

Note

Comparison of discharge tubes for deuterium-specific gas chromatographic detection with a microwave-induced plasma

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Atomic spectroscopy has developed as a powerful method for interfaced chromatographic detection because of its capacity to monitor any element selectively in the eluate^{1–3}. For gas chromatography (GC), such element-specific detection has been most often accomplished by means of a microwave-induced atmospheric pressure helium plasma (MIP)⁴. The plasma spectrometer system acts as an element-specific detector by monitoring the emission wavelength of a particular element and thus selectively detects compounds which contain the element of interest. Some of the advantages of such a detector are the ability to speciate directly or by derivatization, to tolerate non-ideal elution of components, to achieve high elemental sensitivity and to detect more than one element simultaneously. The most frequently employed GC–MIP system uses plasma discharges maintained within cavities based upon the Beenakker⁵ TM₀₁₀ design, which facilitates operation of a helium plasma at atmospheric pressure, allowing simple direct interfacing of a capillary gas chromatograph to the MIP system⁶.

Although spectroscopic resolution is not generally adequate to discriminate between emission lines from different isotopes of the same element, one instance in which this can be accomplished is for the hydrogen isotope deuterium. Deuterium-specific detection studies using various MIP detectors have been reported in the literature^{7–9}; the Beenakker cavity has been evaluated for deuterium detection¹⁰. Recently, Hagen *et al.*¹¹ described various functional derivatization techniques using deuterium and GC–MIP. Derivatized compounds were monitored with deuterium-specific detection or further derivatization was done with reagents incorporating other elements so that more than one element could be monitored and greater analytical information obtained.

The study now described compares quartz and a boron nitride (BN) discharge tubes for deuterium-specific detection. The latter has proven useful in a number of

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studies for elements such as silicon¹². The BN tube was sealed inside a larger quartz tube to improve the transfer efficiency of microwaves from the generator to the BN tube, and thus allow the operation of a stable helium plasma in the 40–50 W range needed for deuterium-specific detection¹².

Deuterium is used in the study of organic reaction mechanisms, the labeling of biological samples and the alteration of the biological properties of drugs. Such modification of the metabolic pathway of drugs is particularly interesting but relatively undeveloped. If one or more hydrogen atoms are replaced by deuterium, a drug molecule exhibits minimal steric change or changes in its physicochemical properties. The increased bond stability may, however, cause changes in the biological properties of the drug, usually by retarding certain metabolic pathways¹³. Since the metabolic pathway is altered, the drug activity is also altered; this may provide benefits, such as the avoidance of formation of toxic metabolites. Despite the promise of this deuterium isotope effect, work in this area has been limited due to the cost of toxicological testing and clinical trials. Gas chromatography–mass spectrometry (GC–MS) is a favored method of analysis for deuterated compounds, but it can be demanding and expensive since unit mass resolution will not be adequate to discriminate deuterated from undeuterated analogues in many instances. A GC–MIP system could serve as a viable alternative in clinical monitoring and testing, thereby extending the utility of the deuterium isotope effect.

EXPERIMENTAL

Instrumentation

A Varian (Walnut Creek, CA, U.S.A.) Model 1200 gas chromatograph modified for capillary column and split injection use was used. The detection system consisted of a Heath 703 Czerny–Turner configuration monochromator (McPherson Instruments, Acton, MA, U.S.A.) (0.35 m, f 6.8 capable of 0.1 nm resolution), a TM_{010} microwave cavity (J & D, Lexington, MA, U.S.A.) which was able to induce and sustain a helium plasma at atmospheric pressure, a microwave generator (Model HV15A, Scintillonics, Fort Collins, CO, U.S.A.) and a heated interface–transfer line. A coaxial stubstretcher (Model SL-10N tuner, Microlab/FXR, Livingston, NY, U.S.A.) was attached to the cavity to act as an impedance matching device and thus minimize reflected power. The photocurrent from the photomultiplier tube (Hamamatsu R928, 1100 V) was monitored with an electrometer (Model 600A, Keithley Instruments, Cleveland, OH, U.S.A.). The resultant signal was displayed on a strip-chart recorder (Omniscribe, Houston Instruments, Houston, TX, U.S.A.).

Materials

[²H₈]Toluene, [²H₃]acetonitrile, [²H₆]acetone, [²H₆]benzene and [²H₂]dichloromethane were obtained from Aldrich (Milwaukee, WI, U.S.A.). A 30 m × 0.25 mm I.D. DB-5 (5% phenylmethylsilicone bonded phase) fused-silica capillary column with a film thickness of 0.25 μm (J & W Scientific, Folsom, CA, U.S.A.) was used. A 6 mm O.D. × 1 mm I.D. fused-quartz discharge tube and a BN discharge tube were used. The BN tube (1 mm I.D.) was sealed inside a larger quartz tube (6.2 mm O.D. × 4 mm I.D.) by means of a high temperature, chemically resistant sealant (Sauereisen Adhesive No. 1, Sauereisen Cements, Pittsburgh, PA, U.S.A.) to prevent flow leakage

between the two tubes. The plasma gas came into contact only with the BN tube while the outside quartz tube, because of its favorable dielectric properties, improved the transfer efficiency of microwaves from the generator to the BN discharge tube.

Analytical method

The microwave detection system was optimized with respect to total plasma gas flow, power, slit width and axial viewing location. The deuterium atomic emission line (656.1 nm) was found by bleeding a deuterated solvent such as [$^2\text{H}_6$]acetone into the plasma and then scanning with the monochromator until the wavelength was located. The focussing lens was then adjusted to give the greatest response. The slit width was optimized for the best signal-to-noise ratio by repeated injections of a deuterium-containing compound. The plasma gas flow-rate and power were optimized by simplex optimization¹⁴.

After optimization, calibration curves for the deuterated compounds were prepared. Detection limit and linear dynamic range information was obtained from these plots. Selectivity values were also calculated.

RESULTS AND DISCUSSION

The optimum conditions for deuterium-specific detection were at a helium plasma gas flow-rate of 60 ml/min, a plasma power of 45 W and a 50- μm slit width for the quartz discharge tube. Values for the BN discharge tube involved a flow-rate of 53 ml/min, a plasma power of 55 W and a 50- μm slit width. Calibration curves for various deuterated compounds were constructed using both the BN and quartz discharge tubes, a summary of these data being found in Table I. Deuterium *versus* carbon selectivity values against hexane or heptane for the two different tubes are also given.

The detection limit and most notably the linear dynamic range values are much better for the quartz discharge tube than for the BN tube. Deuterium detection limits of *ca.* 50 pg and the wide linear dynamic range are encouraging features for further

TABLE I
ANALYTICAL DATA FOR DEUTERIUM-SPECIFIC DETECTION

Compound	Detection limit (pg)		Selectivity of deuterium versus carbon	Slope	Correlation	Linear dynamic range	Number of points
	Deuterium	Compound					
<i>Quartz discharge tube</i>							
[$^2\text{H}_8$]Toluene	28	174	88	0.984	0.9981	5176	8
[$^2\text{H}_3$]Acetonitrile	55	402	92	1.182	0.9974	3940	5
[$^2\text{H}_6$]Acetone	59	314	84	1.171	0.9974	480	5
[$^2\text{H}_6$]Benzene	51	357	78	1.039	0.9958	5130	5
<i>BN discharge tube</i>							
[$^2\text{H}_3$]Dichloromethane	43	937	87	0.932	0.9976	135	4
[$^2\text{H}_3$]Acetonitrile	233	1710	95	1.008	0.9958	135	5
[$^2\text{H}_6$]Acetone	153	815	78	1.237	0.9945	135	5
[$^2\text{H}_6$]Benzene	116	813	79	1.183	0.9943	112	5

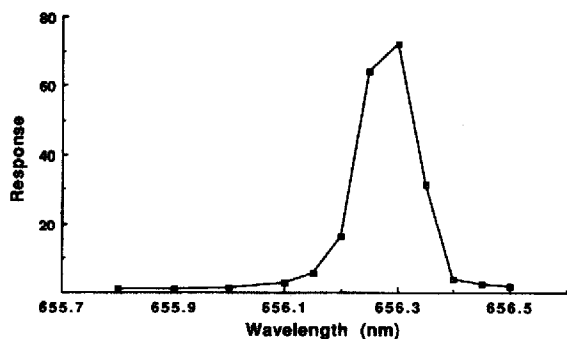


Fig. 1. Helium MIP background response with a quartz discharge tube.

application. However, the deuterium *versus* carbon selectivity is only *ca.* 100 for either discharge tube. It may be that true deuterium to carbon selectivity was not measured because of the contributing response from hydrogen emission at 656.3 nm. In the selectivity determination it was necessary to inject a compound containing carbon and hydrogen along with the deuterated sample, and to measure their responses as they eluted almost simultaneously. This procedure was used for two reasons: to measure responses under virtually identical elution conditions and to make observations for a pair of deuterated and undeuterated species as might be encountered in a practical determination. Since the hydrogen emission line is so close to the deuterium line (656.1 nm), it is possible that the hydrogen emission adds to the emission credited to carbon, thus reducing the measured deuterium *versus* carbon selectivity value, since the calculation does not take into effect such a close and strong interference. Since the hydrogen emission line is so close to the deuterium line, the selectivity value between them would be expected to be low. A selectivity value for deuterium over hydrogen of *ca.* 25 was calculated in this study, from chromatograms such as that shown in Fig. 3; in comparison a value of 50 has recently been reported for measurements at these wavelengths, giving credibility to the above conclusion¹⁵.

Fig. 1 shows the background response of the helium MIP for the mono-

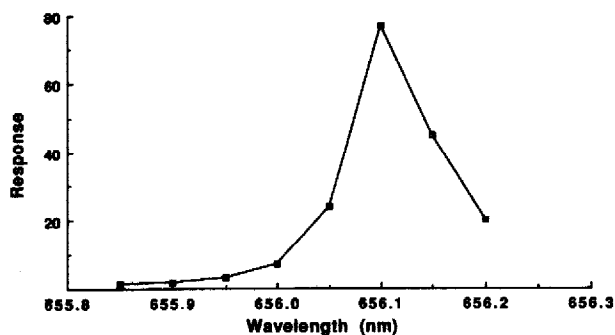


Fig. 2. Helium MIP response with $[^2\text{H}_6]$ acetone bleed and a quartz discharge tube.

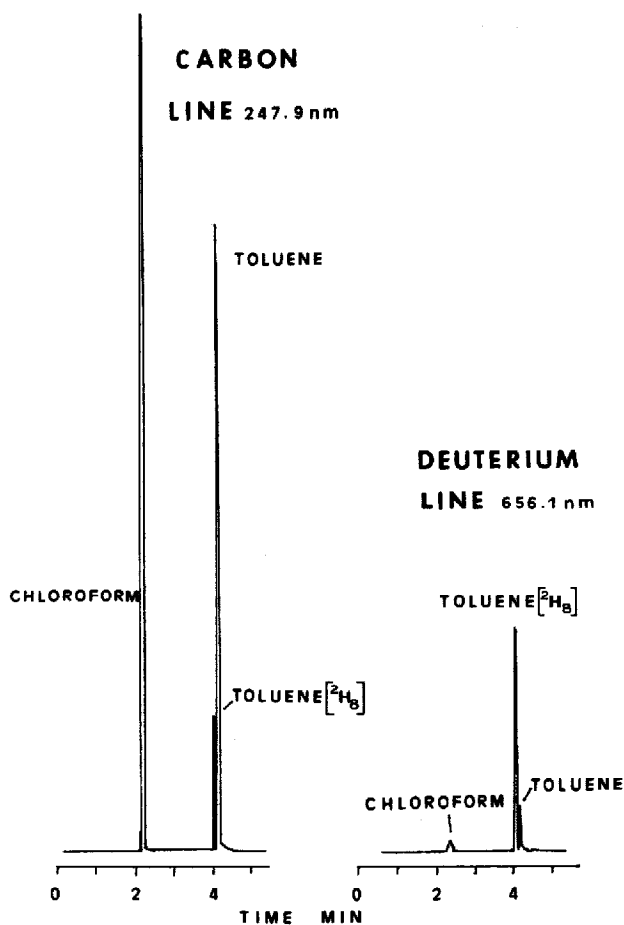


Fig. 3. GC separation of toluene and $[^2\text{H}_6]$ toluene monitored at the carbon (247.9 nm) and deuterium (656.1 nm) emission lines. Helium column flow-rate, 1.4 ml/min; injection volume, 0.1 μl ; inlet split ratio, 53:1; injector temperature, 230°C; detector transfer line temperature, 250°C; column temperature, 57°C isothermal.

chromator used; at 656.1 nm some response is observed. If impurities in the plasma gas are responsible, then a hydrocarbon sample would also be expected to give an enhanced response and thus reduce the selectivity value. Fig. 2 shows the response seen when $[^2\text{H}_6]$ acetone was bled into the plasma. There is a marked decrease in response away from the 656.1-nm emission line and thus no way to avoid the background emission by moving to another measurement wavelength without sacrifice in detectability.

While selectivity between deuterium and carbon is only moderate, Fig. 3 demonstrates that deuterium-specific detection with the MIP system is a useful tool in distinguishing deuterated compounds in a chromatogram. The separation of toluene and $[^2\text{H}_6]$ toluene in a chloroform solution (50:10:500, v/v/v) is shown for two independent chromatograms, monitoring at the carbon emission line (247.9 nm) and at

the deuterium emission line (656.1 nm). Deuterium detection plasma conditions were as noted above while carbon was monitored at 247.9 nm with a plasma power of 65 W and a plasma gas flow-rate of 88 ml/min. The relative responses are as predicted for the response at the carbon line, based upon the amounts of each component in the sample. The deuterium line response demonstrates the selective detection of the deuterated compound, [²H₈]toluene showing a marked increase in response over toluene. The ability to carry out such selective monitoring can simplify the task of finding the deuterated component in complex matrixes, utilizing carbon- and hydrogen-specific chromatograms to gain further information.

The study showed that the quartz discharge tube gave a better detection limit and linear dynamic range for deuterium detection than did the BN tube which, however, has a longer effective operating life since it suffers less from etching of the walls by the plasma. Although the selectivity of deuterium *versus* carbon and hydrogen are both only moderate, GC-MIP shows potential as a useful tool to monitor deuterated compounds.

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