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A novel two-laser interface for coupling capillary electrochromatography with ion-trap time-of-flight mass spectrometry

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ABSTRACT

An interface has been developed for the hyphenation of capillary electrochromatography (CEC) with mass spectrometry (MS). Chromatographic eluate vaporization and selective analyte ionization occur within a quadrupole ion-trap, which permits significant instrument simplification when compared with the atmospheric pressure interfaces typically used for CEC–MS. Vaporization is achieved using laser desorption at 1064 nm while ionization is accomplished through UV photoionization. This two-step approach, through ionization laser wavelength selection, can provide ultratrace analysis with high selectivity. The mass spectrometer is a hybrid ion-trap time-of-flight (TOF) instrument in which the ion-trap is used in radio frequency-only mode, with DC-pulse ejection, to provide decoupling of the different timescales required for CEC separation and TOF mass analysis. The ion-trap is capable of accumulating ions over multiple laser shots. The mass resolution of the demonstration instrument was circa 1500. Preliminary CEC–MS runs have been recorded for mixtures containing polycyclic aromatic hydrocarbons. A concentration detection limit of 500 nM, for naphthalene in acetonitrile, has been determined for the interface.

1. Introduction

Capillary electrochromatography (CEC) can be described as electroosmotic flow (EOF)-driven liquid chromatography (LC). EOF-drive has two significant advantages over pressure-drive. First, the plug flow profile found in EOF-driven LC results in reduced band dispersion when compared with the parabolic flow profile found in pressure-driven LC. Second, band dispersion-minimizing reductions in stationary phase support particle size, which would not place any additional demands on EOF-drive instrumentation, require increased applied pressures in pressure-drive LC [1]. However, these advantages have not yet resulted in widespread popularity [2,3], despite the reporting of numerous CEC applications [4–7]. A key CEC disadvantage is that mobile phase composition influences flow rate, thus adding an extra layer of complexity to method development. Furthermore, when interfacing to mass spectrometry (MS), finding a mobile phase that is ideal for both separation and interface is particularly challenging.

Gordon et al. [8] were first to report the interfacing of CEC to MS, using a continuous flow-fast atom bombardment interface. The earlier report of Verheij et al. [9] is best regarded as describing a pressure-drive system in which an applied potential was used to add an electrophoretic component to the separation. In contrast to the earliest work, most reported CEC–MS interfaces incorporate electrospray ionization (ESI). However, while ESI-based interfaces where eluate is sprayed directly into the mass spectrometer have been reported [10], the incompatibility of typical CEC mobile phases with ESI necessitates the addition of an intermediate step where column eluate is diluted in a compatible make-up flow. The most common means of adding make-up flow is the sheath flow method [11]. Practical operation of such interfaces for CEC–MS has been described by Lane et al. [12,13]. However, since dilution reduces sensitivity and even careful mixing leads to at least some band dispersion, alternative interfacing strategies are clearly required.

Abbreviations: CEC, capillary electrochromatography; EOF, electroosmotic flow; ESI, electrospray ionization; ID, inner diameter; L^2MS, two-step laser mass spectrometry; LC, liquid chromatography; MS, mass spectrometry; PAH, polycyclic aromatic hydrocarbon; REMPI, resonance-enhanced multi-photon ionization; SCX, strong cation exchange; TOF, time-of-flight.

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Laser resonance-enhanced multi-photon ionization (REMPI) exploits resonant absorption to selectively ionize gas-phase molecules that absorb significantly at a chosen wavelength. Target analytes can be ionized in the presence of high concentrations of non-absorbing background species [14]. Naturally, REMPI must be paired with a method for producing gas-phase neutrals to complete an interface with a liquid-phase separation. The recently introduced atmospheric pressure laser ionization interface combines a heated nebulizer with REMPI at atmospheric pressure [15]; this interface, with the addition of ESI, has also been demonstrated for CEC–MS [16]. However, REMPI is most often used under vacuum with laser desorption, which can be used to provide plumes of vaporized neutrals. Long-wavelength laser desorption produces few ions directly, allowing independent optimization of desorption and ionization processes. This combination is known as two-step laser mass spectrometry (L^2MS) [17–19]. While it is possible for the same laser to be used for desorption and ionization, this can lead to complicated mass spectra as reactions occur in the resulting plume of desorbed neutrals and ions [20].

Laser-based mass spectrometry interfaces that operate under vacuum typically operate with solid samples. A notable example of an interface where laser irradiation is applied to a liquid is the laser induced liquid beam ionization/desorption approach [21]. Furthermore, matrix-assisted laser desorption ionization from the hyperbolic inner surface of an ion-trap ring electrode has been demonstrated using a solid sample presented on a probe [22] and a flowing liquid probe [23]. Using this concept we have constructed an L^2MS CEC–MS interface that requires no make-up flow and that avoids the ion transfer losses associated with atmospheric pressure interfaces. The interface is selective for analytes with significant absorbance at the ionization laser wavelength. Desorption and ionization occurs within the quadrupole ion-trap, using cross-bored apertures in the ring electrode to allow laser access. One such aperture is used for presentation of chromatographic eluate. Mass spectra are obtained by ejecting product photoions from the trap into a time-of-flight (TOF) mass analyzer, a configuration chosen chiefly for speed (ejection into the TOF mass analyzer is faster than the scanning out process used in ion-trap mass analysis). Thus, no compromise is required between resolution and scanning speed, and flexibility is retained for options such as switching to higher repetition rate laser systems.

Instrument performance was evaluated with polycyclic aromatic hydrocarbons (PAHs) since they are important environmental pollutants and are amenable to laser ionization at 266 nm. Complex mixtures of PAHs have often been targeted using L^2MS [24]. Chromatographic efficiency was largely maintained, even though a transfer capillary in which pressure-drive conditions existed was used to connect the CEC column terminus to the interface. The use of a transfer capillary was beneficial because it allowed columns to be exchanged without opening the high-vacuum chamber. Expressed as a number of theoretical plates per meter, obtained from measurements of half-height peak widths and retention times, an average chromatographic efficiency of 94,000 was obtained with a test mixture that consisted of acenaphthene, biphenyl, fluorene, naphthalene and phenanthrene. A concentration detection limit of 500 nM was obtained for naphthalene in acetonitrile.

2. Experimental procedures

2.1. Materials

Acenaphthene, biphenyl, naphthalene, and phenanthrene were obtained from Sigma–Aldrich (Saint Louis, MO, USA); fluorene and ammonium acetate were supplied by BDH (Poole, UK). Acetone, acetonitrile, acetic acid, and methanol were purchased from Fisher Scientific (Pittsburgh, PA, USA); water was double distilled in house. Fused-silica capillaries were from Polymicro Technologies (Phoenix, AZ, USA). Strong cation exchange (SCX) combined with reversed-phase (mixed mode) chromatographic stationary phase (3 μm particles) was supplied by Hypersil (Runcorn, UK).

2.2. Capillary electrochromatography

Capillaries were packed largely as described by Boughtflower et al. [25,26]. SCX combined with reversed-phase stationary phase was chosen over reversed-phase alone because the SCX character provides surface charges that increase EOF [27]. Briefly, a slurry of stationary phase particles suspended in acetone was driven rapidly into an empty fused-silica capillary using an applied pressure of 800 bar; a WellChrom K-1900 pneumatic LC pump (Knauer, Berlin, Germany) was used to quickly reach this operating pressure. Stationary phase particle suspension in the packing bomb was maintained using a Miniprobe 55T ultrasonic probe (Kerry Ultrasonics, Hitchin, UK). Particles were initially retained using a Valco (Houston, TX, USA) steel screen (thinner than a frit so reduced resistance to solvent flow). Packing was allowed to proceed for 15 min. After careful depressurization to avoid disturbing the newly packed bed, the system was reconfigured without the packing bomb. Water was then passed through the new CEC column for 12 h, using an applied pressure of 800 bar, in an attempt to collapse any voids that formed during the packing process. An electric heating coil (Innovatech, Stevenage, UK) was then used to create a sintered frit at the high-pressure end of the column. The column was reversed for production of the second retaining frit. With this approach a number of short columns can be made simultaneously. The electric heating coil can also be used to create windows for absorbance detection.

A Waters (Milford, MA, USA) Capillary Ion Analyzer was used for stand-alone CEC measurements (214 nm absorbance detection module installed) and as a high-voltage power supply (−30 to +30 kV) for CEC–MS. The instrument was equipped with an autosampler. Electrokinetic sample injection was performed by applying a potential of 5 kV for 5 s while the column inlet was immersed in a vial containing the sample solution. The system required circa 3 s to ramp up to 5 kV, indicating that the injection might be better described as the application of 3.5 kV for 5 s. An Agilent (Palo Alto, CA, USA) 8453 spectrophotometer was used to obtain molar absorptivity constants in mobile phase at 214 nm. To simplify CEC–MS operation, a transfer capillary was used to carry column eluate to the MS-interface. For electrical isolation, a grounded junction was constructed using a Supelco (Bellefonte, PA, USA) Capillary Column Butt Connector, effectively a double-tapered ferrule in a compression unit; electrical connection was achieved by externally coating the inlet end of the transfer capillary with copper using an Edwards (Crawley, UK) E12E4 vacuum coater. Since EOF terminates at the grounded junction, the flow profile in the transfer capillary is parabolic and chromatographic efficiency will be reduced. To minimize this degradation in performance, the transfer capillary was much narrower than the separation column [28]. In this work, a CEC column having an inner diameter (ID) of 100 μm was paired with a transfer capillary having an ID of 25 μm.

2.3. Mass spectrometry

The mass spectrometer and associated power supplies were manufactured by R.M. Jordan (Grass Valley, CA, USA). Michael et al. [29] have described the design and operation of this instrument. For easy access, the source region of the mass spectrometer was housed in a cubic vacuum chamber (30 cm × 30 cm × 30 cm) equipped with three fused-silica windows for laser access