J. Am. Soc. Mass Spectrom. (2016) 27:1789–1795
DOI: 10.1007/s13361-016-1463-4

RESEARCH ARTICLE

Isobutane Made Practical as a Reagent Gas for Chemical Ionization Mass Spectrometry

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Abstract. As a reagent gas for positive- and negative-mode chemical ionization mass spectrometry (CI-MS), isobutane (i-C_4H_{10}) produces superior analyte signal abundance to methane. Isobutane has never been widely adopted for CI-MS because it fouls the ion source more rapidly and produces positive CI spectra that are more strongly dependent on reagent gas pressure compared with methane. Isobutane was diluted to various concentrations in argon for use as a reagent gas with an unmodified commercial gas chromatograph-mass spectrometer. Analyte spectra were directly compared using methane, isobutane, and isobutane/argon mixtures. A mixture of 10% i-C_4H_{10} in argon produced twice the positive-mode analyte signal of methane, equal to pure isobutane, and reduced spectral dependence on reagent gas pressure. Electron capture negative chemical ionization using 1% i-C_4H_{10} in argon tripled analyte signal compared with methane and was reproducible, unlike pure isobutane. The operative lifetime of the ion source using isobutane/argon mixtures was extended exponentially compared with pure isobutane, producing stable and reproducible CI signal throughout. By diluting the reagent gas in an inert buffer gas, isobutane CI-MS experiments were made as practical to use as methane CI-MS experiments but with superior analytical performance.

Key words: Isobutane, Chemical ionization, CI, Electron capture, Ion source, Electron filament, GC-MS

Received: 28 June 2016/Revised: 27 July 2016/Accepted: 28 July 2016/Published Online: 15 August 2016

Introduction

Chemical ionization mass specrtrometry (CI-MS) has been a valuable analytical tool for 50 y. After the technique was disclosed by Munson and Field [1], it became widely adopted, modified, and commercialized. Methane was the first reagent gas used for CI and remains by far the most common, almost to the total exclusion of other gases in contemporary experiments. The principal positive reagent ions from methane, CH_5^+ and $C_2H_5^+$, react with almost all organic molecules, and methane CI spectra are largely independent of reagent gas pressure in the ion source [2, 3]. When resonance electron capture (EC) ionization was adapted for negative chemical ionization (NCI) mass spectrometry, methane was used as reagent gas to thermalize electrons [4–6]. Although more efficient gases for EC-NCI-MS have long been identified [7], methane continues to be the most popular choice [8, 9].

Isobutane was implemented as a reagent gas in the same seminal publications referenced above that established positive and negative CI-MS methods, and it has historically been used as an alternative to methane when necessary to acquire maximum molecular adduct ion signal. Because isobutane reagent ions have a significantly higher proton affinity than methane reagent ions, analyte fragmentation upon proton transfer from a reagent ion is reduced or eliminated, and the abundance of the intact adduct ion is increased. Isobutane has been used for applications where it was critical to identify the analyte protonated molecule and for maximum sensitivity [10–16]. Isobutane is also more efficient at creating thermal electrons than methane [7] and has been used for increased EC-NCI analyte signal [17].

There are two reasons for the limited use of isobutane regardless of its clear advantages. Unlike methane, spectra from positive CI with isobutane are dependent on reagent gas pressure in the ion source. The isobutane reagent ion $C_3H_7^+$ reacts with i-C_4H_{10} to form the reagent ion t-$C_4H_9^+$. The

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Electronic supplementary material The online version of this article (doi:10.1007/s13361-016-1463-4) contains supplementary material, which is available to authorized users.

Correspondence to: Braden C. Giordano; *e-mail:* braden.giordano@nrl.navy.mil changing pressure of i-C_4H_{10} affects the ratio between reagent ions, which have different acidities and produce differing amounts of fragmentation [3]. Because modern commercial instrumentation for CI-MS does not directly measure reagent gas pressure in the source, conditions cannot be duplicated easily between instruments. More notoriously, isobutane is difficult to work with because it fouls the ion source more rapidly than methane and shortens the operative lifetime of electron filaments [15, 18–20]. Methane CI experiments can be reliably performed for weeks or perhaps months, but CI with isobutane causes the filament to fail within hours or days of use. Such instrumental down-time is impractical in many laboratory settings.

A variety of modifications to the CI source have been created to extend filament operative lifetime. The polarity of the current on the electron filament can be reversed periodically to slow carbon buildup [21], but such a modification is not available on commercial instrumentation. The filament can be operated continuously to prevent the strain of power-cycling [22], but the powered filament would be exposed to gas chromatography (GC) solvent elution. Filaments can be coated with thoria or yttria so that they will produce an equal electron flux at a lower, less strenuous temperature/ionization energy [23–25]. Available coated filaments increase operational lifetime two to three times [26], a modest improvement upon isobutane CI results. The filament may be entirely replaced with a Townsend discharge at the expense of higher signal-to-noise [27, 28].

To maintain the analytical advantages of isobutane CI, minimize ion source fouling, and use commercial instrumentation without modification, a practical chemical alternative must be employed. Reagent gases can be substituted effortlessly. Neopentane produces similar positive CI spectra to isobutane and doubles the electron filament lifetime [20] but is many times more expensive than isobutane to obtain at high purity. Dilution of deleterious analytical gases, including isobutane with inert gases, has been performed for CI [29–32], but the experiments were not constructed for isobutane to directly interact with an analyte. In the present research, a reagent gas mixture of isobutane diluted in argon produces positive CI and EC-NCI spectra of equal or better quality to pure isobutane. The operative lifetime of the electron filament in dilute isobutane is also extended exponentially.

Experimental

All pure gas supplies were purchased at ultra-high purity (UHP): 99.97% methane and 99.95% isobutane (Matheson Tri-Gas, Montgomeryville, PA, USA), and 99.99999% argon (Earlbeck Gases and Technologies, Baltimore MD, USA). References herein to "pure gas" denote an unadulterated supply directly from a purchased, UHP-rated gas cylinder. Two commercially-produced gas mixtures, 10 and 100 ppm UHP isobutane in UHP argon (Matheson Tri-Gas), were also purchased for comparison to serial dilution mixtures.

The gas cylinders used to create reagent gas dilution mixtures were cleaned by repeated fills with pure supply argon and evacuations to <1 Torr. To produce 5% or 10% isobutane in argon, isobutane from a pure supply cylinder was flowed to an evacuated cylinder at a pressure set by the supply regulator. The gas transfer produced an audible hiss that ended to signify equilibrium. A regulated pressure of pure supply argon diluent was then added to the mixture cylinder in the same manner. Serial dilutions of isobutane in argon were further produced in the same mixture cylinder. The isobutane concentration was reduced an order of magnitude by evacuating the mixture cylinder to 10 psi and then refilling to 100 psi with pure argon diluent. Separate dilution series were produced for positive- and negative-mode analyses so that experiments in either mode could be run consecutively. Reagent gases and gas mixtures were supplied to the ion source without filtration except where noted.

All experiments were performed with an un-modified GC-MS (Agilent 7890-5975C; Santa Clara, CA, USA). New rhenium/tungsten electron filaments (Agilent G7005-60072) were installed and the ion source baked at 300 °C for 8 h under vacuum. Except in the case of operative lifetime experiments, the filament was conditioned with at least 1 d of runs in methane reagent gas before beginning analytical runs. For analysis in positive mode, samples of 50 ng nicotine in acetonitrile were injected into the GC inlet at 200 °C with a 1:1 split and a 5 mL/min helium flow. A 15 m long, 0.25 μm i.d. Agilent RTX 5GC column introduced analyte to the ion source. The temperature of the ion source was set to 250 °C, and the quadrupole was set to 150 °C. The column temperature was held at 50 °C for 0.5 min and ramped to 250 °C in 4.5 min. The ion filament was powered for 4 min after a 1 min delay to allow solvent peak elution. The total time for a run, including autosampler/injector operation, separation, and oven equilibration was 8.2 min. The quadrupole was scanned from *m/z* 80 to 300 for analytical runs and from *m/z* 20 to 100 for reagent ion spectra.

Some settings were adjusted for analysis by EC-NCI. Samples of 100 pg trinitrotoluene (TNT) and cyclotrimethylenetrinitramine (RDX) in acetonitrile were injected into the GC split inlet at 250 °C. The ion source temperature was set to 150 °C. The column temperature was held at 100 °C for 0.5 min and ramped to 280 °C in 4.6 min. The ion filament was powered for 4.1 min per run, and the total time for a run was 8.2 min. The quadrupole was operated in selected ion mass mode, scanning for the three most abundant analyte ions: *m/z* 227 ($M^{-\bullet}$), *m/z* 211 ($[M-O]^-$), and *m/z* 197 ($[M-NO]^-$) from TNT; and for *m/z* 176 ($[M-NO_2]^-$), *m/z* 129 ($[C_3H_5N_4O_2]^-$), and *m/z* 102 ($[C_2H_4N_3O_2]^-$) from RDX [33].

Default settings for auto-tuning the Agilent 5975C CI ion filament use –70 eV electron energy and 100 μA emission current. The minimum power settings provide adequate sensitivity for most applications and maximize the operative lifetime of the filament [34]. For this research, filament potential was increased to –100 eV electron energy and 250 μA emission current in order to maximize analyte signal and to highlight any deficiencies in operative lifetime resulting from other experimental conditions.

Like most commercial GC-MS instruments today, the Agilent 5975C does not directly measure reagent gas pressure in the ion source and is not calibrated for different gases. The mass flow controller built into the instrument was used to regulate the reagent gas supply by adjusting a mass flow controller orifice size based on a programmable setting, described in the software as “percent flow.” The mass flow controller had been factory-calibrated to supply 1 mL/min of methane at 20% flow. Using this configuration, flow was optimized for maximum analyte signal with each reagent gas in both positive and negative mode. Each reagent gas was connected in turn to the mass flow controller with a backing pressure of 20 psi. Gas lines were purged to the atmosphere for ~30 s before connection and purged to the vacuum housing for 6 min with the mass flow controller after connection. Methane was supplied at 18% flow for positive mode CI experiments and at 40% flow for EC-NCI experiments. Isobutane, argon, and all gas mixtures were supplied at 15% flow for positive mode CI and at 11% flow for EC-NCI. With reagent gas flowing, the uncalibrated ion gauge pressure measurement was 1.1 to 1.4 × 10^{-4} Torr. The performance of CI reagent gases was characterized by measuring intact analyte adduct ion abundance, total ion signal, and percent fragmentation,

$$\%fragmentation = 100 \times \frac{\sum_i F_i}{M + \sum_i F_i} \tag{1}$$

where M is total abundance of the intact molecular adduct ion(s) and F is the abundance of each fragment ion originating from the intact molecular adduct ion(s).

Results and Discussion

Positive Chemical Ionization

CI analyses using pure isobutane as reagent gas to ionize TNT, nicotine, and other analytes under default source settings repeatedly caused the electron filament to fail within a day or two of use, depending on the quantity of experiments performed. In failing, the formerly straight filament warped and bent toward its assembly reflector plate, shorted the applied voltage, and broke. Failure was preceded by drastic changes in background and analyte signal abundance in the final 3–5 runs. Background ion signals from water and air were less intense with isobutane than with methane reagent gas. Although no contamination was apparent in the reagent ion signal, a CI gas purifier (Agilent G1999-80410; Santa Clara, CA, USA) was installed in the isobutane reagent gas supply line. The gas purifier did not significantly extend the filament lifetime. The rapid source fouling was therefore not attributed to supply contamination but to the greater carbon content of isobutane compared to methane. An yttriated filament (Scientific Instrument Services, Ringoes, NJ, USA) was tested to slow carbon buildup from isobutane, but analyte signal was less abundant at the lower filament energy used for coated filament operation. Neither modification was used for further experiments.

Mixtures of isobutane and argon appeared to produce a comparable CI signal to pure isobutane but did not cause rapid filament failure. Different concentrations of isobutane in argon were produced and tested as reagent gas using the same flow setting regulating gas pressure. The density of isobutane is slightly different from that of argon (2.53 kg/m^3 and 1.69 kg/m^3 at STP, respectively [35]). Mixtures of 5% and 10% isobutane in argon (% i-C_4H_{10}/Ar) have different average density and, therefore, different molar concentrations in the source, and cannot be as easily approximated to pure argon as mixtures of 1% i-C_4H_{10}/Ar and lower. Regardless, there was no significant difference in the optimum flow rate necessary for maximum analyte signal with pure isobutane, argon, or mixtures. For the purposes of the comparison, total reagent gas pressures used for each mixture were considered equal.

A complete dataset comparing different reagent gases was acquired by performing experiments in close succession to minimize any temporal effects on the filament. To minimize any cumulative physical and chemical effects on the filament, the number of replicate injections with each isobutane reagent gas mixture was limited to five. Control CI experiments with methane were also performed immediately before and after experiments with isobutane and mixtures. Methane CI produced two molecular adduct ions at larger mass-to-charge in addition to MH^+, $[M + C_2H_5]^+$, and $[M + C_3H_5]^+$. All concentrations of isobutane above 0.1% in argon produced MH^+, $[M + C_3H_5]^+$, $[M + C_3H_7]^+$, and $[M + C_4H_9]^+$. At 0.1% i-C_4H_{10}/Ar and below, the largest adduct ion was not observed. No additional analyte adduct ions (Online Resource 1) or isobutane reagent ions (Online Resource 2) were observed in meaningful abundance as a result of diluting isobutane. CI with pure isobutane produced 2.3 times the molecular adduct ion signal of methane, and three times the protonated molecule signal ratio to larger adduct ions (Table 1). Fragmentation of intact ions was also reduced more than 3-fold by pure isobutane compared to methane CI. Signal abundance acquired with 10% i-C_4H_{10}/Ar was not significantly different from pure isobutane. As the concentration of isobutane in argon was reduced to 5% and below, intact adduct ion signal also decreased. The lowest isobutane concentration at which results were improved relative to methane CI was 1% in argon, and lower concentrations produced spectra that resembled electron impact. The equivalent control results demonstrate that response was attributable to reagent gas composition and not filament effects.

The ratio between the isobutane reagent ions t-$C_4H_9^+$ at m/z 57, and $C_3H_7^+$ at m/z 43, was changed 5% by 10-fold dilution (10% i-C_4H_{10}/Ar) of the reagent gas in argon (Table 2). As a result of further dilution to 5% i-C_4H_{10}/Ar, percent fragmentation of the nicotine protonated molecule and other intact adduct ions, as well as the ratio between intact analyte adduct ions, was essentially unchanged. Analyte spectra resembled electron impact spectra below 5% i-C_4H_{10}/Ar. The results suggest that the constant total gas pressure is more critical for reproducible

Table 1. Observed Nicotine Ion Signal Using CI Reagent Gases, ± Standard Deviation

	MH^+ relative abundance	Ratio of MH^+ to larger adduct ions	Percent fragmentation of intact adduct ions
Methane	42 ± 3	3.17 ± 0.07	22.6 ± 0.5
Isobutane	95 ± 3	9.8 ± 0.2	6.3 ± 0.3
10% i-C_4H_{10}/Ar	100 ± 7	8.6 ± 0.1	7.7 ± 0.3
5% i-C_4H_{10}/Ar	66 ± 3	8.4 ± 0.3	7.5 ± 0.1
1% i-C_4H_{10}/Ar	53 ± 5	5.7 ± 0.3	13.3 ± 0.5
0.1% i-C_4H_{10}/Ar	30 ± 5	3.23 ± 0.04	32.9 ± 0.6
0.01% i-C_4H_{10}/Ar	14.6 ± 0.3	2.7 ± 0.1	64.9 ± 1.0

spectra than the concentration (above a certain threshold) of proton supply gas species. The reagent gas serves as both a source of proton-donating reagent ions and as a buffer gas to deactivate and prevent additional fragmentation of intact analyte adduct ions. If the total gas pressure were significantly lower, or if the collisional cross-section of the bath gas molecules were smaller than that of argon, fragmentation would be higher at dilute isobutane concentrations.

Electron Capture Negative Chemical Ionization

The performance of diluted isobutane in argon for EC-NCI was also tested. Signal instability with pure isobutane was far more pronounced for EC-NCI than positive CI. Because the detrimental effects of pure isobutane on analyte signal appeared more significant with EC-NCI, all dilute isobutane mixtures were tested before pure isobutane. Like positive CI experimentation, control EC-NCI experiments with methane and argon were repeated after isobutane mixture experiments. Experiments with the various regent gases were performed in close succession.

All reagent gases produced a mass spectrum of the molecular ion $M^{-\bullet}$ and fragment ions. Pure argon yielded 2.8 times the TNT molecular ion signal and 2.3 times the RDX signal compared with methane (Figure 1), consistent with observations of EC-NCI relative efficiency in literature [7]. The first analytical run with pure isobutane produced far more abundant analyte signal than argon, but signal decreased more than 5-fold in the four subsequent replicate injections. The rapid decrease is a direct consequence of the effects of pure isobutane on the filament; as the conditions were significantly altered by each run, the results cannot be compared statistically and are plotted as individual injections. The lowest signal replicates from the pure isobutane sequence were comparable to methane. In contrast, all dilutions of isobutane in argon produced highly reproducible EC-NCI signal. Unlike positive CI, where intact analyte adduct ion signal was unchanged or decreased by decreasing isobutane concentration, EC-NCI signal of TNT and RDX was significantly increased by isobutane dilution from 10% to 1% in argon. The optimum 1% i-C_4H_{10}/Ar reagent gas mixture produced 3.6 times the TNT molecular ion signal of methane and 5.4 times the total RDX signal of methane, both with 3% or less relative standard deviation (RSD).

Isobutane diluted to trace concentration in argon was experimentally distinct from pure argon. Between 1000 ppm (0.01%) and 10 ppb (1×10^{-6}%) i-C_4H_{10}/Ar, observed analyte EC-NCI signal was significantly lower than with pure argon. The lowest concentration in the dilution series was below the purity rating of the diluent argon supply. It is highly unlikely that isobutane would interfere with the production of UHP argon by isolation from air, making it plausible that 10 ppb i-C_4H_{10}/Ar is not the same as pure argon. Control runs with pure argon performed immediately before and after the dilution series were identical, producing higher signal than trace isobutane. Commercially-produced supplies of 10 and 100 ppm i-C_4H_{10}/Ar generated similar EC-NCI signal to serially-diluted trace isobutane, demonstrating that there were no systematic dilution errors.

Filament Operative Lifetime

The operational lifetime of a new electron filament in 1% i-C_4H_{10}/Ar was measured by performing consecutive GC-MS blank runs using acetonitrile. Periodic EC-NCI analyses of TNT were also performed to determine what effect continuous use had on the filament. The initial analyses performed after the filament was installed produced extremely high signal, which decreased upon subsequent runs. Signal had stabilized by the second day of operation, similar to operation with methane as reagent gas. Over 160 h of uninterrupted operation, total ion chromatogram signal abundance had up to 3.7% RSD. Power to the filament was ultimately cycled over 3500 times (478 h of runs, 239 h with the filament powered) without filament failure.

No significant change in analyte signal was observed after pauses in the consecutive run cycle lasting less than 8 h.

Table 2. Observed Reagent Ion Signal Using CI Reagent Gases, ± Standard Deviation

	$C_3H_7^+$ (m/z 43) abundance	t-$C_4H_9^+$ (m/z 57) abundance	Ratio of t-$C_4H_9^+$ to $C_3H_7^+$
Isobutane	$4.5 \times 10^5 \pm 2 \times 10^4$	$3.18 \times 10^6 \pm 6 \times 10^4$	7.14 ± 0.09
10% i-C_4H_{10}/Ar	$3.91 \times 10^5 \pm 5 \times 10^3$	$2.62 \times 10^6 \pm 2 \times 10^4$	6.82 ± 0.03
5% i-C_4H_{10}/Ar	$3.87 \times 10^5 \pm 5 \times 10^3$	$2.42 \times 10^6 \pm 2 \times 10^4$	6.33 ± 0.02
1% i-C_4H_{10}/Ar	$3.75 \times 10^5 \pm 5 \times 10^3$	$1.76 \times 10^6 \pm 1 \times 10^4$	4.70 ± 0.02

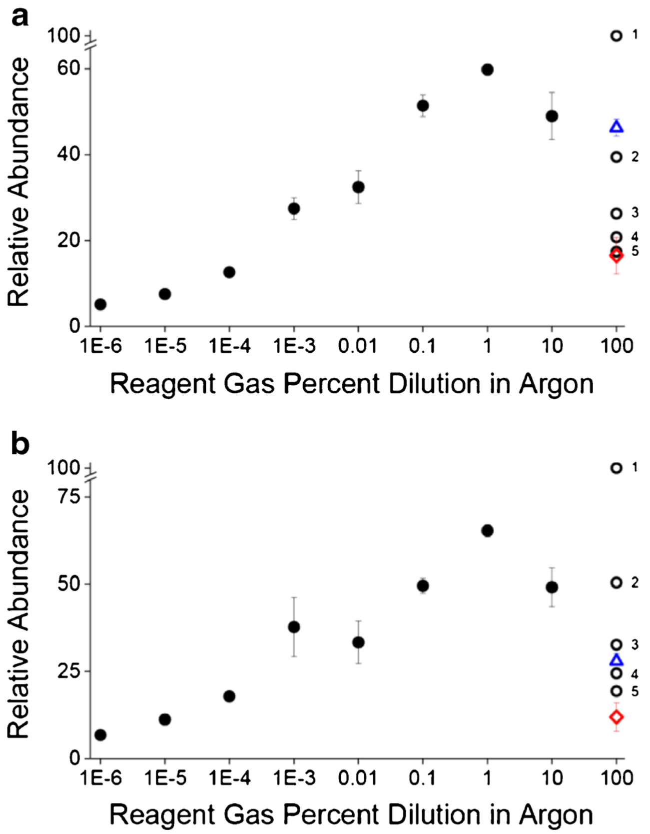

Figure 1. EC-NCI signal relative abundance observed with methane (◊), pure argon (Δ), pure isobutane (○), and diluted isobutane reagent gas (●) of (**a**) TNT molecular ion $M^{-\bullet}$, and (**b**) RDX total ion chromatogram. Individual run results with pure isobutane are noted with injection order. Statistical results with all other reagent gases and mixtures are shown with standard deviation error bars

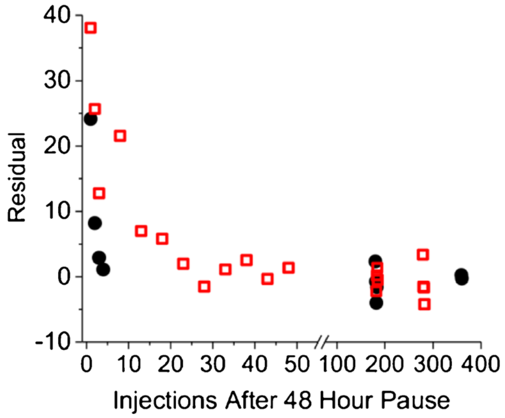

Figure 2. Residual plot of TNT total ion chromatogram EC-NCI signal relative to mean using 1% i-C_4H_{10}/Ar as reagent gas, following 48 h-long pauses in the consecutive run sequence after 500 runs (●), and after 3400 runs (□)

Realistically, experiments are often separated by more significant periods of instrument idleness such as nights and weekends. To test the effects of prolonged inactivity, the run sequence was paused twice in the total sequence for 48 h each. The 1% i-C_4H_{10}/Ar reagent gas was supplied throughout inactive periods. When injections resumed, successive analyte signals produced a similar pattern to the first operation of a new filament. Initial signal abundance was much larger than previous analyses but regressed to a lower stabilized mean value (Figure 2). With 500 total runs already performed before the interruption, early in the filament operative lifetime, two runs were required for signal to return to a stabilized mean with 2.9% RSD. After a cumulative 3400 runs and another 48 h pause, 20 runs had to be performed before acquiring an analytical series with 3.3% RSD.

The ion source was inspected after over 3500 runs in 1% i-C_4H_{10}/Ar had been performed without filament failure. The stainless steel surface around the electron-admitting orifice was covered with ion burn, typical of use with any organic reagent gas. Although the filament assembly reflector plate was blackened from carbon buildup, the electron filament itself was notably straight (Figure 3a). The persistent straightness of the filament used in 1% i-C_4H_{10}/Ar suggested that it had a significant remaining operative lifetime under the present conditions. Considering that the filament energy was increased for the present studies, the filament can be expected to serve for longer when using lower default settings. Ion burn and carbon buildup in the source might sooner degrade performance over the long run, although no such performance effects were observed in the sequence of 3500 runs. Carbonization would also proceed more slowly with the default, lower filament energy.

As a final test of robustness, the filament used with 1% i-C_4H_{10}/Ar was reinstalled in the instrument after 3 wk at atmospheric pressure in a covered box. Ion burn around the electron-admitting orifice was cleaned according to standard procedures, but the filament reflector and assembly were not cleaned or altered. Performing further EC-NCI analyses of TNT with 1% i-C_4H_{10}/Ar, observed analyte signal returned to a reproducible mean level.

After the successful demonstration of extended filament operation with 1% i-C_4H_{10}/Ar, isobutane concentration was increased to further tax the ion source. A new filament was tested with positive CI analyses of nicotine using 10% i-C_4H_{10}/Ar. Like EC-NCI experiments, analyte signal stabilized after filament conditioning on the first day. Unlike EC-NCI experiments, the stabilized positive CI signal mean was approximately equal to the very first run. Nicotine total ion chromatogram signal abundance had up to 6.7% RSD over 160 h of uninterrupted operation. Power to the filament was cycled 3500 times (478 h of runs, 233 h with the filament powered) in total without filament failure.

The consecutive run cycle with 10% i-C_4H_{10}/Ar was also paused twice in the total sequence for 48 h each with reagent gas supplied during inactivity. The first runs after the pause produced lower analyte signal than before the interruption, but signal reverted upward to the stabilized mean value (Figure 4). Early in the filament operative lifetime at 300 total runs, approximately 30 runs were required for signal to return to a stabilized mean with 3.3% RSD. After a cumulative 2400 runs and

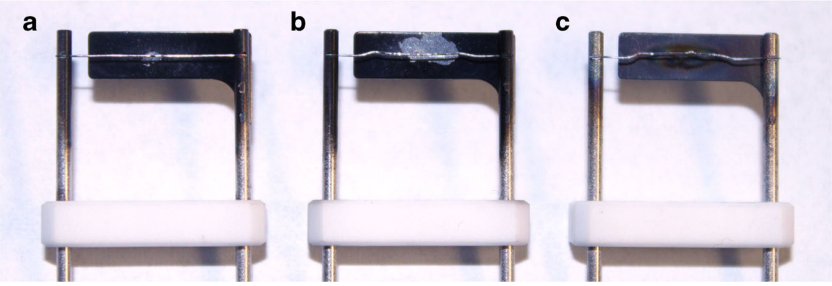

Figure 3. Electron filament and reflector plate assemblies (**a**) after 3500 power cycles in 1% i-C_4H_{10}/Ar, (**b**) after 3500 power cycles in 10% i-C_4H_{10}/Ar, and (**c**) after less than 50 power cycles in pure isobutane

another 48 h pause, less than 10 runs had to be performed before acquiring an analytical series with 6.3% RSD. The higher isobutane content conditioned the filament more rapidly and minimized recovery time after inactivity. Similar to runs in 1% i-C_4H_{10}/Ar, analyte signal was unchanged by brief pauses lasting less than 8 h.

The ion source was likewise inspected after 3500 runs in 10% i-C_4H_{10}/Ar had been performed without filament failure. The ion burn on the filament assembly reflector plate and the surfaces around the electron orifice was moderately more extensive than observed after an equal number of runs in 1% i-C_4H_{10}/Ar. Power-cycling in 10% i-C_4H_{10}/Ar left the filament somewhat warped (Figure 3b). In comparison, thousands fewer runs in pure isobutane caused a filament to be more misshapen (Figure 3c). In keeping with observations of analyte signal performance, filament condition was directly dependent on isobutane concentration in the bath gas.

Conclusions

Dilution of isobutane in argon for use as reagent gas causes the ion source to be fouled at no greater rate than methane without sacrificing analyte signal performance. Using 10% i-C_4H_{10}/Ar for positive CI produces equal signal to pure isobutane. EC-NCI analysis with 1% i-C_4H_{10}/Ar yields abundant, highly-reproducible analyte signal, unlike the unstable results from pure isobutane. The ratio of positive isobutane reagent ions and fragmentation of analyte ions is largely unchanged by moderate dilution in argon buffer gas, suggesting a weak spectral dependence on pressure. Positive CI experiments performed with 10% i-C_4H_{10}/Ar could be more accurately repeated using different instrumentation than experiments with pure isobutane.

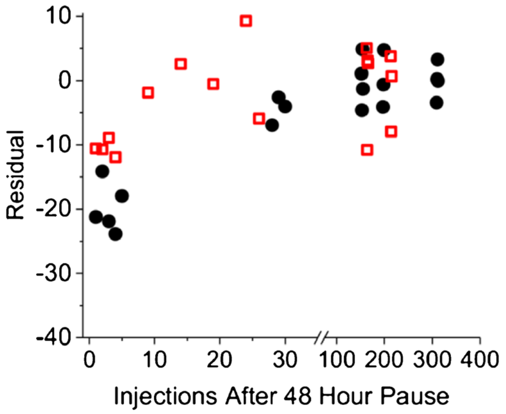

Figure 4. Residual plot of nicotine total ion chromatogram CI signal relative to mean using 10% i-C_4H_{10}/Ar as reagent gas, following 48 h-long pauses in the consecutive run sequence after 300 runs (●), and after 2400 runs (□)

By using dilute isobutane in argon as a reagent gas in place of methane, positive CI and EC-NCI-MS results can be significantly improved with virtually no additional operational costs. Practical use of isobutane for quantitative CI necessitates fronting analyses with blank runs to power-cycle and condition a filament that has been newly installed or inactive for a significant period of time. Such conditioning is also a requirement of analysis with methane CI. Isobutane and argon supply gas costs are also comparable to methane, and custom mixtures are readily obtained from compressed gas vendors. Commercial instrumentation auto-tune sequences are programmed for methane, but optimization of reagent gas pressure for i-C_4H_{10}/Ar is no more complex than tuning any other ion source parameter. Many laboratories are modifying routine GC-MS methods to use hydrogen as a carrier gas in place of standard but increasingly expensive helium. Dilute isobutane CI methods can similarly replace inferior but prevalent methane CI methods for GC-MS analysis.

Acknowledgments

The authors thank Bob Bolander of Agilent Technologies and Alfred Yergey of the National Institutes of Health for advice about chemical ionization; Adam L. Lubrano of Nova Research, Inc. for assistance troubleshooting the GC-MS; and Kevin J. Johnson of the U.S. Naval Research Laboratory for loaning equipment.

The authors acknowledge the U.S. Department of Homeland Security, Science and Technology Directorate, Homeland Security Advanced Research Projects Agency, Explosives Division, for funding this research.

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