ESI-IMS-QTOF: a regioselective Michael addition study

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Keywords: Michael addition, ion mobility, mass spectrometry

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. Lately, the ion mobility spectrometry (IMS) may become an important approach to study reaction mechanisms.

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 to the bromoquinone 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.

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\text{Scheme 1. 1,2- and 1,4- additions of pyrrolidine to 2-bromo-1,4-naphthoquinone.}
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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.

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\text{Figure 2. The signal of m/z 228 separated by IMS analysis.}
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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.

ACKNOWLEDGEMENTS

This research was supported by grants from the CNPq, CAPES, FAPDF, FAPESP, UFMG and DPP.

REFERENCES