

DIRECT CHARACTERIZATION OF SOLID PHASE RESIN-BOUND MOLECULES BY MASS SPECTROMETRY

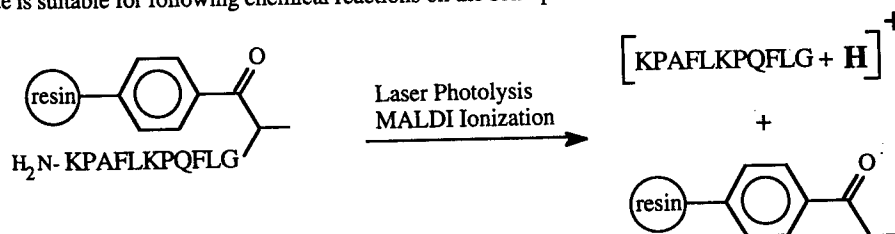
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Abstract: In this work we demonstrate that analytes, covalently linked to a polymeric support through a photolabile linker, can be directly analyzed by matrix-assisted laser desorption/ionization (MALDI). Mass spectral analysis is performed in a single step requiring no pretreatment of the sample to induce cleavage from the support. Our results show that the UV laser light in the MALDI experiment can be used to simultaneously promote an analyte's photolytic cleavage from a solid support and its gas phase ionization for subsequent mass spectral analysis. In this manner, MALDI facilitates the dissociation and identification of resin-bound analytes in a single analytical procedure without the need for any prior chemical treatment. Copyright © 1996 Elsevier Science Ltd

Introduction

Mass spectrometry is playing an increasingly important role in the molecular characterization of combinatorial libraries, natural products, and biopolymers¹. The recent development of soft ionization techniques such as matrix-assisted laser desorption/ionization (MALDI) and electrospray ionization (ESI) have significantly extended the application of mass spectrometry to a wide variety of compounds previously inaccessible because of their low volatility and thermal lability. Several reports²⁻⁶ have also shown that mass spectrometry can be very useful in characterizing compounds from solid polymeric supports. These reports illustrated that compounds covalently bound to a single polymeric bead (~50 µm in diameter) or set of beads were amenable to mass spectral analysis subsequent to their chemical cleavage from the resin. Preliminary results⁷ in another report suggested that MALDI could be used to analyze selected Fmoc-protected amino acids that were bound to a solid-phase resin through a photolabile link. In this report we demonstrate that peptides covalently linked to a polymeric support through a photolabile linker can be directly analyzed by MALDI mass spectrometry. We also show that the technique is suitable for following chemical reactions on the solid phase.



Scheme 1. Schematic representation of the products generated upon laser photolysis and MALDI ionization of a peptide covalently attached to a solid phase resin through a photolabile α -methylphenacyl-ester linker.