Maximizing MS/MS Fragmentation in the Ion Trap Using CID Voltage Ramping

Technical Note

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Introduction

A seldom-discussed obstacle to obtaining good, consistent MS/MS results with triple-quadrupole and ion-trap mass spectrometers is the compound-dependent nature of collision optimization. Collision-gas pressure and collision energy both have a significant effect on sensitivity, mass spectral quality, and ion yield. In chromatographic analyses with multiple analytes, it can be difficult or impossible to find a single set of collision parameters that yield optimum product ion spectra for all analytes.

This note discusses the effect of these collision parameters in triple-quadrupole and ion-trap mass spectrometers. It shows how the new SmartFrag feature in the Agilent 1100 Series LC/MSD Trap ion-trap mass spectrometer overcomes compound dependency to generate optimum information from every analyte.

Triple-quadrupole mass spectrometers yield useful fragment ions—at a price

In a triple-quadrupole mass spectrometer, and similar quadrupole/quadrupole/time-of-flight instruments, the precursor ion is selected by the first quadrupole and collision takes place in the collision cell (second quadrupole). The collision-induced dissociation (CID) is “slow” because it takes place along the entire length of the collision cell. In one sense this is an advantage, because the slow nature of this process allows cascading fragmentation to take place. Product ions generated by collision of the precursor ion are themselves fragmented by further collisions. The result is a wide range of product ions that are useful in compound identification and structure elucidation.

There are, however, several corresponding disadvantages. In a triple-quadrupole mass spectrometer, both collision-gas pressure and collision energy, which

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is controlled by the collision-cell voltage, have significant effects on analytical results. Both must be optimized in order to achieve the best analytical results. Because optimum settings are compound dependent, settings that produce good results for the first compound to elute may yield poor results for the next compound. A triple-quadrupole mass spectrometer must be able to change settings for each analyte to produce optimum results.

Traditional ion traps have a different set of challenges

The ion trap works somewhat differently. The precursor ions are held near the center of the trap in a confined space. The collision time tends to be shorter (faster), allowing little or no time for further fragmentation of the product ions. The result is fewer product ions and less structural information. Traditionally, this was compensated for by using the ion trap's ability to perform more levels of MS analysis to continue selecting and fragmenting product ions. Indeed, this is a very powerful technique that allows structure to be determined in a very controlled fashion. Recent innovations, however, allow the Agilent ion trap to generate more structural information with fewer steps of MS and at the same time overcome the compound-dependent nature of collision optimization.

In the ion trap, the collision gas, generally helium, reduces the kinetic energy of the incoming ions as they approach the center of the trap. The amount of gas in the trap is generally fixed and is not changed for different compounds. This leaves one variable, collision energy, with a significant and compound-dependent influence over fragmentation.

CID voltage ramping in the ion trap provides the best of both worlds

A new feature, CID voltage ramping (SmartFrag), is built into firmware of the Agilent 1100 Series LC/MSD Trap. CID voltage ramping eliminates the need to optimize the collision energy for different compounds. Each time MS/MS is performed, CID voltage ramping quickly ramps the collision voltage over a range of energies. This ensures that each compound receives the correct energy for optimum fragmentation. It also results in a higher level of fragmentation, providing more structural information with fewer steps of MS/MS.

Figure 1a shows the full-scan mass spectrum of prednisone, an anti-inflammatory steroid having a protonated molecular ion $[M+H]^+$ at *m/z* 359. Figure 1b depicts the MS/MS full-scan spectrum obtained at a fixed collision energy of 0.8v. The MS/MS spectrum yields a large precusor ion and a few product ions which show *m/z* losses for a water molecule and for a water molecule and CO (total of 46). Figure 1c shows the same MS/MS full-scan spectrum obtained using the CID voltage ramping. The spectrum is rich with product ions providing much structural information.

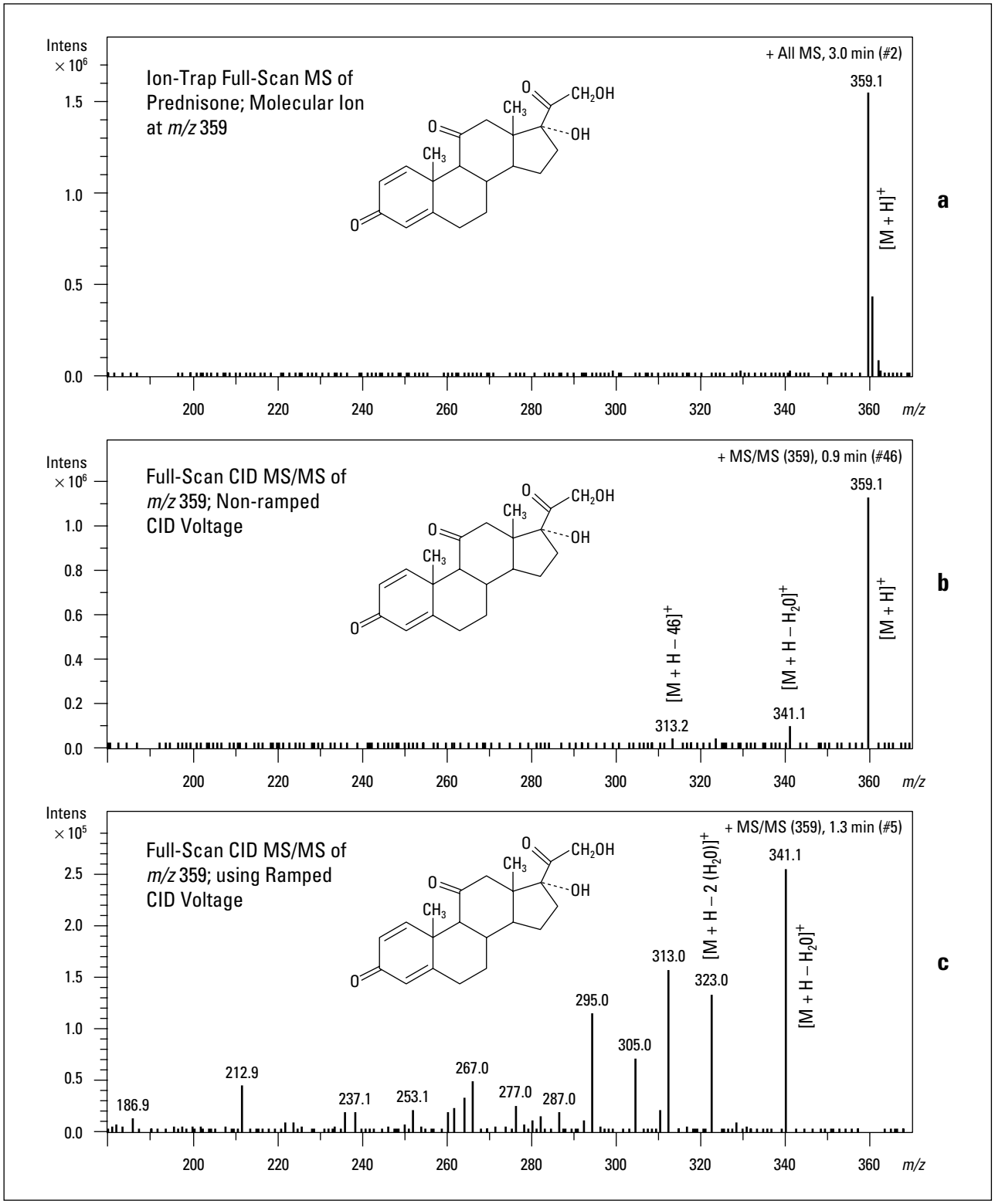

Figure 1. MS/MS of Prednisone using CID voltage ramping

Figure 2a is a full-scan mass spectrum of the antihypertensive, Labetalol, having a protonated molecular ion at *m/z* 329. Figure 2b shows MS/MS of the precursor ion yielding a major ion at *m/z* 311, which corresponds to the loss of a water molecule. The spectrum is nearly bare of product ions, presenting the need for more stages of MS to more fully confirm the molecular structure. If this occurs with a triple-quadrupole system, the option for MS^3 does not exist and other confirmatory approaches may be needed. Figure 2c shows MS/MS of Labetalol using CID voltage ramping. The full-scan MS/MS product ion spectrum is rich with product ions and the most abundant ion in the spectrum is at *m/z* 207. This provides much more structural information than the single ion at *m/z* 311.

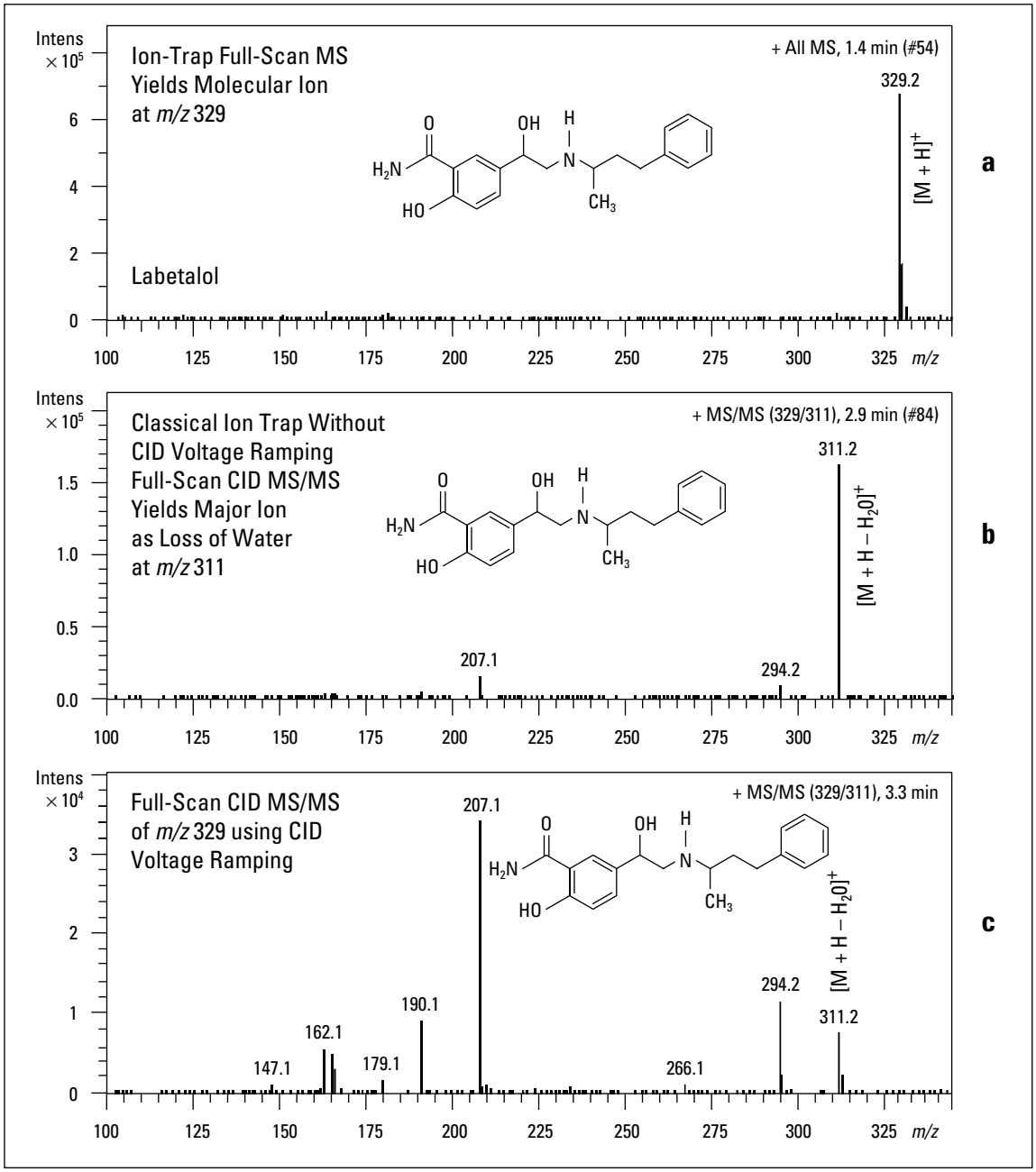

Figure 2. MS/MS of Labetalol using CID voltage ramping

Figure 3 is another example of the use of CID voltage ramping. Figure 3a is the full-scan mass spectrum of 4-hydroxytamoxifen, a compound for the treatment of breast cancer. Figure 3b shows result of MS/MS of tamoxifen at a fixed collision voltage of 0.9 V. Although the spectrum yields six to seven ions useful for structural characterization, the precusor ion is not totally fragmented. Further analysis would be required to find the optimum CID voltage to obtain a more spectral-rich product ion spectrum. Without other experimental changes, switching to CID voltage ramping generated the product ion spectrum shown in Figure 3c.

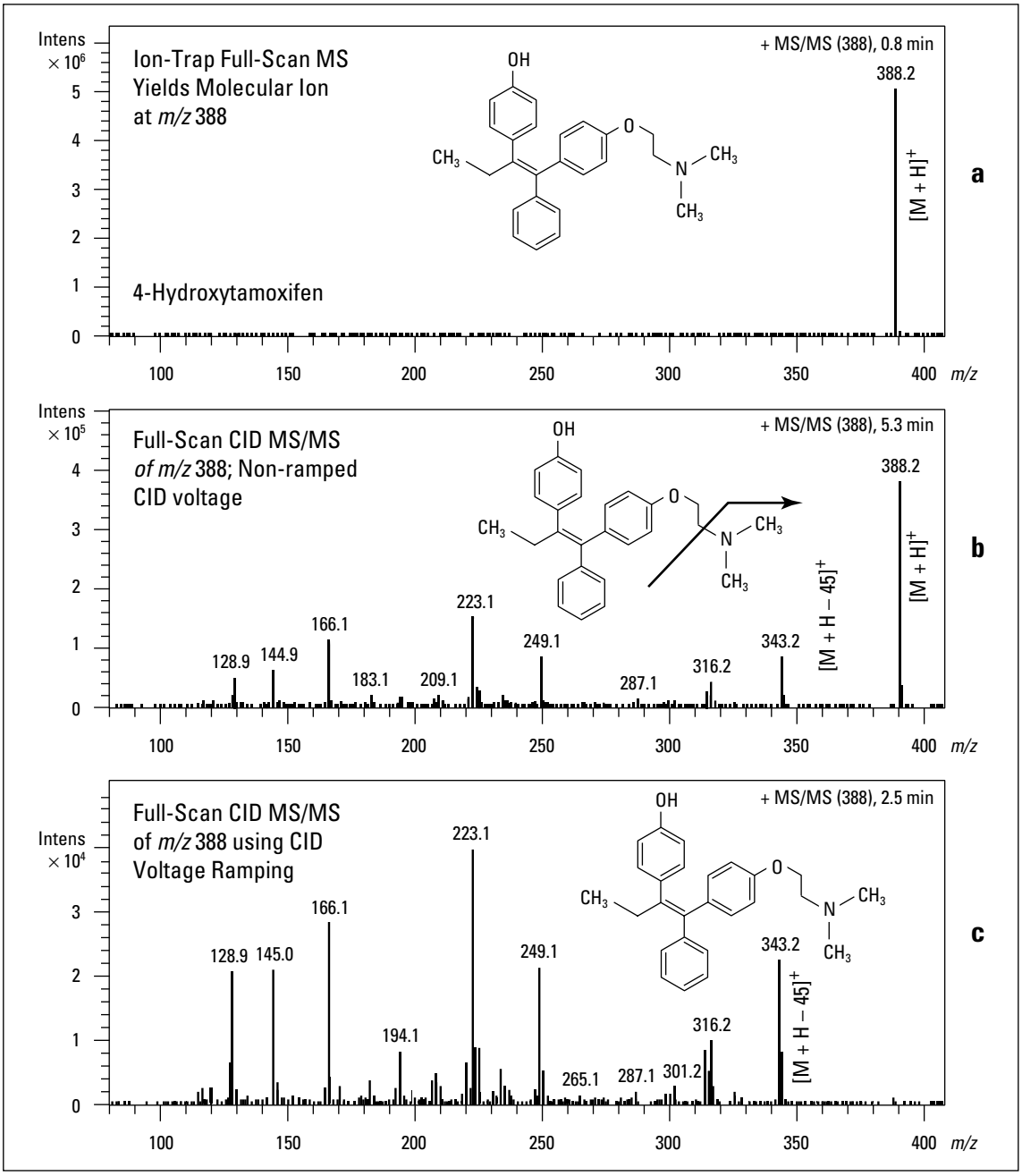

Figure 3. MS/MS of 4-hydroxytamoxifen using CID voltage ramping

Conclusions

Using the CID voltage ramping feature of the Agilent LC/MSD Trap ion-trap mass spectrometer eliminates the need for time-consuming collision-voltage optimization. By setting a range of CID voltages using the SmartFrag setting, an analyst can be certain to obtain fragment-rich, full-scan product-ion spectra for identity confirmation or structure elucidation.

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Printed in the U.S.A. November 2000
(23) 5988-0704EN

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