane is a key pharmacophore of a number of plant alkaloids that are widely used in medicine (aconitin, quinidine, tropane, cocaine, garnet, etc.). Among synthetic heterocycles containing a 3-azabicyclo[3.3.1]nonane fragment, compounds with various types of biological activity were found: analgesic and anti-inflammatory, antimicrobial and fungicidal, anti-cancer, antioxidant, etc. We synthesized a number of new derivatives of 3-azabicyclo[3.3. 1]nonane by Mannich condensation of hydride σ-adduct 2-chloro-*N*-(2-hydroxy-3,5-dinitrophenyl)acetamide with formaldehyde and primary amines or amino acids. The synthesis was carried out in two stages. In the first stage, under the action of sodium tetrahydride borate on a solution of 2-chloro-*N*-(2-hydroxy-3,5-dinitrophenyl)acetamide, the C=C bonds of the aromatic ring were reduced to form a 3-charge hydride adduct. The resulting diaduct was isolated from the solution and, while cooling with ice, was introduced into Mannich condensation with formaldehyde and a solution of the primary amine or amino acid. When the reaction mixture was acidified with dilute orthophosphoric acid to pH 4-5, precipitates of the target products precipitated. After recrystallization from ethanol, the yield of the target products, depending on the substituent at the nitrogen atom, was 75-90%. This method is distinguished by relative simplicity, availability of reagents and allows under mild conditions to transfer from the aromatic system activated by nitro groups to 3-azabicyclo[3.3.1]nonane derivatives, containing promising from the point of view of further functionalization nitro, carbonyl, amino groups, and also halogen atom . The structure of the compounds obtained was proved by IR, ^{1}H-, ^{13}C-, two-dimensional correlation NMR spectroscopy, as well as high-resolution mass spectrometry data (HRMS).

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