
Simultaneous Analysis of Butene Isomer Mixtures Using Process Mass Spectrometry

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The feasibility of simultaneous analysis of mixtures containing two to four butene isomers and up to six total components using process mass spectrometry is assessed. As for typical (nonisomeric) applications of process mass spectrometry, simultaneous analysis is based on the assumption that the electron ionization mass spectra of mixtures are linear combinations of the spectra of the individual constituents. Limits of detection for binary isomer mixtures are on the order of 0.1% to 10%, limited by the ability to distinguish small differences between similar spectra. As spectral and mixture complexity increase, both accuracy and precision decrease. Not surprisingly the similarity of the spectra of stereoisomers *cis*- and *trans*-2-butene is greater than that of the other (nonstereoisomeric) isomer pairs, and mixtures containing both *cis*- and *trans*-2-butene are the most difficult to quantitate. However, even for mixtures of all four butenes, accuracy (root-mean-square error = 2.43%), precision (average coefficient of variation = 6.72%), and linearity (correlation coefficient of a plot of measured versus actual concentration $r^2 = 0.985 \pm 0.002$) are reasonably good. (J Am Soc Mass Spectrom 2000, 11, 1079–1085) © 2000 American Society for Mass Spectrometry

Effective industrial process control often requires current, reliable reaction data from sensors monitoring the process in real time [1]. Chemical information from process *analyzers* can be particularly useful for increasing overall reaction yield, product quality, and/or process safety through better reaction control [2]. Where applicable, process mass spectrometry is attractive for providing such information due to its fast analysis speed, compound selectivity, wide dynamic range, and multistream monitoring capabilities [3, 4]. Process mass spectrometers are used for simultaneous analysis in a wide variety of industrial applications, such as environmental air quality assessment and chemical vapor deposition monitoring [1, 3].

Simultaneous quantitation involves treating mixture mass spectra as linear combinations of the characteristic spectra of the contributing pure components:

$$[U] = [R] \times [S] \times [C] \quad (1)$$

where $[U]$ represents the spectrum of an unknown mixture (a $1 \times m$ matrix; m = the number of peaks in the spectrum); $[R]$ represents the pure component ref-

erence spectra (an $n \times m$ matrix; n = the number of components); $[S]$ represents the relative sensitivities (an $n \times n$ diagonal matrix); and $[C]$ represents the desired concentrations (an $n \times 1$ matrix). In practice, $[R]$ is determined from measured spectra of pure (single) components; $[S]$ is determined using the spectrum $[U]_{\text{std}}$ of a calibration mixture of known composition $[C]_{\text{std}}$; and then these are used to determine $[C]_{\text{unk}}$ from measured spectra $[U]_{\text{unk}}$ using simple linear algebra and least-squares routines. All spectra are usually normalized to reduce effects of drift in absolute intensities (e.g., due to filament wander or aging). As a result, only relative concentrations (% composition rather than absolute pressures) are derived.

Typical applications often involve mixture components with "unique peaks" (peaks in the mixture spectrum with contributions from only one component). However, recent studies in our laboratory [5–8] have established that the high precision of process mass spectrometric intensity measurements can enable distinction of even the minor differences in relative ion intensities in the mass spectra of *isomers*, providing a basis for simultaneous quantitation without resorting to tandem mass spectrometry (as, for example, in [9–15]) or derivatization (as, for example, in [16]). Our earlier studies addressed several simple binary mixtures of isomers. This study aims to assess the feasibility of simultaneous process mass spectrometric quantitation

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of more complex mixtures, including up to four butene isomers and a total of six components. The utility of a spectral similarity index [17] as a predictor of analysis feasibility is also addressed.

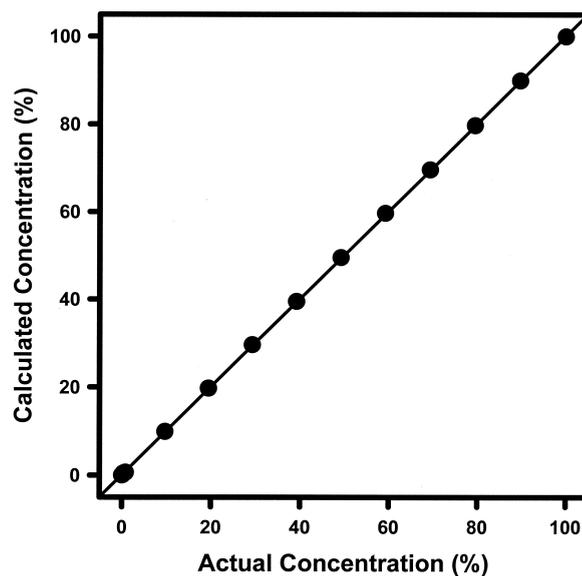
Experimental

Mixtures were prepared on-line using mass flow controllers with 2 μm filters (Brooks Instruments, Hatfield, PA). Samples were prepared from CP grade gases (Matheson Gas Products, Morrow, GA). Gases flowed from the mass flow controllers through 1/8 in. stainless steel tubing into a stainless steel mixing chamber providing up to seven gas inlets and one outlet. The total sample flow to the process mass spectrometer was 30 standard cubic centimeters per minute (SCCM), comprised of 20 SCCM (total) of analyte gas and 10 SCCM of He sweep gas. From the outlet of the mixer the sample flowed through 1/8 in. stainless steel tubing to an ABB-Extrel (Pittsburgh, PA) Questor IV quadrupole mass spectrometer. The spectrometer's "quick inlet" is a "T" splitter which in this case directed $\sim 0.04\%$ of the gas through a 25 μm i.d. silica capillary (Polymicro, Phoenix, AZ) directly into the electron ionization (100 eV) ion source. The balance of the gas mixture was directed to a waste vent. All ion signals comprising $>2\%$ relative abundance in full scan reference spectra were monitored in the selected ion monitoring mode (300 ms dwell time for each ion in each cycle) using a Faraday cup detector for optimum precision. This entailed 33 ions ($m = 33$ for eq 1) for six-component mixtures and 19 ions for all others except the binary methane/ethane mixtures (for which $m = 6$). Ten full cycles were averaged for each final spectrum.

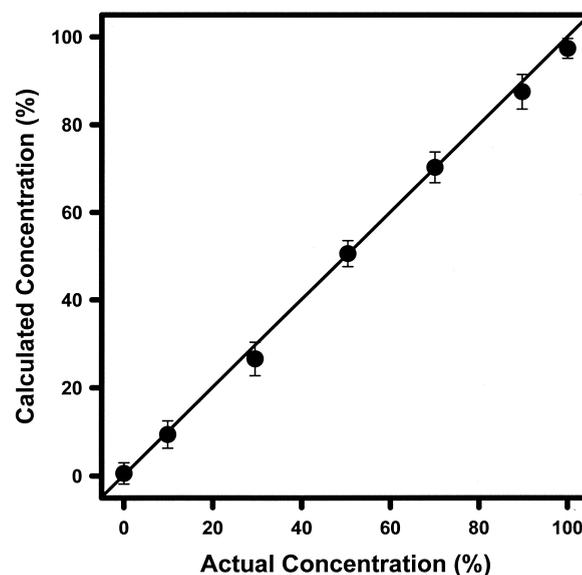
Relative sensitivities ($[S]$ in eq 1) were assessed for each system using the mass spectrum of a calibration mixture with composition approximating the average of a given set of test mixtures. Experimental concentration estimates were obtained from mixture spectra using least-squares routines incorporated into the Questor IV data system or the MATLAB software package (The Mathworks, Natick, MA). One measurement of each mixture comprised a set, and each set was measured three times. The sequence of mixtures within each set was randomized to minimize the effects of any systematic drift. Points plotted represent the mean of the triplicate measurements, and error bars represent \pm one standard deviation ($\pm\sigma$).

Results and Discussion

Figure 1a is a typical "validation plot" of calculated (c_{calc}) versus actual (\hat{c}) concentration for 11 test mixtures of 1-butene in isobutene with concentrations ranging from 10% to 90%. The ideal theoretical line ($c_{\text{calc}} = \hat{c}$) is also plotted. The calibration mixture for determination of $[S]$ was comprised of 50.83% isobutene and 49.17% 1-butene. Three figures of merit can be used to assess the quantitative performance achieved. Analysis



A



B

Figure 1. "Validation plots" for analysis of (a) 1-butene in isobutene and (b) *trans*-2-butene in *cis*-2-butene.

accuracy can be evaluated as the root-mean-square error (ϵ , summed over triplicate tests of N samples each containing n analytes):

$$\epsilon = \sqrt{\frac{\sum (c_{\text{calc}} - \hat{c})^2}{n \times N \times 3}} \quad (2)$$

Averaging the coefficient of variation (%RSD) for triplicate analyses of each component in each test sample provides a measure of precision (\overline{CV}), and linearity can be estimated from the correlation coefficient (r^2) for the validation plot. The data of Figure 1a represent excellent performance based on all three figures of merit: $\epsilon = 0.15$; $\overline{CV} = 0.14$ (error bars are smaller than the points

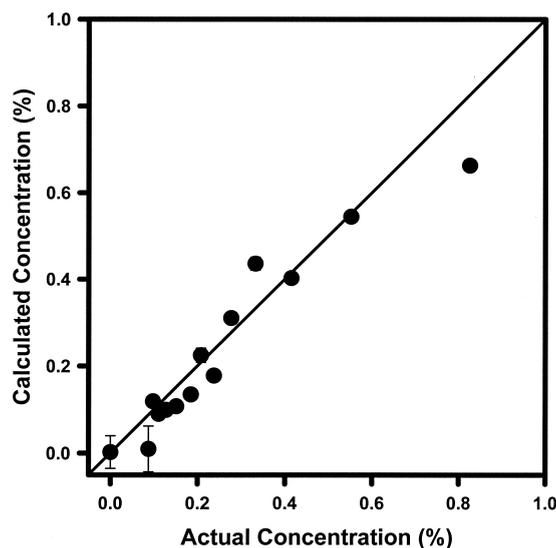


Figure 2. Validation plot for the mixture of Figure 1a, near the limit of detection.

on the curve), and $r^2 = 0.99998 \pm 0.00001$ (\pm based on the standard deviation of r^2 measurements derived from treating the triplicate data sets separately).

Another important figure of merit is the limit of detection (LOD). Figure 2 shows the performance for this system in the region of the LOD (0.087% to 0.90%; calibration at 0.21% 1-butene). As expected, performance is compromised relative to higher concentrations ($\epsilon = 0.23$; $\overline{CV} = 19.14$; $r^2 = 0.80 \pm 0.01$). Much of the error stems from the lowest nonblank point (0.087%), which is below the apparent LOD [average blank plus three times the standard deviation of the blank (100% isobutene) = $0.0027 + 3 \times 0.0375 = 0.12\%$]. Excluding this point, ϵ and \overline{CV} fall to 0.06 and 1.81, respectively, whereas r^2 increases to 0.914 ± 0.008 . Still, the error bars for several points in Figure 2 do not cross the theoretical line, even though the length of the bars is approximately what would be expected from the flow controller specifications (e.g., ± 0.03 absolute for the

lowest point). Further study will be needed to characterize the small apparent systematic errors.

LOD's for the other binary isomer mixtures (Table 1) are considerably higher than that for the mixture without a stereoisomer, reflecting the poorer accuracy and precision that result when the *cis* or *trans* isomer is present. Even the 0.12% LOD is significantly higher than the ppm LOD often cited for process mass spectrometry [18] (e.g., the 10 ppm LOD for ethane in methane; included for comparison in Table 1) because the limiting factors are quite different. The usual expedient of employing an electron multiplier to extend the dynamic range downward by improving sensitivity to ions of low abundance will not work with isomeric mixtures, for which it is necessary to measure small differences in ion signals rather than measuring signals of low intensity.

Because the simultaneous analysis of isomers relies on measurements of small spectral differences, the question arises: how small can spectral differences be before quantitation becomes impossible? Another context in which spectral differences are important is in the matching of unknown and library spectra to confirm compound identification. In an earlier study of parametrization (variable selection) for optimum simultaneous analysis [8], we used the similarity index of Lay et al. [19] (eq 3) to assess the "dissimilarity" of various spectral subsets, in an effort to identify the portion of a mass spectrum best able to distinguish between compounds with similar spectra:

$$SI = \sqrt{\frac{\sum_{m/z} \left(\frac{i - i_0}{i_0} \times 100 \right)^2}{P}} \quad (3)$$

where i and i_0 represent the intensities at a given m/z in two spectra being compared (i_0 is the smaller intensity), and P is the number of different m/z 's being considered. When the spectra are identical, $SI = 0$, confirming a spectral match (the purpose for which the SI was

Table 1. Figures of merit and similarity indices^a for simultaneous analysis of binary mixtures of butene isomers

| Compounds tested (number of mixtures) | Similarity index ^a | RMS error ^b (%) | Correlation coefficient ^c | \overline{CV} ^d (%) | LOD ^e (%) |
|--|----------------------------------|-------------------------------|---|-------------------------------------|-------------------------|
| <i>Trans</i> -2-butene/ <i>cis</i> -2-butene (7) | 0.99926 \pm 0.00007 | 2.06 | 0.997 \pm 0.002 | 7.10 | 7.35 |
| <i>Cis</i> -2-butene/1-butene (11) | 0.9957 \pm 0.0001 | 2.59 | 0.995 \pm 0.004 | 7.27 | 6.04 |
| <i>Trans</i> -2-butene/1-butene (11) | 0.99469 \pm 0.00002 | 2.87 | 0.992 \pm 0.008 | 9.61 | 8.88 |
| Isobutene/ <i>cis</i> -2-butene (11) | 0.9823 \pm 0.0002 | 1.44 | 0.998 \pm 0.003 | 3.93 | 2.18 |
| Isobutene/ <i>trans</i> -2-butene (11) | 0.9796 \pm 0.0001 | 1.75 | 0.997 \pm 0.004 | 5.24 | 4.85 |
| Isobutene/1-butene (11) | 0.96846 \pm 0.00005 | 0.15 | 0.99998 \pm 0.00001 | 0.14 | 0.12 |
| Methane/ethane (11) | 0.0420 \pm 0.0002 | 0.41 | 0.9998 \pm 0.0002 | 0.82 | 0.001 |

^aSI from eq 3.

^b ϵ from eq 2.

^c r^2 for validation plot analogous to Figure 1.

^dAverage coefficient of variation (%RSD) from triplicate analyses of both components in all test samples.

^eLimit of detection for the second listed component (mean blank + $3\sigma_{\text{blank}}$). The "blank" is the calculated concentration of component 2 in pure component 1.

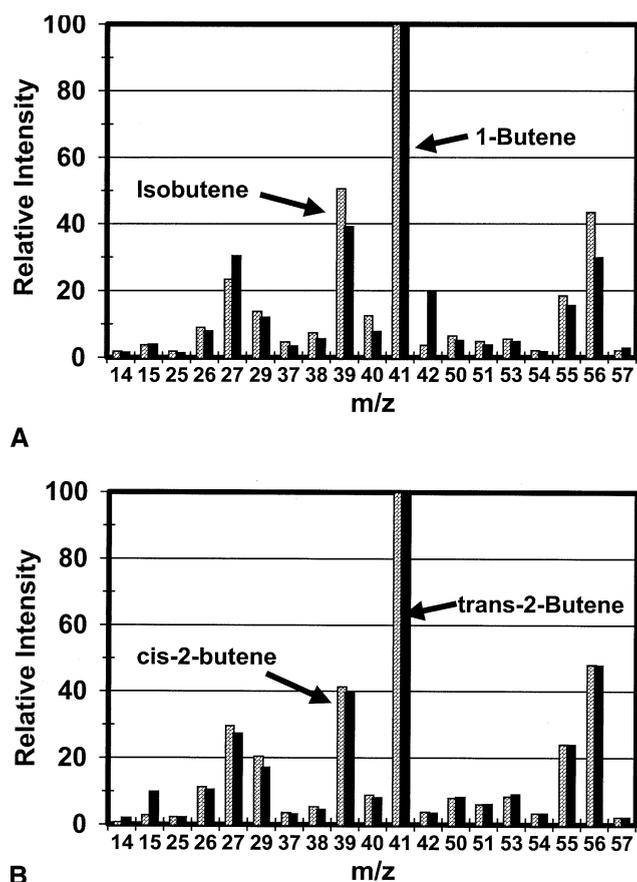


Figure 3. Comparison of partial pure component spectra for (a) isobutene and 1-butene; and (b) *cis*-2-butene and *trans*-2-butene.

originally developed). For parametrization (or distinction), a high value of SI (indicating significant differences between reference spectra) is desirable. The Lay SI has the drawback that the relative contribution from ions of low intensity can become disproportionately large [as $i_0 \rightarrow 0$, the ratio $(i - i_0)/i_0$ may be large, even if the difference is small]. To avoid this, we have turned to the similarity index of Stein [17] (eq 4, adapted from [17]):

$$SI = \frac{(\sum_{m/z} I_x^{0.5} I_y^{0.5})^2}{\sum_{m/z} I_x \sum_{m/z} I_y} \quad (4)$$

This index is based on relative intensities (I , generally normalized so that $I_{\max} = 100$ in a given spectrum) in the reference (x) and test (y) spectra. Contributions are included for all m/z at which there is significant intensity. A perfect match gives a "similarity index" (SI) of exactly 1; otherwise, $SI < 1$. Table 1 includes the SI for pairwise comparison of each of the butene spectra of Figure 3, along with figures of merit for corresponding validation plots analogous to Figure 1. The nonisomeric pair methane and ethane is included, representing hydrocarbon gases with significantly different pure

component spectra. Although a perfect match ($SI = 1$) must preclude quantitation, the correlation between SI and the figures of merit is only fair. Even for the case where the SI is largest (0.99926 ± 0.00007 for the stereoisomers *cis*-2-butene and *trans*-2-butene; Figure 1b) the quantitation figures of merit are reasonable although significantly poorer than for the smallest SI case. Among the isomeric pairs, the three mixtures containing isobutene have the smallest SI's, consistent with the distinct (nonlinear) connectivity among the four carbon atoms in this molecule. As a group, these three also have the best figures of merit, and among them, the isobutene/1-butene system stands out; this is the only case involving neither stereoisomer. The analytical performance for the nonisomeric pair of methane and ethane is not significantly better than the butene mixtures except for the LOD, which is much lower. In this case, the presence of "unique" ions for ethane reduces the LOD challenge to the "normal" regime of detecting small signals, rather than small differences in large signals.

Few "real world" industrial processes involve only two components. Moving toward higher complexity, results for the four possible ternary butene mixtures are summarized in Table 2. The LOD is not included here because in general it can be expected to depend on the overall composition of the mixture (e.g., in a ternary mixture, the LOD for each component will depend on the ratio between the other two). Given the reasonable correlation between the LOD and CV in Table 1, these values can be taken as a rough indication of the expected LOD's. Although the similarity index cannot be readily extended to mixtures with more than two components, it can be seen in Table 2 that there is a reasonable inverse relationship between the figures of merit and SI_{\max} , the largest of the three pairwise SI's for the three components involved in each system. Note that the precision is relatively low in both ternary systems where both *cis*- and *trans*-2-butene are present. Analysis accuracy is also reduced in these cases. In particular, a systematic error is evident in Figure 4; all *cis*-2-butene concentrations are overestimated and all *trans*-2-butene concentrations are underestimated. This may be a calibration error; the test concentrations are generally above and below, respectively, the corresponding calibration concentrations (38.45% *cis*-2-butene, 38.24% isobutene, and 23.31% *trans*-2-butene). The strong similarity of the *cis*- and *trans*-2-butene spectra apparently make these components vulnerable to offsetting errors, leaving the third component unaffected.

Also included in Table 2 are data for simultaneous analysis of all four butenes (Figure 5). Remarkably, the figures of merit are not seriously compromised; in fact, performance is at least nominally *better* than for two of the ternary mixtures! Rather than an intrinsic "improvement," the differences are suggestive of *day-to-day* variability. This was assessed by repeating the entire four-component experiment on a second day, on which

Table 2. Figures of merit and similarity indices^a for simultaneous analysis of mixtures containing multiple butene isomers

| Compounds tested (number of mixtures) | Similarity index ^a | RMS error ^b | Correlation coefficient ^c | \overline{CV} ^d |
|---|----------------------------------|--|---|---|
| <i>Cis</i> -2-butene, <i>trans</i> -2-butene, isobutene (4) | 0.99926 ± 0.00007 | 7.35 (8.85, 9.09, 1.00) | 0.963 ± 0.036 | 17.65 (13.57, 38.68, 0.69) |
| <i>Cis</i> -2-butene, <i>trans</i> -2-butene, 1-butene (4) | 0.99926 ± 0.00007 | 2.70 (3.58, 2.52, 1.65) | 0.991 ± 0.009 | 11.95 (24.54, 5.16, 6.13) |
| <i>Cis</i> -2-butene, isobutene, 1-butene (4) | 0.9953 ± 0.0001 | 0.81 (1.02, 0.58, 0.76) | 0.998 ± 0.002 | 1.70 (1.63, 2.32, 1.17) |
| <i>Trans</i> -2-butene, isobutene, 1-butene (4) | 0.99469 ± 0.00002 | 2.96 (3.26, 0.88, 3.87) | 0.982 ± 0.029 | 8.69 (9.04, 3.72, 13.30) |
| <i>Cis</i> -2-butene, <i>trans</i> -2-butene, isobutene, 1-butene (4) | 0.99926 ± 0.00007 | 2.43 (2.48, 2.81, 2.38, 1.94) | 0.985 ± 0.002 | 6.72 (9.64, 6.94, 5.50, 4.81) |
| Isobutene, 1-butene, methane, ethane, propane, propene (8) | 0.96846 ± 0.00005 | 0.7 (1.15, 0.81, 0.46, 0.62, 0.37, 0.42) | 0.992 ± 0.005 | 2.28 (1.91, 5.57, 1.47, 2.23, 0.76, 1.72) |
| <i>Cis</i> -2-butene, <i>trans</i> -2-butene, 1-butene, ethane, propane, propene (8) | 0.99926 ± 0.00007 | 3.17 (5.37, 4.97, 2.43, 0.38, 0.54, 0.77) | 0.937 ± 0.008 | 5.79 (22.57, 3.02, 6.10, 0.88, 1.19, 0.98) |

^aThe largest similarity index (eq 3) for pairwise comparisons (SI_{\max}) of the components listed in column 1.

^b ϵ from eq 2. Parenthetical values are for individual components, in the order listed in column 1.

^c r^2 for validation plot analogous to Figure 1.

^dAverage coefficient of variation (%RSD) from triplicate analyses of all components in all test samples. Parenthetical values are for individual components, in the order listed in column 1.

accuracy ($\epsilon = 3.21$) and linearity ($r^2 = 0.983 \pm 0.003$) were slightly poorer, even though precision ($\overline{CV} = 4.34$) improved slightly. Thus, somewhat surprisingly, incorporation of the fourth isomer does not appear to significantly compromise the analysis.

Can the performance of isomer quantitation be maintained in the presence of other components? Two six-component systems were investigated to address this point. In the first, methane, ethane, propane, and propene were added to the most easily quantitated binary butene mixture (1-butene/isobutene). The performance was compromised, but still quite comparable to that of the other binary mixtures (compare data in Tables 1 and 2). Similarly, addition of ethane, propane, and propene to ternary mixtures of *cis*-2-butene, *trans*-2-butene, and 1-butene (Figure 6) lowered the figures of merit (included in

Table 2), but gave performance that would still be adequate for many applications.

Conclusions

These studies leave no doubt that accurate and precise simultaneous analysis of complex mixtures of isomers is feasible. Although the number of components in a stream influences analysis accuracy and precision, the effects of component similarity are more important; in this instance, performance was generally compromised when both stereoisomers were present. The Stein SI [17] provides a qualitative but imperfect indicator of performance. When the SI falls below about 0.97, limits of detection below 1% can be achieved, but LOD's for isomer mixtures remain orders of magnitude higher

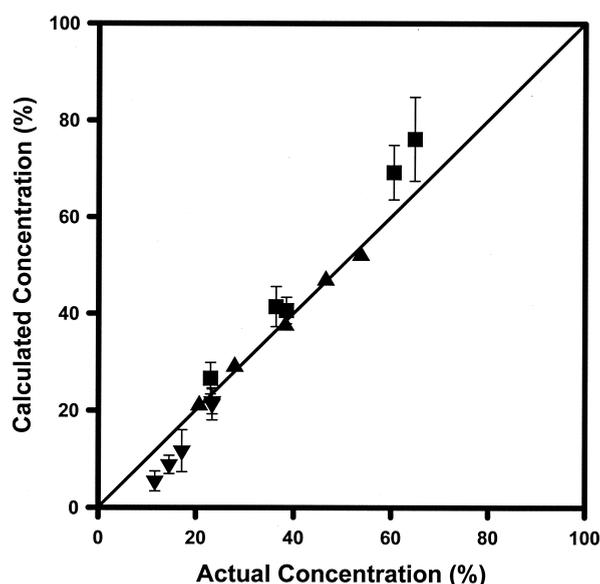


Figure 4. Validation plot for analysis of *cis*-2-butene (filled square), *trans*-2-butene (filled inverted triangle), and isobutene (filled triangle).

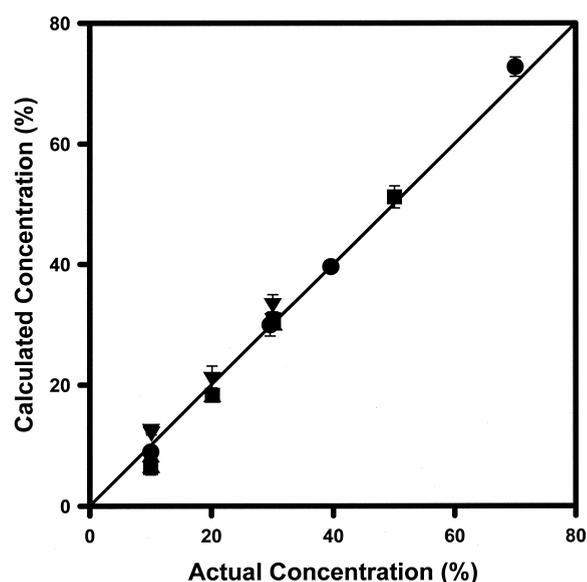


Figure 5. Validation plot for analysis of *cis*-2-butene (filled square), *trans*-2-butene (filled inverted triangle), isobutene (filled triangle), and 1-butene (filled circle).

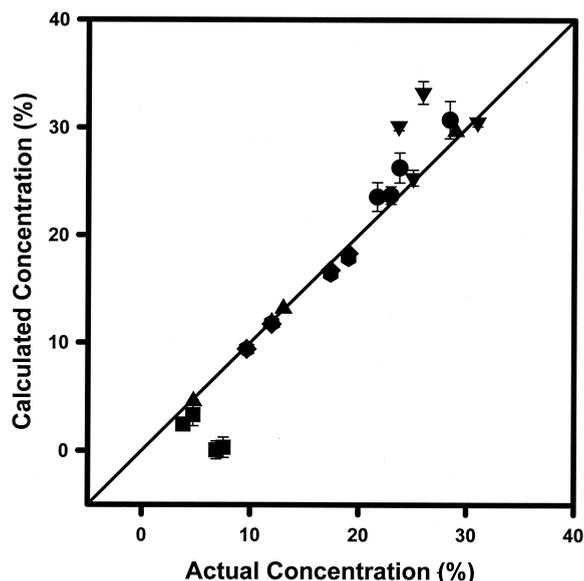


Figure 6. Validation plot for analysis of *cis*-2-butene (filled square), *trans*-2-butene (filled inverted triangle), 1-butene (filled circle), propane (filled diamond), ethane (filled triangle), and propene (filled hexagon).

than those usually cited for nonisomeric systems. This derives from a fundamental limitation to the precision with which small differences can be measured, and seems unlikely to be overcome. However, from other studies [8] we know that parametrization can critically affect quantitation accuracy and precision; we are assessing whether judicious parametrization can extend the dynamic range downward in the systems studied here. These findings should facilitate extending the use of process mass spectrometry to a wider range of time-critical applications.

Finally, it should be noted that impurities can have a large influence on simultaneous analyses. Although unexpected components may be less common in process applications than in other analyses, they may have a particularly strong effect on simultaneous *isomer* analyses, because the reliance on small spectral differences is so great. If an unexpected component contributes significantly to the signals monitored, it can be expected to inflate the estimated concentration(s) of the modeled component(s) with the highest weighted reference spectrum intensity at the conflicting m/z 's. Clearly, the magnitude of the interference will depend on the parametrization; interference can often be avoided by avoiding conflicting m/z 's. In any case, when unexpected (and unmodeled) contaminants do affect quantitation, they will almost certainly increase the residuals (the difference between the measured spectrum and that predicted by eq 1). Thus, monitoring the residuals can provide an operator with an important indication of the presence of an unexpected contaminant.

Acknowledgments

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