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Amino acids in the double Mannich reaction with anionic σ-complexes of 5,7-dinitro-8-hydroxyquinoline

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Abstract

The synthesis of new derivatives of 3-azabicyclononan is one of the urgent tasks of modern synthetic organic chemistry. 3-Azabicyclononan is a structural analogue of the cytisine alkaloid, which is a strong agonist of acetylcholine receptors. Among synthetic heterocycles containing a 3-azabicyclo[3.3.1]nonane fragment, compounds with different types of biological activity have been discovered at present: analgesic, anti-inflammatory, antimicrobial, antioxidant, and others. The introduction of a fragment of azabicyclononan into the amino acid structure can lead to a limitation of the conformational mobility of a new molecule, as a result of which the activity and selectivity of its interaction with the receptor will increase. We synthesized 2-(1,9-dinitro-8-oxo-6,11-diazatricyclo[7.3.1.0^{2,7}]trideca-2,4,6-trien-11-yl)acetic acid and 2-(1,9-dinitro-8-oxo-13-(2-oxopropyl)-6,11-diazatricyclo[7.3.1.0^{2,7}]trideca-2,4,6-trien-11-yl)acetic acid by the interaction of annionic σ-complexes 5,7-dinitro-8-hydroxyquinoline with glycine under Mannich condensation in high yield. At the beginning, when 5,7-dinitro-8-hydroxyquinoline $NaBH_4$ was applied in DMF or acetone carbanion in DMSO, the corresponding anionic complexes were synthesized. The resulting adducts were isolated from the reaction mixture, dissolved in cold water, and an aminomethylating mixture consisting of formaldehyde and an amino acid was added. As a result, 3-azabicyclo[3.3.1]nonane derivatives are formed, annelated with a pyridine ring and containing an amino acid residue. By the methods of NMR and IR spectroscopy, as well as high-resolution mass spectrometry, the structure of the obtained compounds was proved. Thus, in the ^{1}H NMR spectra of the synthesized compounds, a signal of the proton of the carboxyl group in the form of a broadened singlet is detected in a weak spectral region. Equatorial and axial protons of an alicyclic fragment form a characteristic system of signals in the range δ 3.20-3.60 ppm. In the IR spectra of these molecules, the vibrational bands of carbonyl groups at ν 1720 cm^{-1}, as well as the vibrational bands of the C–O bond of the carboxyl group at ν 1198 cm^{-1}, are fixed. The m/z values in the high resolution mass spectra correspond to the molecular weights of the synthesized diazatricycclotridecans.

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