A Fragmentation Study on Four Oligostilbenes by Electrospray Tandem Mass Spectrometry

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Abstract
Oligostilbenes have attracted much interest due to their intricate structures and diverse bioactivities. In this study, two stilbene dimers, (−)-7,8-cis-ε-viniferin (1) and carasiphenol A (2), and two trimers, suffruticosol A (3) and suffruticosol C (4), were investigated by electrospray ionization ion-trap time-of-flight multistage mass spectrometry (ESI-IT-TOF-MSn). Based on the MSn study, the fragmentation pathways and diagnostic ions of four oligostilbenes in both positive and negative modes were proposed. The consecutive elimination of phenol (C₆H₆O) and resorcinol (C₆H₆O₂) moieties were the particular dissociation for oligostilbenes due to the presence of 1,2-diphenylethylene nucleus. The present MSn fragmentation study will provide valuable information for the fast characterization of oligostilbenes from complicated natural mixtures.

Graphical Abstract

Keywords ESI-IT-TOF–MSn · Fragmentation rules · Oligostilbenes

1 Introduction
Natural stilbenes are an important group of polyphenols characterized by the presence of 1,2-diphenylethylene nucleus [1]. Naturally occurring stilbenes always have intricate structures with different numbers of stilbenes and polymeric types [2]. Stilbenes as the defensive chemicals of plants are revealed with diverse bioactivities including anti-tumor, anti-oxidant, anti-inflammatory,
anti-fungal, anti-diabetic and anti-Alzheimer’s disease effects [3–7], whereas their natural distribution is quite limited, mainly in Cyperaceae, Dipterocarpaceae, Gnetaceae, Iridaceae, Leguminosae, Moraceae, Orchidaceae and Polygonaceae plants [2]. Thus, it is necessary to develop and establish a rapid and systematic method to profile stilbenes from natural resources.

Mass spectrometry (MS) with high sensitivity and resolution is one of the most efficient methods in analyzing natural products [8–10]. Tandem MS techniques have advantages in ascertaining the relationship between precursor and product ions, by which the fragmentation rules and diagnostic ions of complicated compounds can be proposed [11, 12]. In this paper, we report the MSn fragmentation rules of four oligostilbenes, (−)-7,8-cis-ε-viniferin (1), carasiphenol A (2), suffruticosol A (3) and suffruticosol C (4), by electrospray ionization ion-trap time-of-flight (ESI-IT-TOF) mass spectrometer to provide reference for their fast characterization from natural sources.

2 Results and Discussion

The first-stage MS of compounds 1–4 (Fig. 1) in both positive and negative ion modes were acquired in automatic pattern, by which their protonated ([M+H]+) and deprotonated ([M−H]−) molecule ions were readily detected. For compounds 1, 3 and 4, the [M+HCOO]− ions in negative mode were also obtained due to the application of formic acid in the solvent [13]. The subsequent MSn studies on compounds 1–4 in both positive and negative modes were performed, from which their fragmentation pathways were proposed (Figs. 2, 3, 4, 5, 6, 7, 8, 9). It should be noted that alternative ways of fragmentation that can reasonably interpret the product ions are also possible in addition to the proposed pathway. For example, the negative charge can be present at any hydroxy group rather than the position denoted.

2.1 MSn Fragmentations of (−)-7,8-cis-ε-Viniferin (1) in Positive Mode

In the single-stage mass spectrum of (−)-7,8-cis-ε-viniferin (1), the [M+H]+ ion at m/z 455 (1A), [M−H]− ion at m/z 453 (1b) and [M+HCOO]− ion at...
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$m/z$ 499 (1a) were readily obtained, corresponding to the molecular formula of C$_{28}$H$_{22}$O$_{6}$. The subsequent MS$^2$ experiment on [M+H]$^+$ (1A) gave rise to multiple product ions (1B–1L). The ion 1A lost a C$_6$H$_6$O or a C$_7$H$_6$O moiety to provide the ions of 1B ($m/z$ 361) and 1C ($m/z$ 349) [14]. Then, the subsequent elimination of two H$_2$O molecules from 1B generated ions at $m/z$ 343 and $m/z$ 325. The ion 1C was present in high abundance, which might be due to the rearrangement of 1C into tropone derivative. The ions 1G ($m/z$ 267) and 1I ($m/z$ 251) were proposed from 1B by the elimination of a C$_6$H$_6$O or a C$_6$H$_6$O$_2$ part.

The similar fragmentation was also observed for ion 1C, from which two product ions at $m/z$ 255 (1H) and $m/z$ 239 (1J) were obtained corresponding to neutral loss of a C$_6$H$_6$O or a C$_6$H$_6$O$_2$ part. When ion 1H was selected as the precursor ion to perform MS$^3$ experiment, two ions 1K ($m/z$ 227) and 1M ($m/z$ 199) were formed by the successive loss of two CO molecules. Similarly, the ion 1F ($m/z$ 315) was well explained by the loss of a molecule of CO from 1D [15–17]. In addition, a MS$^2$ ion at $m/z$ 215 (1L) was also observed from 1A, but its fragmentation pathway was still unclear (Fig. 2).
Fig. 5  Proposed fragmentation pathways of carasphenol A (2) in negative mode

Fig. 6  Proposed fragmentation pathways of suffruticosol A (3) in positive mode
Fig. 7  Proposed fragmentation pathways of suffruticosol A (3) in negative mode

Fig. 8  Proposed fragmentation pathways of suffruticosol C (4) in positive mode
2.2 MS\(^n\) Fragmentations of (−)-7,8-cis-ε-Viniferin (1) in Negative Mode

Similar to that in positive mode, the [M−H]\(^−\) ion 1b gave rise to ions at \(m/z\) 359 (1c) and \(m/z\) 347 (1d) by the loss of a \(\text{C}_9\text{H}_8\text{O}_2\) or a \(\text{C}_2\text{H}_2\text{O}\) moiety. When ion 1c was chosen to perform MS\(^3\) experiment, three product ions at \(m/z\) 289 (1f), \(m/z\) 265 (1h) and \(m/z\) 253 (1i) were obtained, corresponding to the elimination of \(\text{C}_9\text{H}_8\text{O}_2\), \(\text{C}_6\text{H}_6\text{O}\) and \(\text{C}_7\text{H}_6\text{O}_2\) moieties [15–17]. The MS\(^3\) study on 2D gave rise to ions at \(m/z\) 371 (2g) and 359 (1c) by the loss of \(\text{C}_2\text{H}_4\text{O}\) and \(\text{C}_6\text{H}_6\text{O}\) parts. The ions at \(m/z\) 273 (1g) and \(m/z\) 197 (1k) were tentatively deduced from 1f and 1j by the loss of an O or a CO moiety. Due to the presence of hydroxy groups in the structure, the elimination of \(\text{H}_2\text{O}\) from 1d generated 1e (Fig. 3).

2.3 MS\(^n\) Fragmentations of Carasiphenol A (2) in Positive Mode

The [M+H]\(^+\) ion 2A gave rise to fragments at \(m/z\) 385 (2B), \(m/z\) 335 (2D) and 323 (2E) by the elimination of \(\text{C}_9\text{H}_8\text{O}\), \(\text{C}_6\text{H}_6\text{O}\) and \(\text{C}_7\text{H}_6\text{O}_2\) moieties [15–17]. The ions 2E might undergo a rearrangement and further loss a \(\text{C}_2\text{H}_2\text{O}\) part to provide 2J (\(m/z\) 281). By the loss of a CH\(_2\) from 2B, the ion at \(m/z\) 371 (2C) was yielded, and further provided ion 2K (\(m/z\) 277) by the loss of a \(\text{C}_6\text{H}_6\text{O}\) moiety. When the ion at \(m/z\) 309 (2G) was chosen for MS\(^3\) experiment, diverse ions at \(m/z\) 291 (2I), 267 (2M), 215 (2O) and 199 (2P) were obtained. The ion at \(m/z\) 269 (2L) was deduced from 2G by the elimination of \(\text{C}_9\text{H}_4\) part. The subsequent MS\(^3\) study on 2L generated ions at \(m/z\) 241 (2N), 175 (2S) and 147 (2T). With the elimination of \(\text{H}_2\text{O}\), \(\text{C}_9\text{H}_8\text{O}\) or \(\text{C}_7\text{H}_6\text{O}_2\) part from 2D, three ions at \(m/z\) 317 (2F), 293 (2H) and 187 (2Q) were obtained. The ion at \(m/z\) 183 (2R) was tentatively deduced from 2H by the loss of resorcinol moiety (Fig. 4).

2.4 MS\(^n\) Fragmentations of Carasiphenol A (2) in Negative Mode

The MS\(^2\) experiment on [M−H]\(^−\) ion generated prolific fragments at \(m/z\) 385 (2b), 369 (2c), 343 (2d), 333 (2e), 321 (2f), 307 (2g) and 267 (2k). The following MS\(^3\) experiment on 2b and 2c gave rise to 2i (\(m/z\) 291) and 2j (\(m/z\) 275), respectively, corresponding to the neutral loss of a phenol moiety. The ions at \(m/z\) 301 (2h) and 223 (2m) were produced from the precursors 2d and 2e, by the elimination of \(\text{C}_2\text{H}_2\text{O}\) and \(\text{C}_7\text{H}_6\text{O}_2\) [15–17]. When ion at \(m/z\) 307 (2g) was performed the MS\(^3\) study, three ions at \(m/z\) 265 (2l), \(m/z\) 213 (2n) and \(m/z\) 187 (2o) were formed. The ion 2p (\(m/z\) 145) was affirmed from the precursor 2l by the loss of a molecule C\(_8\)H\(_6\)O (Fig. 5).

2.5 MS\(^n\) Fragmentations of Suffruticosol A (3) in Positive Mode

The MS\(^2\) study on [M+H]\(^+\) ion gave rise to the fragments at \(m/z\) 587 (3B), 575 (3C), 493 (3D), 481 (3E) and 321 (3J). The production of ion 3E (\(m/z\) 481) was verified as the successive elimination of a \(\text{C}_7\text{H}_6\text{O}\) and a \(\text{C}_9\text{H}_8\text{O}\) part from 3A. The ion 3E could further generate ion at \(m/z\) 387 (3G) and 371 (3H) by the neutral loss of a phenol (\(\text{C}_6\text{H}_6\text{O}\)) and a resorcinol (\(\text{C}_6\text{H}_4\text{O}_2\)) moiety [15–17]. With the elimination of a molecule of \(\text{H}_2\text{O}\), the ion at \(m/z\) 369 (3I) was obtained from 3G. Similarly, the fragment 3F was produced from 3D by the loss of a phenol (\(\text{C}_6\text{H}_6\text{O}\)) part (Fig. 6).

2.6 MS\(^n\) Fragmentations of Suffruticosol A (3) in Negative Mode

When the [M−H]− ion was chosen for MS\(^2\) study, the product ions at \(m/z\) 585 (3c) and 573 (3d) were generated due to the loss of \(\text{C}_6\text{H}_6\text{O}\) and \(\text{C}_7\text{H}_6\text{O}_2\) moieties [15–17]. The following MS\(^3\) investigation on ion 3c gave rise to fragments at \(m/z\)
was well explained by the consecutive loss of two phenol (C₆H₆O) which gave rise to smaller ions. Two MS³ fragments at m/z 357 (3k) and 341 (3l) were obtained from 3i, which were well in accordance with the departure of a phenol (C₆H₆O) and a resorcinol (C₆H₆O₂) parts (Fig. 7).

2.7 MSⁿ Fragmentations of Suffruticosol C (4) in Positive Mode

The [M+H]⁺ ion of 4A gave rise to MS² fragments at m/z 587 (4B) and 575 (4C) due to the neutral loss of a molecule of C₆H₆O and C₇H₆O parts. The successively loss of two C₆H₆O moieties was further observed in the MS³ experiment on ions 4B, and thus gave rise to the fragments at m/z 493 (4D) and 399 (4G). The ions 4E (m/z 481) and 4H (m/z 371) were generated from 4C by the successive loss of a C₆H₆O and a C₆H₆O₂ moieties [15–17]. The ion at m/z 453 (4F) was deduced from 4E by the elimination of a molecule of CO, and further gave rise to 4I (m/z 359) and 4J (m/z 265) which was well explained by the consecutive loss of two phenol (C₆H₆O) moieties. The ion at m/z 371 (4H) was generated from 4E by the departure of a C₆H₆O₂ moiety (Fig. 8).

2.8 MSⁿ Fragmentations of Suffruticosol C (4) in Negative Mode

In the negative MS² experiment, the neutral loss of C₆H₆O from the [M–H]⁻ ion (4b) gave rise to the fragment at m/z 585 (4c). When the ion 4c was chosen to perform the MS³ study, diverse ions at m/z 543, 491, 479, 451 and 447 were obtained. The ions 4c and 4f were well consistent with the elimination of C₆H₆O₂ and C₇H₆O₃ parts from the precursor 4c [15–17]. However, the formation of ions 4d (m/z 543), 4g (m/z 451) and 4h (m/z 447) was difficult to explain due to the complicated structure (Fig. 9).

3 Experimental

3.1 Apparatus and Analytical Conditions

All of the MSⁿ experiments were performed on the LCMS-IT-TOF mass spectrometer (Shimadzu, Kyoto, Japan). Accurate masses were calibrated using sodium trifluoroacetate (CF₃CO₂Na) clusters. MS experiments were performed in automatic pattern, and MSⁿ experiments were achieved in direct mode. The MS parameters are in accordance with the previous report [18].

3.2 Chemicals and Samples

Acetonitrile (CH₃CN) of HPLC grade was purchased from Merck Co., Ltd., Germany, and formic acid was bought from Aladdin Chemistry Co., Ltd., China. Deionized water was purified using a MingChe™-D 24UV Merck Millipore system (Merck Millipore, Shanghai, China). Compounds 1–4 were isolated from the seeds of Paeonia lactiflora Pall. in our previous investigation. Samples were diluted in MeOH at the concentration of 0.5 mg/mL.

4 Conclusion

The ESI multi-stage mass spectra (MSⁿ) of four oligostilbenes were studied for the first time by LCMS-IT-TOF, by which their fragmentation pathways were deduced. The consecutive elimination of phenol (C₆H₆O) and resorcinol (C₆H₆O₂) moieties from the precursor ions was the particular dissociation due to the presence of 1,2-diphenylethylene nucleus in the structure. Interestingly, the elimination of a C₆H₆O moiety was always detected due to the fracture of the double bond in 1,2-diphenylethylene nucleus, and this fragmentation pathway might be impelled by the rearrangement of the free radical into a stable conjugated system (e.g. tropone). Based on the fragmentation rules deduced above, (−)-7,8-cis-e-viniferin (1), carasiphenol A (2), suffruticosol A (3) and suffruticosol C (4) could be well differentiated by their respective ion pars of 455–215, 429–267, 681–321 and 679–447 in positive mode, and 453–359, 427–307, 679–451 and 679–447 in negative mode. The present MSⁿ fragmentation study will provide valuable information for the fast characterization of oligostilbenes from complicated natural mixtures.

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Compliance with Ethical Standards

Conflict of interest These authors have no conflict of interest to declare.

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