Synthesis and Structural Analysis of Some Isotopically Labeled Amadori Products

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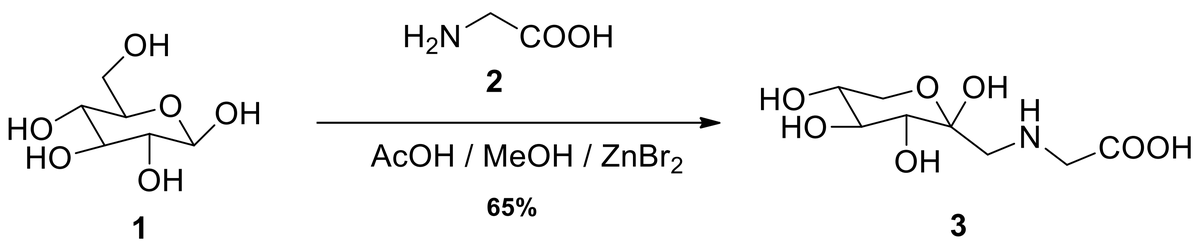
Introduction

Amadori rearrangements are milestone reactions of carbohydrate chemistry, mainly because these products combine the structural characteristics that derived from both core units, an amino acid unit and a carbohydrate unit. The aim of this work was the synthesis of some Amadori products following a multi-step strategy and using some isotopically labeled amino acids, which further, could act as building-blocks in synthesis of some biocompatible systems, specially adapted for the monitoring of specific biological processes.

Results

The proposed route to obtain a labeled Amadori product involves the reaction between a labeled carbohydrate and a labeled amino acid moieties. In order to develop the most efficient reaction conditions (in terms of yields), we initiated the tests starting from unlabeled reagents, in our case D-Glucose and Glycine (Scheme 1)[1]. For product **3**, we have obtained a good yield (ɳ = 65 %), and the structure of final product was confirmed by ^{1}H NMR (D_2O, 500 MHz) and mass-spectrometry (ESI+) (Figure 1).



Scheme 1

Further we initiate the synthesis of the corresponding labeled Amadori product, starting from commercially available D-Glucose-D_{12} and Glycine-D_2-^{15}N. The final product was obtained also in good yield (ɳ = 72,8 %) and the absence of signals in ^{1}H NMR (D_2O) demonstrates the lack of protons and confirms the presence of deuterons in all the corresponding positions; the mass-spectrometry analysis is currently underway.

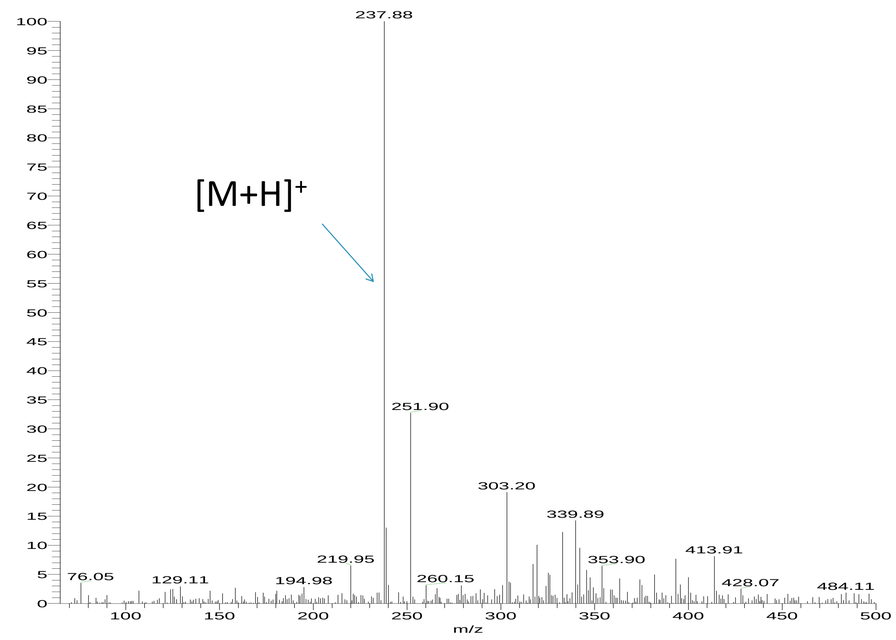
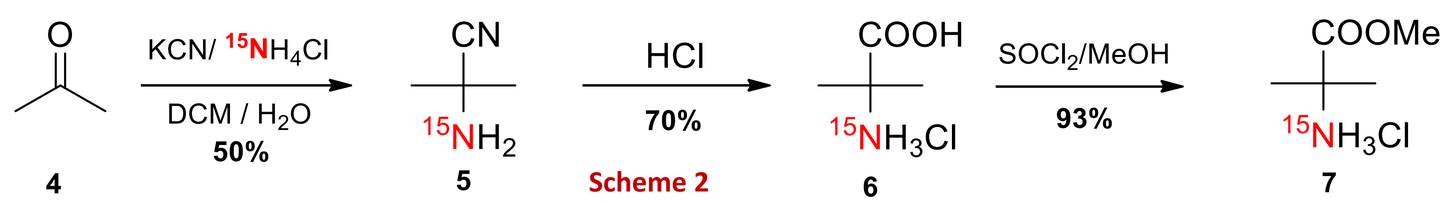


Figure 1. Fragment of ESI-MS spectrum of compound **3**

Simultaneously, we tried to develop some methods to obtain labeled aminoacids, which will be reacted further with a carbohydrate, in order to obtain another labeled Amadori products. One of the proposed strategies involves a Strecker-type reaction, a two-step procedure for synthesis of amino acids. In our case, it begins with the addition of a labeled cyanide to acetone to form an α-aminonitrile (**5**) (Scheme 2) which was further hydrolyzed (in acidic conditions) to give a salt of α-aminoacid (**6**)[2]. The next step was to obtain the salt of ester **7**[3], which will be used in the future in the reaction with D-Glucose to obtain the corresponding ^{15}N labeled Amadori product[4] . The structure of derivative **6** was confirmed by NMR spectra (Figure 2, Figure 3) and the structure for compound **7** was confirmed by NMR spectroscopy and mass-spectrometry (Figure 4).



Scheme 2

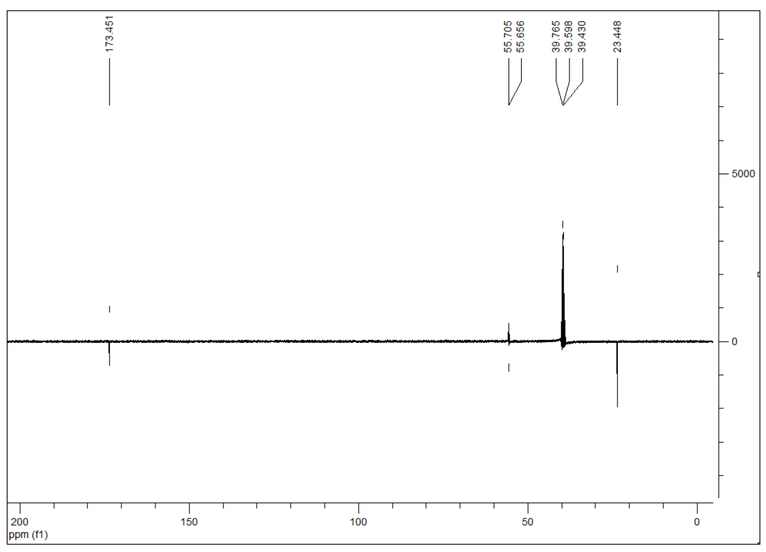


Figure 2. Fragment of ^{1}H NMR for derivative **6** (dmso-d_6, 500 MHz)

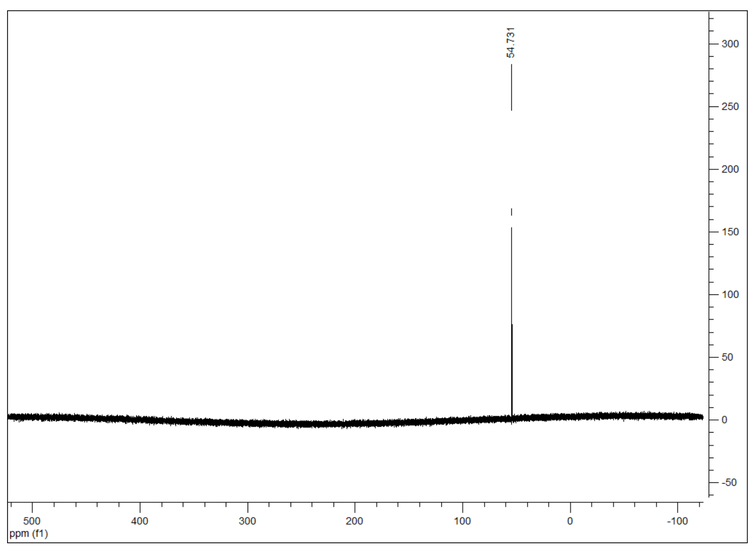


Figure 3. Fragment of ^{15}N NMR for derivative **6** (dmso-d_6, 500 MHz)

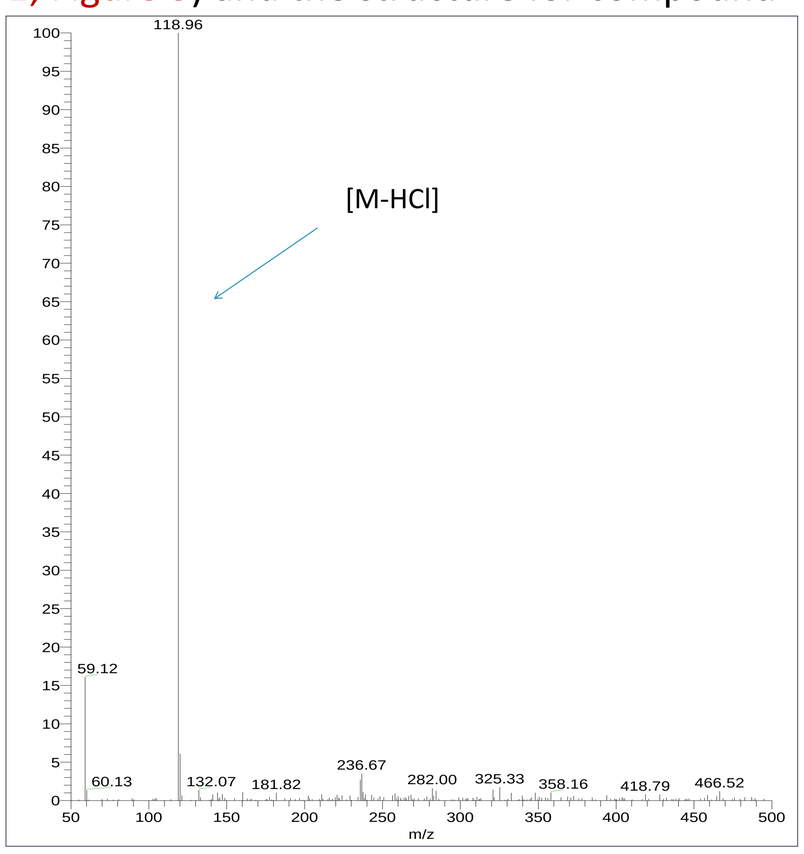


Figure 4. Fragment of ESI-MS for ester **7**

Acknowledgements

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References

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