

crude extracts, there is the potential for significant interference with the assay. Such interferences include nonspecific inhibition of targets by ubiquitous classes of natural products like fatty acids, or the presence of a highly potent cytotoxic agent that kills the host cell designed for the specific assay. These issues are not insurmountable, but require diligence in evaluating screening results. Some solutions for these issues are presented in Section 4.5.

7.4.4 DEREPICATION

Dereplication is a term that when used by natural products chemists refers to the rapid identification of a compound (or class of compounds). How is this different from the usual process encountered in the isolation of natural products? It is different in that the process refers to the identification of expected (or nuisance) compounds. These nuisance compounds will vary depending upon the particular assay system that is being followed, and therefore it takes some experience with a given bioassay to identify the classes of interfering compounds. Before the advent of high-throughput LC/MS systems, specific tests were developed to identify the nuisances. In the early days of antibiotic discovery paper chromatography was used, as were thin layer chromatography with specific detection, and liquid chromatography with diode-array detection, and so on. This process has been greatly expedited by the use of LC/MS such as the system diagrammed in Figure 7.7. The system is based upon the separation of a mixture by reversed phase HPLC, the continuous recording of UV/visible absorption spectra and mass spectra throughout the chromatogram, and the correlation of these data with biological activity. Once the active wells in the bioassay plate are related to a retention time, the optical and mass spectral data are correlated and used for querying suitable databases that provide matches of known compounds. Once an active compound is identified in this way, one can simply rely on the chromatographic and spectral data for dereplication of future samples.

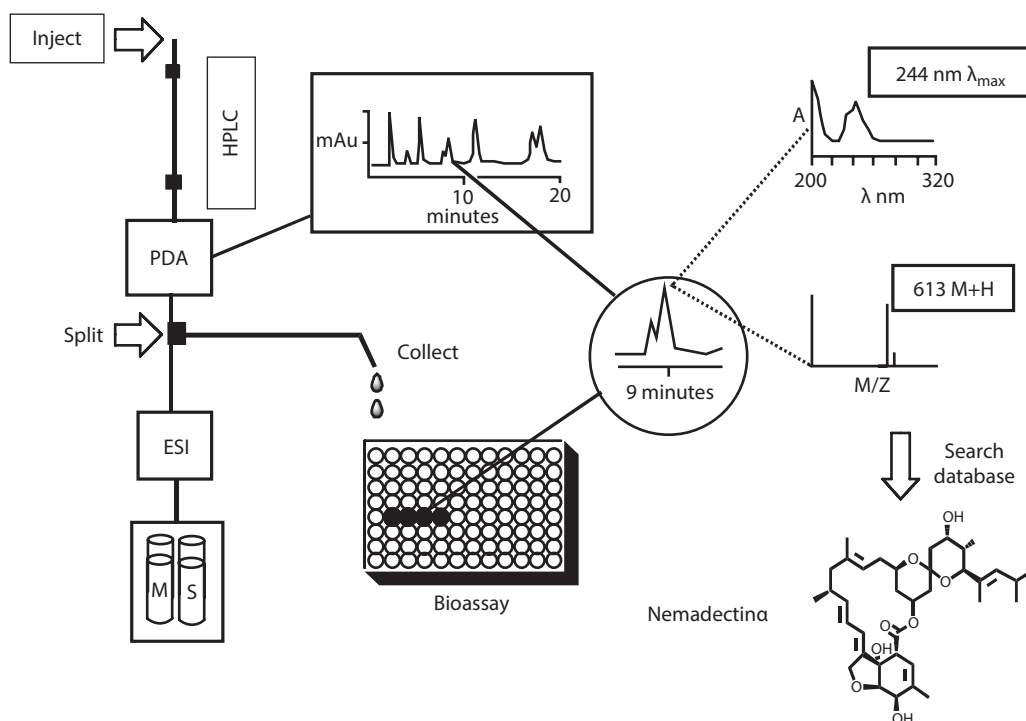


FIGURE 7.7 Schematic of HPLC/UV/MS system for dereplication of natural products.