Reduction of Nitriles to Amines in Positive Ion Electrospray Ionization Mass Spectrometry

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Introduction

It was observed that acetonitrile was reduced to ethylamine to form [M+46]+ adduct ions during LC(+)-ESI-MS analyses. Here, we report the phenomenon and mechanism of nitrile (C≡N) reduction under (+)-ESI-MS conditions that may facilitate characterization of unknown chemical entities having a nitrile functional group.

Experimental

Liquid chromatography:

- Pump: Agilent 1200 Series pump
- Mobile Phases: A: CH3CN-H2O (1:1) w/ 1% HCOOH and 1% NH4OH; B: CH3OH-H2O (1:1) w/ 0.01% (CH3)2CH2CH2NH2 and 1% HCOOH and 1% NH4OH

Mass Spectrometry:

- MS System 1: Finnigan LCQ Bruker Mass Spectrometers
- Ion spray (IS): 4.5 kV
- Capillary temp: 200 °C
- Sheath gas: 40
- Auxiliary gas: 20
- MS System 2: AB QSTAR XL LC/MS/MS System
- IS: 5.5 kV
- Curtain gas: 15
- Gas 1: 15
- Gas 2: 10

Results and Discussion

1. An [M+46]+ adduct ion was observed for some compounds, e.g., fluticasone proprionate, during LC(+)-ESI-MS analysis with CH3CN-H2O (1:1) as mobile phases (Figure 1a). The adduct ion is identical to that found when the HPLC mobile phase contained 0.01% CH3CN, CH3NH2 (Figure 1b).

2. The [M+46]+ ion was proposed to be an adduct ion of ethylamine, which was determined through use of deuterated agents to be derived from CH3CN in the mobile phase (Figure 1c and 1d).

3. The product ions of the [M+46]+ adduct further confirmed the phenomenon (Figure 2).

4. Both [M+46]+ and [M+74]+ ions were observed when fluticasone propionate was prepared in (a) CH3CN-(CH3)2CH2CN-H2O (1:1:0.5) and only [M+74]+ was observed when fluticasone propionate was prepared in (b) CH3OH-H2O (1:1) containing 0.01% (CH3)2CH2CH2NH2 (Figure 3).

5. Reduction of other nitriles was also observed. For example, benzonitrile was reduced to benzylic anion in CH3CN-H2O and was completely reduced to benzylamine in CH3OH-D2O (Figure 5).

Conclusions

- Nitriles (acetonitrile, isobutyronitrile, benzonitrile) are readily reduced to their respective amines under (+)-ESI-MS conditions.
- The source of the reducing hydrogen was determined to originate from electrolysis of water.
- This finding may facilitate the characterization of the nitrile-moiety in a variety of chemical entities of interest.
- Since water electrolysis occurs readily within the ESI source, other reduction products via a similar reaction mechanism with reducing hydrogen may also be anticipated.