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SYNTHESIS OF ADVANCED GLYCATION END PRODUCTS AND THEIR EFFECT ON METABOLISM OF *RHIZOBIUM LEGUMINOSARUM**

Keywords: glycation, advanced glycation end products, *Rhizobium leguminosarum*.

Advanced glycation end products (AGEs) represent stable peptide and lipid transformation modifications resulting from a series of reactions beginning with attachment of a sugar to the amino groups. In mammals, these compounds exert clearly pro-inflammatory and atherogenic properties. On the other hand, accumulation of AGEs accompanies ageing and stress response in plants. However, the role of glycation products in bacterial metabolism still remains unknown [1]. Our recent data on accumulation of AGEs during nodule ageing indicate possible involvement of these modifications in. Thus, the finding of possible response to glycation stimuli might be quite important for legume-rhizobial symbiosis [2].

Indeed, inter alia, site-specific glycation of plant nodule proteins could potentially modulate physiological state of the bacterial symbiotic partner. To address the possible unknown regulatory systems several of the most common AGE-modified amino acids (MG-H1, Glarg, CML) (fig. 1) and corresponding 10-mer peptides (fig. 2) were synthesized [2, 3].

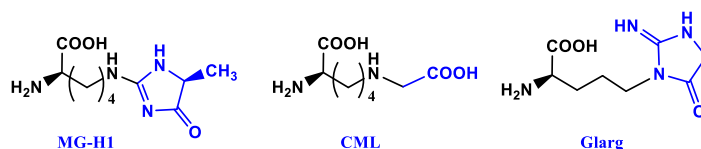
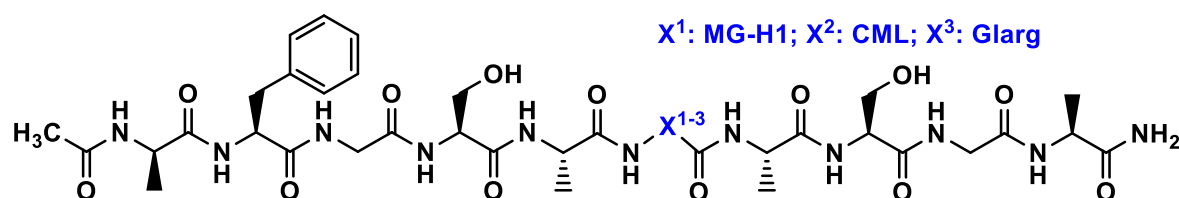


Figure 1. Structure of the glycated amino acids



Ac-Ala-Phe-Gly-Ser-Ala- X^{1-3} -Ala-Ser-Gly-Ala X - glycated amino acid

Figure 2. Structure of the peptides containing *glycated amino acids*

Further, their fluorescent derivatives were obtained for determine the fact of entry to the cells and the distribution of AGEs in them. The introduce of 5(6)-carboxyfluorescein (CF) as a fluorophore at the N-terminus of all peptide chains was done and dipeptides as analogues of amino acids were synthesized and labeled with the NBD (7-nitrobenz-2-oxa-1,3-diazol-4-yl) group (fig. 3).

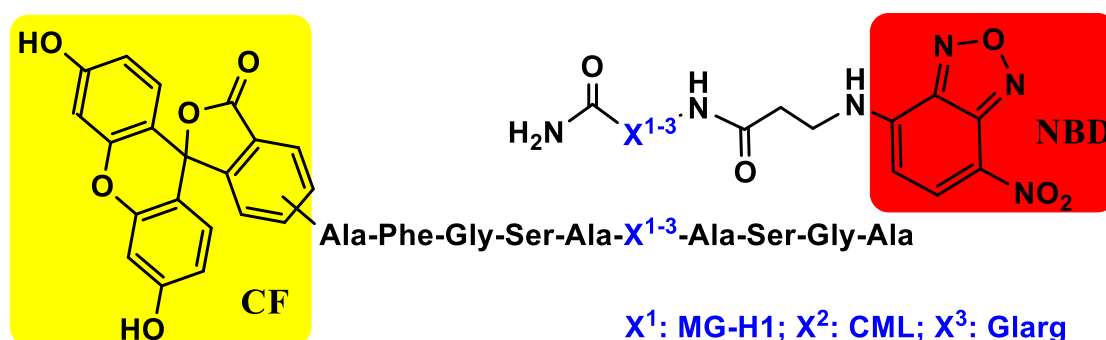


Figure 3. Structures of the fluorescent derivatives

Finally, photoaffinity probes capable to the covalent bond formation with a biological target by irradiation were needed to identify AGEs-protein interactions on the surface, in the periplasmic space and in the cytoplasm of a bacterial cell. Photoleucine (Photo-Leu) was used as a photoreactive amino acid for the synthesis both of photo active peptides and dipeptides (fig. 4).

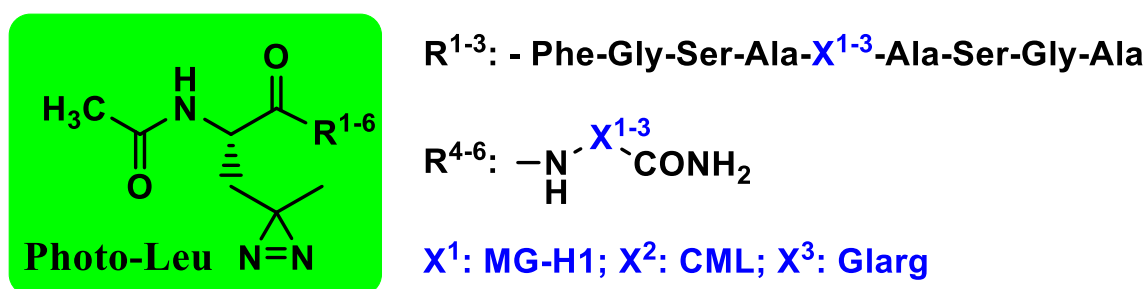


Figure 4. Structures of the photoactive derivatives

Under the action of both glycated and non-glycated amino acids and peptides, the metabolic and proteomic changes that are usually occur due to environment were found to disappear. All studied objects are therefore signaling molecules for rhizobial bacteria. However, this is achieved for a variety of reasons, since these changes differ according to kind of substances.

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* Работа выполнена при поддержке гранта РФФИ 18-016-00190.

УДК 547.866.5

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PSEUDOPERICYCLIC DEAROMATIVE 1,6-CYCLIZATION OF 1-(2-PYRIDYL)-2-AZABUTA-1,3 DIENES: SYNTHESIS AND RING-CHAIN VALENCE EQUILIBRIA OF 4H-PYRIDO[1,2-*a*]PYRAZINES*

Keywords: nitrogen heterocycles, fused-ring systems, rhodium, 2*H*-azirines, electrocyclic reactions.

The 1,6-electrocyclization of diazahexa-1,3,5-trienes is a promising and atom-economic method for the synthesis of heterocyclic compounds, such as dihydropyrimidine/pyrimidine, dihydropyrazine/pyrazine and pyridazine [1–4]. Of particular interest are the 1,6-electrocyclizations of diazatrienes in which the C=N-termini is a part of an aromatic system, for example pyridine. Such cyclizations should proceed with dearomatization of the C=N bond containing substituent and formation of non-aromatic fused heterocycles.

In this work, we studied 1,6-electrocyclizations of 1-(2-pyridyl)-2-azabuta-1,3-dienes **3** as representatives of 1,4-diazahexatrienes with the C=N bond incorporated in aromatic pyridine system. 2-Azadienes **3** for the study were synthesized by the Rh(II)-catalyzed reaction of triazolopyridines **1** with 2*H*-azirines **2**.

It was found that these 1,6-electrocyclizations can afford stable 4*H*-pyrido[1,2-*a*]pyrazines **4** despite the fact that the reaction proceeds with irreversible dearomatization of the pyridine aromatic system.

Azadienes **3** containing an electron-withdrawing substituent at the C1 and a hydrogen, alkyl or aryl group at the C4 were able to undergo such 1,6-