

Rational Design of Molecularly Imprinted Plastics for Solid Phase Extraction by MS and NMR.

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Molecularly Imprinted Plastics (MIPs) are polymers produced in the presence of a compound of interest (template), that leave voids with the shape and size complementary to the template molecule. Reintroduction of the template to the MIP should result in the trapping of the template in these voids to the exclusion of other compounds. The degree of selectivity and capacity of the MIPs is dependent on the strength of the interaction between the template and the molecular surface of the void. MIPs are most commonly formulated using methacrylic acid and these do, in general, produce only weak hydrophobic forces of attraction.

MIPs based on methacrylic acid have been produced to selectively extract nerve agent degradation products from sera (1). However, we found that selectivity and retention for a variety of MIPS using different templates on solid phase extraction (SPE) columns produced with methacrylate was poor. In an attempt to generate stronger interaction we chose some methacrylic acids esterified with moieties containing heteroatoms in a study with nerve agent degradation products.

Electrospray (ESI) sources on mass spectrometers readily produce ion clusters and this tendency has been harnessed for production of calibration compounds covering thousands of Daltons using low molecular weight components (2). It seemed plausible to use mass spectrometry (MS) to investigate mixed cluster formation of template and functional monomer in the gas phase by ESI. Results from screening several monomers with alkyl phosphonates and MPA by Fourier Transform Ion Cyclotron Resonance (FTICR) MS produced one mixture showing strong interaction. The spectrum of a mixture of diethylaminoethyl methacrylate (DEAEM) and MPA showed the protonated functional monomer ion and a mixed cluster of two monomer molecules with MPA. This association appeared only on the FTICR spectrometer and could not be reproduced with a quadrupole instrument.

The notion that formation of a mixed cluster in the gas phase could be replicated in solution was confirmed by nuclear magnetic resonance (NMR) spectrometry. Addition of MPA to a solution of DEAEM resulted in significant shifts in the proton, carbon spectrum of the monomer and variations in the phosphorus spectrum of MPA. NOESY and selective NOE experiments confirmed that the interaction between MPA and DEAEM was not restricted to acid/base proton exchange but also involved the methyl protons of the MPA and protons along the backbone of DEAEM.

Polymers using the DEAEM and MPA were synthesized, crushed, sieved and packed into SPE tubes. These were then challenged with MPA and a series of alkyl phosphonates. The results of the analysis by positive-negative switching LCMS showed some very interesting trends. Nonpolar solvents for introduction and elution of the analyte showed weak binding of the alkyl phosphonates and some tendency to selectively attract compounds carrying the P-Me group. MPA was found to bind very strongly to both the imprinted and blank polymer made from DEAEM and could be quantitatively extracted from water with both polymers. However significant distinction between blank and imprinted polymer could be achieved by lowering the polarity of the eluting solvents. Additionally the MPA-DEAEM MIP was shown to have strong selectivity over compounds structurally related to MPA.

MPA is the final degradation product of nerve agent and is considered to be an important marker compound for determination of present or past use of nerve agents. The production of this polymer for selective extraction of MPA from environmental matrices should be of great value in the verification of the Chemical Warfare Convention.

1. Meng Zi-Hui, Lui Qin, *Anal. Chim. Acta*, **435**, 121, (2001)
2. David J. Bourne, *Advances in Mass Spectrometry*, **14**, A04_5030 (1997)