

ESI-IMS-QTOF: a regioselective Michael addition study

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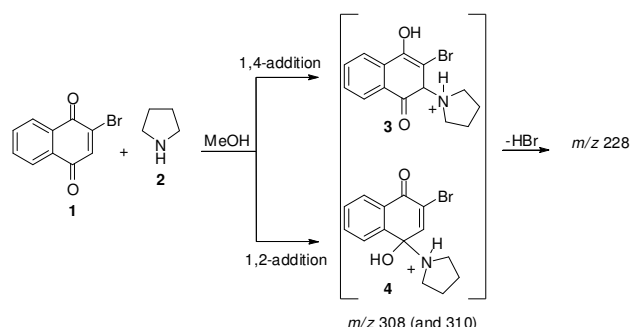
INTRODUCTION

1,2- and 1,4- additions of nucleophiles to α,β -unsaturated carbonyl compounds are among the most useful transformations in organic synthesis. 1,4-Naphthoquinones have been reported as important active compounds and are interesting substrates for studying the regioselectivity of a nucleophilic addition reaction.¹ Lately, the ion mobility spectrometry (IMS) may become an important approach to study reaction mechanisms.²

Herein, we describe ESI and IMS as tools in the study of the 1,2 vs. 1,4-regioselective addition of amines to 2-bromo-1,4-naphthoquinone.

RESULTS AND DISCUSSION

Upon mixing the reagents, the reaction mixture was analyzed by ESI-IMS-QTOF after 15 min. Two more intense signals of m/z 306 (and 308) and m/z 228 were noted. It is interesting that no signal of m/z 308 (and 310) of the direct addition of pyrrolidine (**2**) to the bromoquinone **1** was detected. The other important signal observed is that of m/z 228, attributed to the direct loss of HBr from the intermediates **3** and/or **4**, as seen in Scheme 1.



Scheme 1. 1,2- and 1,4- additions of pyrrolidine to 2-bromo-1,4-naphthoquinone.

The suggested formation of the ion of m/z 228 derived from the 1,4-addition occurs from two different pathways that lead to the same ion, independently if the addition takes place at the bromine-containing carbon or at the adjacent carbon.

The proposed formation of the ion of m/z 228 derived from 1,2-addition can be occurs by the direct attack of amine at the carbonyl group provides protonated specie that can produce a five-membered ring cyclic and after HBr eliminates the fragment ion m/z 228 can be observed.

Envisaging the separation of the structural isomers **3** and **4**, the signal of m/z 228 was submitted to IMS. The chromatogram is showed in Figure 2.

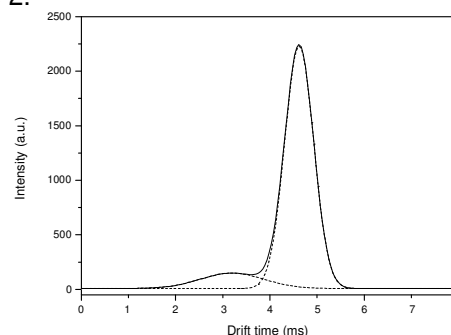


Figure 2. The signal of m/z 228 separated by IMS analysis.

Considering the areas of the graphics it is possible to quantify the relation among both isomers. The ratio of Area A (right, 1704.81 a.u.) /Area B (left, 238.37 a.u.) was 7.15 indicating the proportion of 7:1 favoring the regioisomer from the 1,4-addition.

CONCLUSION

It has been demonstrated that IMS and ESI-QTOF analyses are a powerful combination to study the regioselectivity addition in systems such as quinone derivatives. The 1,4-addition of pyrrolidine is preferred to 2-bromo-1,4-naphthoquinone system.

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