

A V-EASI-MS Study of the Ugi Reaction Mechanism

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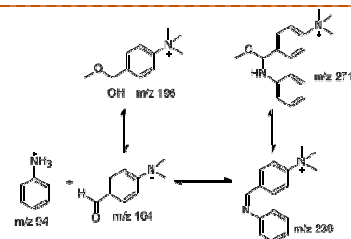
INTRODUCTION

Multicomponent reactions are defined as those where more than two substances react and essentially most of their atoms are incorporated in the product. In the case of the Ugi four component reaction an isocyanide, aldehyde, amine and carboxylic acid react to form a tripeptide. One important characteristic of the multicomponent reaction is the difficulty to elucidate the molecular sequence of events that take place in order to form the products.

Venturi easy ambient sonic-spray ionization (V-EASI)¹ is an ambient ionization technique based on the Venturi effect that provides self-pumping and online monitoring of the Ugi reaction giving representative snapshots of the ionic composition of the reaction solution and therefore key information with respect to the mechanism(s). In this study, we have used V-EASI and charged tagged reagents to improve detection of otherwise neutral or zwitterionic species. The model reaction employed 4-trimethylammonium benzaldehyde iodide, acetic acid, aniline and cyclohexylisocyanide, in equimolar quantities and at ambient temperature in methanol.

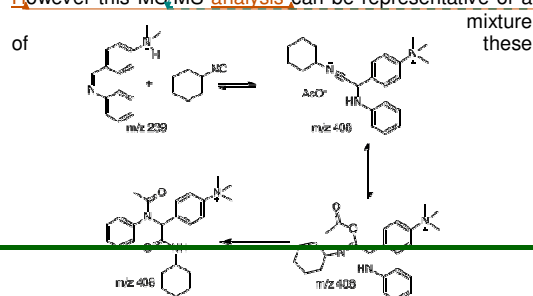
RESULTS AND DISCUSSION

After initiation of the reaction, the first sample was analyzed after 10 minutes. At this time the ions detected in the reaction corresponded to the equilibrium involving the formation of the imine. The structures presented in scheme 1 were confirmed by MS/MS experiments on the corresponding ions. The ion m/z 239 corresponding to the imine was the most intense signal in the spectrum.



Scheme 1

After 2 hours of mixing at ambient temperature an appearance of an ion of m/z 408, was detected in the reaction media. This molecular mass is consistent with the acetate, presented in scheme 2 as well as with the expected product of the reaction. The MS/MS analysis of this peak reveal a important fragment of m/z 223, also present in the MS/MS analysis of imine presented in scheme 1. This result indicates the presence the acetate or intermediate before the Mumm rearrangement. However this MS/MS analysis can be representative of a mixture of these



compounds, leading at the present moment to an inconclusive analysis.

Scheme 2

In order to ascertain about the nature of these species in the solution, an MS/MS experiments of the ion of m/z 408 over time will be carried, as well as the synthesis of the product in order to compare the MS/MS spectra.

CONCLUSION

In the present work important advances towards the understanding of the Ugi reaction mechanism was undertaken, however the presence of different isobaric intermediates complicates the interpretation of the data, and additional experiments will be performed to overcome these difficulties.

ACKNOWLEDGEMENTS



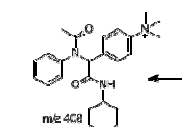
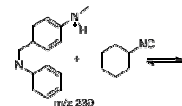
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