A Triple Ionization Source for LC/MS

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Abstract

We report on the development of a triple ionization source consisting of ESI, APCI and APPI sources. The source uses two probes, one for ESI and a nebulizer/vaporizer for APCI and APPI. The dual probe configuration greatly improves on the multimode approaches currently in use for ESI/APCI and ESI/APPI dual sources where at high flow rates the ESI sprayer does not fully desolvate compromising the APCI and APPI performance. The dual probe approach; however, requires splitting the LC flow and maintaining a high precision ratio in order to achieve coincident elution from both sprayers. The triple source can operate in several operating modes including (i) simultaneous operation of all three or any two ionizers, (ii) fast switch between all three or any two ionizers, and (iii) a custom method in which the ionizer most suited to the eluting compound is turned on. We believe the latter mode is an extremely effective method for optimizing analysis of screens of many disparate or difficult-to-ionize compounds such as are encountered in food safety and environmental monitoring.

Flow split characterization

Flow-gradient matrix for split ratio			
Flow (µL/min)	ACN (%)		
	10	50	90
200	1.487	1.498	1.495
500	1.491	1.495	1.493
1000	1.491	1.497	1.489

1:1 water:methanol	
Flow (µL/min)	Split ratio
200	1.487
500	1.491
1000	1.494

Shift in APCI/APPI peak arrival time (s) relative to calibration point			
Flow (µL/min)	ACN (%)		
	10	50	90
200	0.015	0.000	0.004
500	0.004	0.002	0.003
1000	0.002	0.000	0.002

Splitting is achieved using two PEEKsil tubing. The split ratio is monitored over a week and the measurements fall in the range 1.495-1.498 for 50% ACN at 200 uL/min. Arrival times for ESI and APPI/APCI are matched at calibration point using 50% ACN and 200 µL/min solvent flow. Peak matching remains within a few ms across wide range of flow rates and solvents compositions.

Single mode versus tri-mode operation

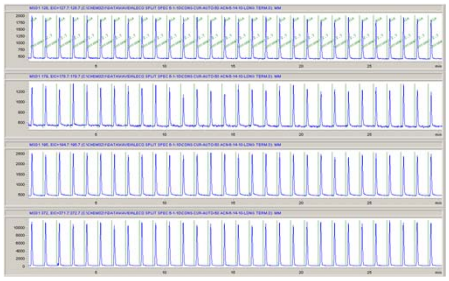
Injection amounts: 20 ng naphthalene, 2 ng anthracene, 200 pg caffeine, 34 pg crystal violet
Mass spectrometer: Agilent single quadrupole. No dopants are used for this study.

Average of five 2uL-auto injections at 200 uL/min, 50% ACN+0.05% formic acid						
		FWHM (s)	area	area RSD%	height	height RSD%
ESI	caffeine	5.13	7323	2.62	1427	1.77
	crystal violet	4.00	77962	1.17	18670	1.41
APPI	naphthalene	3.28	21493	0.95	6108	0.69
(no dopant)	anthracene	3.66	420	4.33	115	2.46
	caffeine	3.65	71	6.60	19	5.16
APCI	naphthalene	3.42	5122	1.86	1424	1.56
	anthracene	3.40	16781	0.33	4646	1.30
	caffeine	3.66	24406	0.60	6272	1.32
tri-mode	naphthalene	4.77	6582	0.73	1244	1.18
	anthracene	4.73	4752	2.48	911	5.90
	caffeine	4.95	12329	1.36	2274	3.31
	crystal violet	4.08	16162	2.96	3699	4.74

The entire flow is directed to one probe for single mode measurements. A split ratio of 1.495 in favor of APCI/APPI is utilized for tri-mode. Probe positions and voltages may be adjusted to achieve the desired comprise in sensitivity. Typically, a factor of 3-5 loss in sensitivity is observed for simultaneous operation of all three modes versus the best performance in a single mode.

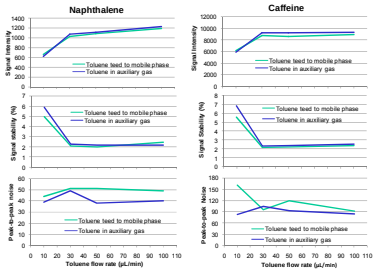
Signal stability in tri-mode operation

30 injections of 20 ng naphthalene, 2 ng anthracene, 200 pg caffeine, 34 pg crystal violet
Flow: 200 µL/min, 50% ACN+0.05% formic acid; Split ratio: 1.634 achieved using 0.0025" PEEK tubings



30 flow injections in 30 minutes			
analyte	contributing mode	area RSD%	height RSD%
naphthalene	APPI	2.3	3.5
anthracene	APCI	5.5	7.6
caffeine	APCI/ESI	2.6	3.0
crystal violet	ESI	1.7	2.9

Dopant introduction for APPI



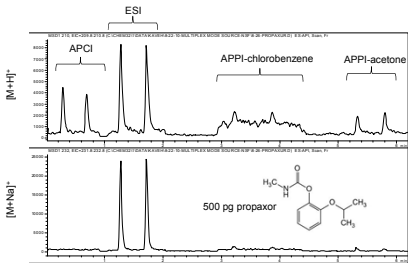
Gas-phase dopant delivery into the auxiliary gas of the vaporizer shows identical performance to dopant introduction via solution. This eliminates complications of post-column dopant addition.

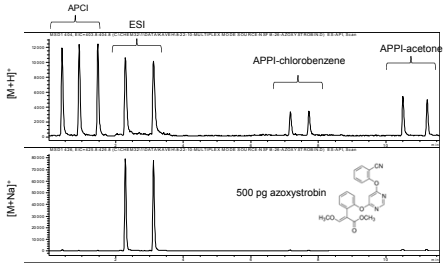
Experimental conditions: 2 minute background measurement followed by 2 minute signal measurement; dopant delivered using a 1mL syringe, Analyte infused into the mobile phase flow of 1mL/min ACN.

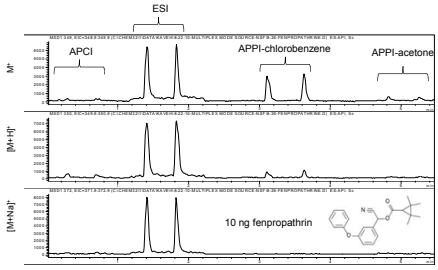
Online mode switching

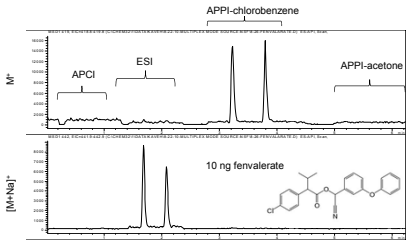
Mode switching can be used to operate each mode at its best efficiency. A mode selection program maybe implemented during a chromatographic run based on chemical properties of analytes. Feasibility is shown below by manual switching for detection of pesticides relevant to food safety.

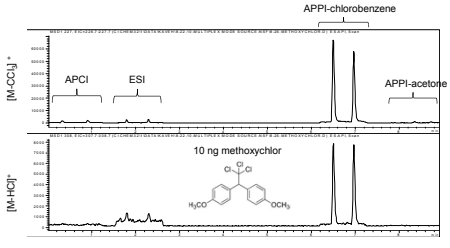
Experimental conditions: 200 µL/min flow, 75% ACN, 25% Water, 0.05% formic acid; Manual flow injection: 2 µL; Dopant: 5 µL/min in the gas phase
Flow splitting: 3:2 split ratio in favor of APPI/APCI achieved using PEEKsil tubing, Data acquisition: scan mode
Dopant selection is implemented by introducing dopants through two separate syringe pumps and lines secured to the source by a dual lumen sleeve.

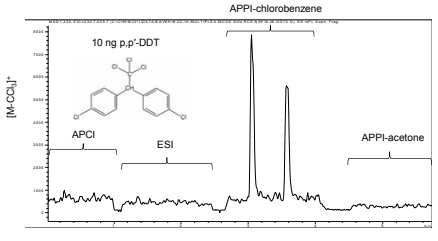












Conclusions

- Operation of a triple mode ion source in simultaneous and switching modes with stable flow splitting is demonstrated.
- Sensitivity is compromised in simultaneous mode by a factor of 3-5.
- Mode switching allows use of dopants to enhance APPI performance and operation of each mode at its optimum conditions.
- ESI and APPI show the most complementary behavior for the analytes studied.
- Dopant switching from chlorobenzene to acetone improves the APPI signal for high proton affinity compounds by a factor of ~2 for the solvent and flow rate used in this study.
- ESI-APPI combination is expected to provide better coverage of analytes compared to dual dopant APPI. However, high gas and liquid velocity from ESI probe in mode switching reduces the APPI signal by a factor of 2-3 compared to a dedicated APPI source.

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