

# Model for the Estimation of Electron Impact Gas Chromatography/Mass Spectrometry Response Factors for Quadrupole Mass Spectrometers

A. D. Sauter\* and J. J. Downs

A. D. Sauter Consulting, 2356 Aqua Vista, Henderson, Nevada 89015

J. D. Buchner, N. T. Ringo, D. L. Shaw, and J. G. Dulak

Extrel, Inc., P.O. Box 11512, Pittsburgh, Pennsylvania 15238

**A simple method for the estimation of electron impact GC/MS response factors (RF) is presented. Intralaboratory estimated/observed RF values for polynuclear aromatic hydrocarbons, chlorinated priority pollutants, and polychlorinated biphenyls were found at  $1.03 \pm 0.171$ ,  $1.02 \pm 0.180$ , and  $1.05 \pm 0.088$ . The utility of the model to yield response factor estimates for compounds for which standards are not available or for "unknowns" is asserted in a proper quality control context. The powers and limitations of the model are considered, and the utility of the model in the quality assurance and quality control of "laboratory" functions is discussed. The extension of the model to other chromatographic MS or MS/MS based instrumental analytical techniques is also proposed.**

Internal standard (IS) based quantification is the principal strategy employed for the quantification of organic compounds by electron impact (EI) GC/MS in U.S. EPA programs related to the characterization of hazardous wastes (1) and hazardous waste sites (2). Even the isotopic dilution (ID) based quantification GC/MS methods employed for the characterization of industrial effluents and other environmental samples (3) currently require IS based quantification for the analysis of compounds for which labeled standards are not available. IS based quantification will probably always be utilized in certain environmental measurements for practical and other reasons. For example, ID based quantification of the 209 PCB congeners is, of course, precluded by the nonavailability of standards and by the fact that all congeners cannot be completely chromatographically and mass resolved using fused silica capillary column (FSCC) GC/MS (4). Similarly, these problems hinder IS based quantification because the determination of the response factors in the standardization process is precluded for technical or practical reasons. A similar dilemma exists for thorough characterization of samples containing mixtures of dibenzodioxins, dibenzofurans, and other analytes for which the response factor has not been determined (i.e., "nontargeted" analytes). The latter category of analytes has been shown by Shackelford in a national GC/MS study to represent the major fraction of analytes identified as pollutants of industrial origin (5).

Currently, crude approaches are employed to quantitate "nontargeted" analytes. For example, in U.S. EPA's Superfund program when "nontargeted" analytes are identified, a response factor (RF) value of 1.00 is assumed for subsequent IS based quantification using total ion current ratios (2). This procedure presumes incorrectly that the ionization cross section of the "nontargeted" analyte and internal standard is the same. Moreover, when peaks are eluted that are not chromatographically resolved, this assumption can result in sample-dependent, quantitative errors of unknown magnitude.

Examination of previously published RF values (6, 7) demonstrates that RF values for extractable priority pollutants have a range of approximately 20, and therefore, if the assumption were applied to the more traditional response factors, which are based on the ion current generated at given  $m/z$  values, large quantitative errors would result. Therefore, a formalism that could provide a procedure to estimate RF values for "non-targeted" organic compounds identified in extracts of samples would be of considerable utility for the quantification of organic compounds identified at hazardous waste sites, in hazardous wastes, and in other areas of applied GC/MS.

The U.S. EPA currently utilizes RF value monitoring as important quality assurance/quality control (QA/QC) criteria in the Superfund program, and it is currently compiling a data base of response factors (2). The establishment of a reference set of RF values for organic compounds measured by EI GC/MS would be of significant utility in the quality control/quality assurance of inter- and intralaboratory multianalyte GC/MS based methods commonly used in environmental programs. Just as libraries of reference mass spectra facilitate qualitative processes in applied GC/MS, a reference set of RF values could be utilized to facilitate the verification of the quantitative standardization process and other routine analytical functions performed in such work. Previously we have demonstrated the utility of RF values in the monitoring and in the troubleshooting of inter- and intralaboratory multianalyte quantitative GC/MS data (8). At that time we demonstrated the need to encode first pass data review because of the massive volume of data generated in laboratories that utilize the U.S. EPA's EI GC/MS based methods. Clearly, data review that is not performed in near "real time" can result in error propagation into subsequent analyses. As RF values encode the multilevel multianalyte standardization process, the establishment of a "correct" set of EI GC/MS RF values and related statistics could be utilized to facilitate the verification of the complex GC/MS standardization process. Hence, a reference set of RF values could be of utility in the data review of the previously referenced programs and in related applications of U.S. EPA's GC/MS Methods 624, 625, 1624, and 1625. Furthermore, such information could be utilized to great advantage in the design of expert systems (9).

A model to provide analytically useful estimates of EI GC/MS RF values has significant technical and practical benefits in applied GC/MS. However, the realization of such a model presents a number of technical difficulties such as sample introduction, analyte ionization, ion transmission, ion detection, and other phenomena which are complex. Moreover, the segregation of the sources of errors from theoretical considerations, from the temporal condition of the "system", and from common laboratory operations in multianalyte quantitative GC/MS is difficult. Therefore, technical and

other factors complicate the attainment of a "true" set of RF values. However, we have demonstrated that interlaboratory EI GC/MS RF values are "similar" in previous studies (10). Therefore, we have presumed that the development of a practically useful RF predictive model was feasible.

We derive below a simple model for the estimation of electron impact GC/MS response factors for quadrupole mass spectrometers. The simplifying assumptions employed in this work are considered. Estimated and observed values are given for polychlorinated biphenyls (PCB's), polynuclear aromatic hydrocarbons (PNA's), and chlorinated priority pollutants. The utilization of this model in environmental measurements is considered, and the extension of the model to other chromatographic MS and MS/MS configurations is discussed. Limitations on the application of the predictive scheme are also presented.

## EXPERIMENTAL SECTION

**Standards.** The analytical standards of priority pollutants employed in this work were purchased from Supelco, Inc., Bellefonte, PA. For this work, analytes were analyzed at nominal injected weight levels of 20, 40, 80, 100, and 160 ng/ $\mu$ L with internal standards at a constant 40 ng/ $\mu$ L. The ion abundance calibrant, decafluorotriphenylphosphine (DFTPP), was purchased from P.C.R., Inc., Gainesville, FL.

The PCB's employed in this work were also purchased from Supelco, Inc. RF values were determined from two sets of triplicate injections of the DCMA mixture using 40 ng/ $\mu$ L of the internal standards solution utilized in the priority pollutant experiments.

**Instrumentation.** The GC/MS data were acquired on an Extrel, Inc. (formerly Extranuclear Laboratories, Inc.), ELQ-400 quadrupole mass spectrometer equipped with a switchable EI/CI ion source and a Galileo Model 4770 continuous dynode electron multiplier with the conversion dynode maintained at -4.0 kV. The conditions for electron impact ionization were as follows: electron energy, 70 eV; emission current, 2.5 mA; source temperature, 275 °C. The mass range scanned was 41-450 amu at 750 amu/s.

Data acquisition and GC and MS control were performed with the Extrel Model 750 data system. This system uses a Motorola 68000 computer to acquire data and to control the GC/MS system. A DEC 11/73 host computer is utilized to perform data manipulation, enhancement, and archiving. An Amcodyne 50MB disk drive was employed for mass storage.

The Extrel Extract software was used to automatically detect compounds, perform integrations, and view spectra and chromatograms. Response factors and related statistics were output in standard EPA format. Also, all spectra and areas were manually verified.

The quadrupole mass spectrometer was mass calibrated by using perfluorotri-*n*-butylamine, PFTBA, and ion abundance calibration was performed in accordance with the specifications for DFTPP (2).

Gas chromatography was performed on a fused silica capillary column (DB-5, 30 m  $\times$  0.32 mm i.d.) purchased from J. & W. Scientific, Inc., Rancho Cordova, CA. The column was coupled directly to the ion source. A Varian 3400 gas chromatograph with Grob-type split/splitless injector under data system control was used to provide splitless injections. After 40 s the split valve was opened. The carrier gas was helium at a column head pressure of 18 psig. The split flow rate was approximately 30 mL/min, and the sweep exit was capped. The carrier gas linear velocity was 85 cm/s at 30 °C. For priority pollutants, the column temperature was held at 30 °C for 4 min and then ramped at 8 °C/min and maintained at 300 °C until all components had eluted. Total data acquisition time was approximately 45 min. For PCB's the GC conditions were the same except that the column temperature was increased at a rate of 16 °C/min with data acquisition time of approximately 25 min.

## RESULTS AND DISCUSSION

For primary species under constant source conditions, the total ion current ( $I_t$ ) obtained from the ionization of molecules by 70-eV electrons was described by Harrison as being directly

proportional to the ionization cross section ( $Q_i$ ) and a molar term (eq 1) (11). This effort noted regular increases in the

$$I_t \propto Q_i N_i \quad (1)$$

production of ion current for a variety of organic compounds as the ionization cross section was increased by, for example, a methylene group. While Harrison's work concluded that his results neither fit a simple additivity rule nor a simple correlation with molecular polarizability, it was noted that a modified additivity rule did correlate well within homologous series (e.g., between alkanes, alkenes, and ketones).

Based in part on this work, Fitch and Sauter derived equations for the estimation of relative ionization cross section after normalization and averaging interlaboratory cross section values relative to hexane for 179 compounds (12). Equation 2 was shown to give an average relative cross section error for the previously cited test set of 4.69%. In eq 2  $k$  is the re-

$$Q_{rel} = k + \sum_{i=1}^{10} a_i n_i \quad (2)$$

gression constant,  $a_i$  is the derived coefficient, and  $n_i$  is the number of atoms of a given type in the molecule of interest. Coefficients were derived for C, H, O, Cl, Br, I, F, N, D, and S. While the simple additivity approach can be susceptible to errors based, for example, on the tendency of molecules to undergo neutral dissociation, such errors were apparently not large in the subject test set. The response factor model presented herein presumes that eq 1 and 2 adequately describe the major fraction of ion current production by 70-eV electrons under the experimental conditions described above.

Dawson has described the transmission of quadrupole mass spectrometers in the analyzer-limited regime as an inverse power of resolution (13). Measurements made in this mode lead him to conclude that transmission was related to the inverse square of resolution rather than the anticipated first-order inverse dependence. In routine environmental applications of quadrupole mass spectrometry the transmission function is not determined explicitly. In addition, temporal phenomena such as analyzer cleanliness, alignment of rods and source, and other factors can cause departure from some theoretical, ideal dependence while the system remains in an analytically useful mode. Moreover, measurements made in this and other routine application of GC/MS in environmental programs employ the ion abundance calibrant, DFTPP. In order to meet the ion abundance criteria of this compound we have found it necessary on a number of quadrupole mass spectrometers to increase low-mass resolution and hence artificially suppress "low" mass transmission. Therefore, the transmission of quadrupoles tuned to DFTPP is unlikely to be identical to that described by Dawson where transmission was presumably maximized across the mass range of study. Hence, we describe the dependence of ion transmission as some inverse power of resolution:

$$\% T_{m/z} \propto 1/R^p \quad (3)$$

The resolution of a quadrupole mass spectrometer is dependent on the resolution constant ( $k$ ) and the square of the number of rf cycles ( $N$ ) that an ion experiences in transmission through the analyzer (14). The latter

$$R = m/\Delta m = k(N)^2 \quad (4)$$

is directly related to the length of the rods ( $l$ ), the radio frequency of the analyzer ( $f$ ), and the inverse velocity of the ion ( $v$ )

$$N = fl(1/v) \quad (5)$$

where the velocity is expressed in terms of the electronic

charge ( $e$ ) and the axial ion potential ( $V_z$ ) applied to the ion of mass  $m$  as follows:

$$v = (2eV_z/m)^{1/2} \quad (6)$$

Upon substitution, we derive the ion transmission equation given by

$$\% T_{m/z} \propto \frac{1}{\left(kf^2l^2\left(\frac{m}{2eV_z}\right)\right)^p} \quad (7)$$

A simple relative transmission equation ( $T_r$ ) for analyte  $x$  and internal standard is can be written (eq 8) with constants collected in  $K$ . The relative transmission of two ions then

$$T_r = \frac{\left(K\left(\frac{m_{is}}{V_{z_{is}}}\right)\right)^p}{\left(K\left(\frac{m_x}{V_{z_x}}\right)\right)^p} \quad (8)$$

reduces to a function of its mass, the axial ion potential, and the transmission exponent ( $p$ ).

The relative transmission term can be restated as

$$T_r = \left(\frac{V_x m_{is}}{V_{is} m_x}\right)^p \quad (9)$$

Note that when the masses of the analyte and internal standard ions are similar in systems with linearly driven axial ion drawout potential, the relative transmission term above will approximate unity for reasonable values of  $p$ . Also note that the offset voltages applied in quadrupole mass spectrometers are typically on the order of a few to 10 V. This fact and the fact that effective and applied voltages can differ due to a variety of temporal conditions of the system will probably always limit the accuracy of any RF estimation model as small changes in offset voltages can result in large percentage changes in ion velocity and hence ion transmission. Effects of this nature are inherent in the "slow ion" technology of quadrupole mass spectrometers. Study of eq 9 also demonstrates that the use of multiple internal standards not only helps in chromatographic aspects of GC/MS measurement (15) but also provides the important property of correcting for relative ion transmission.

The source-generated ion current ( $I_{m/z_s}$ ) is related to the total ion current ( $I_t$ ) via the fractional ion abundance ( $F_{m/z_s}$ )

$$I_{m/z_s} = F_{m/z_s} I_t \quad (10)$$

The detected ion current at value  $m/z$  ( $I_{m/z_d}$ ) is reduced by transmission

$$I_{m/z_d} = \% T_{m/z} G_{m/z} I_{m/z_s} \quad (11)$$

( $\% T_{m/z}$ ) and increased by the gain ( $G_{m/z}$ ). The ratio of detected ion current for analyte  $x$  and internal standard is is given as shown in eq 12. We assume that for primary species

$$\frac{I_{m/z_{dx}}}{I_{m/z_{dis}}} = \left(\frac{m_{is} V_x}{m_x V_{is}}\right)^p \frac{G_{m/z_x}}{G_{m/z_{is}}} \left(\frac{F_{m/z_{dx}}}{F_{m/z_{dis}}}\right) \frac{I_{t(dx)}}{I_{t(is)}} \quad (12)$$

acquired in the "DFTPP tune regime" the ratio of fractional ion abundances for analyte and internal standard in the source can be represented as the ratio of the detected  $F$  values. This approximation can be shown to be valid when analyte-internal standard pairs have virtually identical spectra, as would be the case for isomers (e.g., anthracene relative to phenanthrene), or when spectra are similar in pattern and fragment  $m/z$  values (e.g., pyrene relative to benz[a]anthracene). Addi-

tionally, when the ratio of  $F$  values is dominated by, for example, isotopic effects (e.g., hexachlorobenzene relative to phenanthrene- $d_{10}$ ), the ratio of source  $F$  values is presumed to be approximated by the ratio of detected  $F$  values.

Essentially, these three cases represent situations where relative fractional ion abundance values of analyte and internal standard are not strongly gain or transmission dependent. This simplification limits the model's applicability, where the above approximation is a priori expected to be invalid. Nevertheless, there are many analytes of environmental interest wherein the approximation is valid.

Using this assumption, we express the total ion current as a function of ionization cross section and a molar term where the former is estimated by the model of Fitch and Sauter. Eliminating the gain term (see below) and converting the molar term to weight/molecular weight ( $W/M$ ) with rearrangement yields the response factor estimation model (eq 13).

$$RF_{est} = \frac{I_{m/z(dx)} W_{is}}{I_{m/z(dis)} W_x} = \left(\frac{m_{is} V_x}{m_x V_{is}}\right)^p \frac{F_{m/z(dx)} Q_{rel_x} M_{is}}{F_{m/z(dis)} Q_{rel_{is}} M_x} \quad (13)$$

The estimated model tested herein contains relative terms for ion transmission, fractional ion abundance, ionization cross section, and molecular weights. The gain term above is explicitly ignored as is chromatographic injection discrimination (16). Previously we have demonstrated that to a first approximation such simplifications produce analytically useful RF estimates for polychlorinated biphenyls, polynuclear aromatic hydrocarbons, phenols, and phthalates for on-column and splitless injection techniques (17). The use of multiple internal standards aids such simplifications, and we speculate that because injection discrimination can increase as volatility decreases and because gain of conversion dynode multipliers, as reported for example by Stafford (18), increases slightly with mass, these factors partially offset each other. A complete model would treat such effects, but significant practical difficulties exist, as for example, analyte transfer in splitless injections can depend on a variety of nebulous factors (16). Concurrently, gain determinations could further complicate an already cumbersome standardization procedure in environmental applications of GC/MS (2). Therefore, a practically useful predictive model should be robust to such problems, by experimental design. The use of multiple internal standards and other important quality control quality assurance factors previously discussed in our inter- and intralaboratory GC/MS studies (6, 8, 10, 15) facilitates the adoption of analytically useful simplifications.

**Polychlorinated Biphenyls.** Response factors were estimated for 10 chlorinated biphenyls using eq 13. Relative ionization cross sections were calculated after Fitch and Sauter. The mass of the ions of primary species ( $m$ ) of analyte and internal standard were multiplied by the offset voltage at that given mass as shown in eq 13 using an exponent which presumed that transmission decreased as a simple inverse function of resolution.  $F$  values were determined for each analyte and internal standard by simply observing the percent ionization of the quantitation mass in the EI mass spectra. The relative products of transmission, fractional ion abundance, and relative ionization cross sections were corrected for molar effects by multiplication of molecular weights ( $M$ ) as shown in eq 13.

In Table I we present the estimated/observed (E/O) values for PCB's experimentally determined as presented above. In Table I the relative ion mass ( $m_r$ ) is presented as is the relative axial ion drawout potential ( $V_r$ ). The  $m_r V_r$  product is simply the relative transmission of two ions when transmission is assumed to be a simple inverse function of resolution. The relative ionization cross section function ( $Q_r$ , an estimate of

Table I. Estimated Observed (E/O) Response Factors for Polychlorinated Biphenyls

PCB	$m_r$	$V_r$	$Q_r$	$M_r$	$F_r$	$\bar{R}F_{est}$	$\bar{R}F_{obad}$	E/O
2-chlorobiphenyl <sup>a</sup>	1.00	1.00	1.01	1.00	0.593	0.593	0.526	1.13
3,3'-dichlorobiphenyl <sup>a</sup>	0.847	1.02	1.13	0.847	0.474	0.392	0.383	1.02
2,4,5-trichlorobiphenyl <sup>a</sup>	0.730	1.04	1.25	0.730	0.315	0.218	0.200	1.09
2,2',4,4'-tetrachlorobiphenyl <sup>a</sup>	0.640	1.05	1.37	0.640	0.253	0.149	0.153	0.974
2,3',4,5',6-pentachlorobiphenyl <sup>a</sup>	0.576	1.07	1.49	0.525	0.259	0.124	0.129	0.961
a pentachlorobiphenyl <sup>ab</sup>	0.576	1.07	1.49	0.525	0.240	0.116	0.134	0.866
2,2',3,4,5,5',6-heptachlorobiphenyl <sup>c</sup>	0.609	1.08	1.63	0.612	0.164	0.108	0.0996	1.08
2,2',3,3',4,4',5,5'-octachlorobiphenyl <sup>c</sup>	0.558	1.10	1.73	0.563	0.133	0.0795	0.0722	1.10
2,2',3,3',4,4',5,5',6-nonachlorobiphenyl <sup>c</sup>	0.517	1.11	1.92	0.521	0.113	0.0649	0.059	1.10
2,2',3,3',4,4',5,5',6,6'-decachlorobiphenyl <sup>c</sup>	0.482	1.13	2.04	0.486	0.124	0.0669	0.059	1.13

<sup>a</sup> Internal standard was phenanthrene-*d*<sub>10</sub>. <sup>b</sup> A pentachlorobiphenyl whose congener was not determined. <sup>c</sup> Internal standard was chrysene-*d*<sub>12</sub>.

relative total ion current production between analyte and internal standard) and the relative fractional ion abundance values ( $F_r$ ) observed for analyte and internal standard quantitation  $m/z$  values are also presented in Table I along with the relative molecular weights ( $M_r$ ). The product of all five relative functions gives the estimated response factor, so the increasing/decreasing trends of each relative function can be easily observed. For the 10 compounds listed, the model gave estimated values in excellent agreement with observed values. On average the model was accurate to approximately 5%  $\pm$  approximately 9% at 1 standard deviation. This work and data previously reported (17) employed a transmission constant, i.e.,  $p = 1$ . That is, relative transmission as described herein and within the "DFTPP regime" was found to be consistent with a simple inverse function of resolution. Experiments recently repeated by Fite support the contention that ion transmission is a simple inverse function of resolution in the DFTPP tune regime (19). Statistically estimated and observed RF values were well correlated giving a correlation coefficient of 0.996 with linear regression analysis slope and intercept of 1.11 and -0.0100, respectively.

Examination of Table I is instructive as to how the individual terms serve to estimate the RF value. Considering the first six entries, which are relative to phenanthrene-*d*<sub>10</sub>, we note that the relative transmission term (the  $m_r V_r$  product as written) decreases from unity for 2-chlorobiphenyl to approximately 62% for the pentachlorobiphenyls. The quantitation  $m/z$  values for phenanthrene-*d*<sub>10</sub> and 2-chlorobiphenyl are identical ( $m/z = 188$ ); hence, relative transmission does not affect the estimated RF value. For the pentachlorobiphenyls, however,  $m/z$  326 has, according to this model, a relative transmission term of approximately 62% that of the previously cited analyte/internal standard pair.

The relative cross section term ( $Q_r$ ) estimates the total ion current ratio produced, relative to phenanthrene-*d*<sub>10</sub>, in going from mono- to pentachlorobiphenyls. As shown, pentachlorobiphenyl produces almost 50% more current relative to the 2-chlorobiphenyl. The latter analyte has a relative cross section term whose value is approximately equal to that of the internal standard when calculated according to the model of Fitch and Sauter.

The relative fractional ion abundance reflects the fragmentation pattern, increasing chlorine substitution through the series, and the exact tune of the spectrometer. The relative molecular weight term ( $M_r$ ) corrects the model for molar consideration. Similar trends can be seen for the second group of PCB's in Table I.

Both the data listed in Table I and previous application of the model (17) give some important observations. For example, it appears that the model works well *between* compound classes of ions of primary species as the analytes were chlorinated biphenyls and the internal standards were deuterated PNA's. We anticipate that this model should be of

utility in estimating RF values for chlorinated dibenzodioxins and chlorinated dibenzofurans, and we are working to verify this fact. As above, we predict that when tetrachlorodibenzodioxins are quantitated relative to an appropriately labeled tetrachlorodibenzodioxin under QA/QC protocols designed to verify system linearity and stability by providing a reference set of RF values (10, 20), that only the relative fractional ion abundance term can be used to estimate the RF value. Note that virtually all functions given in Table I would approximate unity in such application of the model and that the only significant difference between labeled and unlabeled TCDD's is the fragmentation pattern and the exact tune of the mass spectrometer when molar ratios are preserved during analysis.

Finally, the "pentachlorobiphenyl" entry in Table I demonstrates the utility of the model in quantitating "unknowns". In this work, we observed that the standard contained two pentachlorobiphenyls and no hexachlorobiphenyl as stated by the supplier. While we did not determine the exact congener, we were able to estimate the RF value knowing the functions given in Table I and to compare it to the observed value with good agreement. In a similar fashion, RF estimates could be determined for "nontargeted" analytes tentatively identified in environmental samples, as relative transmission, cross section, fractional ion abundance values, and molecular weights can often be calculated from EI GC/MS observations and the references described herein. Once the response factors are estimated, analyte concentration estimates in the sample extracts can be obtained by using the estimated RF values.

In Table II we present additional estimated/observed RF values for chlorinated and polynuclear aromatic priority pollutants. Both the accuracy and precision of estimated and observed values are similar. The latter compound class gives observed and estimated values near unity as the relative functions discussed previously center on values that approach 1. A notable exception to this is acenaphthylene, which was determined relative to the internal standard acenaphthene-*d*<sub>10</sub>. The mass spectrum of the internal standard shows a strong loss of deuterium from the molecular ion, which reduces the detected fractional ion abundance of the molecular ion to roughly half that of the value observed for the analyte. As the product of the other four relative functions in the model is 1.12, we see that the strong loss of deuterium from the internal standard is reflected as expected in the observed RF value for the analyte acenaphthylene. This observation also serves to demonstrate how the qualitative and quantitative aspects of the GC/MS measurement process are interrelated.

The observed and estimated RF values for the chlorinated priority pollutants demonstrate that the model agrees reasonably over a range of RF values of approximately 20. Observed and estimated values are correlated with a correlation coefficient of 0.980 and with linear regression analysis slope and intercept of 0.967 and -0.0421, respectively. These data

**Table II. Estimated and Observed Response Factors (RF) for Chlorinated and Polynuclear Aromatic Priority Pollutants**

pollutant	IS <sup>a</sup>	$\overline{RF}_{est}^b$	$\overline{RF}_{obsd}^b$	E/O
PNA's				
naphthalene	d8	1.11	1.03	1.08
acenaphthylene	d10A	2.05	2.31	0.887
acenaphthene	d10A	1.12	1.37	0.818
phenanthrene	d10P	1.08	0.929	1.16
anthracene	d10P	0.995	1.12	0.888
fluoranthene	d10P	0.964	0.970	0.994
pyrene	d12C	1.45	1.98	0.732
benzo[a]anthracene	d12C	1.26	1.29	0.977
chrysene	d12C	1.231	1.26	0.976
benzo[b]fluoranthene	BaP	1.15	1.03	1.12
benzo[k]fluoranthene	BaP	1.16	1.16	1.00
indeno[1,2,3-cd]pyrene	BaP	1.02	0.794	1.28
dibenzo[a,h]anthracene	BaP	1.01	0.752	1.34
benzo[ghi]perylene	BaP	0.845	0.751	1.13
				E/O = 1.03 ± 0.171
PCB's				
1,3-dichlorobenzene	d4	1.79	1.50	1.19
1,4-dichlorobenzene	d4	1.89	1.76	1.07
1,2-dichlorobenzene	d4	2.06	1.65	1.25
1,2,4-trichlorobenzene	d8	0.247	0.271	0.911
hexachlorobutadiene	d8	0.0914	0.115	0.795
hexachlorocyclopentadiene	d10A	0.259	0.198	1.31
2-chloronaphthalene	d10A	1.17	1.41	0.833
4-chlorophenyl phenyl ether	d10A	0.540	0.574	0.941
4-bromophenyl phenyl ether	d10P	0.185	0.181	1.02
hexachlorobenzene	d10P	0.159	0.181	0.878
				E/O = 1.02 ± 0.180

<sup>a</sup>The internal standards employed for response factor calculation were 1,4-dichlorobenzene-*d*<sub>4</sub> (d4), naphthalene-*d*<sub>8</sub> (d8), acenaphthene-*d*<sub>10</sub> (d10A), phenanthrene-*d*<sub>10</sub> (d10P), chrysene-*d*<sub>12</sub> (d12C), and benzo[a]pyrene (BaP). The latter compound was used instead of terphenyl-*d*<sub>14</sub> at injected weight equal to injected weight of analyte. <sup>b</sup>RF values are mean values determined at nominal injected weights of 20, 40, 80, 120, and 160 ng/μL.

demonstrate the analytical utility of the model, and, as with other data we have presented previously (17), it demonstrates the degree to which the model can estimate EI GC/MS RF values.

Examination of Table II shows that certain E/O values are potential outliers (e.g., pyrene and hexachlorocyclopentadiene). We note that E/O values are representative of the entire procedure from standard integrity to data reduction, including the simplifying assumptions of the model. In the aggregate the model provides analytically useful RF estimates within the complete measurement process. However, there are a number of situations where application of the model is inappropriate (see below). Concurrently, we note that it is commonly known that halogenated compounds of a wide variety represent a "class" of analytes of major environmental significance. Simply assuming an RF value of 1 as is currently the practice in the previously referenced U.S. EPA program is obviously formally incorrect. More disturbing is the fact that this practice can bias quantitative results by an unknown, sample-dependent factor when total ion current concentrations are employed for nonresolved components. Furthermore, if this assumption were applied to the traditional response factors, which utilize ion current measurements at selected *m/z* values, then simply assuming RF values of 1 would bias analytical results low by an analyte-dependent factor that could approach or exceed 1 order of magnitude. Because of the known importance of halogenated compounds in the environment, and as the referenced procedure is used nationally in the characterization of hazardous waste site samples and

in other areas, we assert that our formalism, properly applied, is a useful and fundamentally more accurate way to perform internal standard based quantification of "unknowns" or "nontargeted" analytes in such samples. At the same time, we caution that our model should not be utilized indiscriminately.

An inappropriate application of the model can occur for certain volatile priority pollutants. For these low-molecular-weight compounds, a significant fraction of the ion current that is created in the ion source is not detected as the mass range typically recorded in Method 624 is limited to exclude ion current below approximately 41 amu. This artificially increases the measured fractional ion abundance of the analyte, relative to the source-generated value. Hence, estimated values have been found to be considerably larger than observed values for many volatile priority pollutants (17). Therefore, application of the model to analytes whose spectra are truncated by selection of experimental parameters is inappropriate, unless corrections are made to this effect. Other organic pollutants classified as extractable (e.g., alkyl nitrosamine and nitro compounds) also have artificially enhanced measured *F* values. The model should not be utilized to estimate RF values for compounds without correcting the measured *F* value to the "nontruncated" value. Application of the model is also inappropriate in any case where the molar ratios implied in the model are disturbed during analysis as would be the case when an analyte was thermally degraded during GC analysis. The aforesaid offers interesting diagnostic potential in applied GC/MS, but discussion of this aspect of RF value estimation is beyond the scope of this paper.

A priori, use of the model should be restricted to analyses where analytical extrapolations are minimized (e.g., retention time, compound classes, quantitation mass, and fragmentation patterns). Although we have not yet defined such limits explicitly, simple experiments can be performed to test extension of the model to other compound classes. Perhaps, most importantly, study of the model and the papers referenced herein can be utilized to help design analytical protocols for environmental and other GC/MS analysis that minimize analytical extrapolations of what we term "analytical distance" of analyte to internal standard. By design then the model can be "forced" to fit the analytical problem at hand whether it is of environmental, energy-related, or biomedical significance.

Additional examination and testing of the model is warranted, but analytically useful results have been attained based on our formalism even given our assumptions. We suggest that application of this approach to the quantitative determination of "nontargeted" analytes identified in samples of hazardous waste or sample extracts of material from hazardous waste sites will increase the accuracy of such determinations compared to current practices. Additionally, our formalism with some extensions could be utilized to define a reference set of EI GC/MS RF values for QA/QC purposes in the analysis of many compounds of environmental interest.

In other areas, we speculate that this model could be utilized to help derive RF estimation formulae for other ionization techniques. For example, observed RF values could be employed to derive ionization functions for other ionization techniques such as positive or negative chemical ionization. Furthermore, in principal, relative transmission functions could be derived for mass spectrometers of different geometry with known relative ionization functions. For example, we have correlated EI GC/MS RF values for PCB's published by others for magnetic sector and quadrupole mass spectrometers using this model (17) with good results. We further speculate that the model could be utilized to derive transmission functions for MS/MS analyses when the ionization function is known. Each application of the model would

require a demonstration of its applicability by demonstration of the agreement of estimated and observed values.

This model has general properties, which provides an important starting point to allow for the establishment of a universal approach to the characterization of introduction, ionization, transmission, detection, and other phenomena in MS instrumentation employed in environmental measurements. Carried to its logical ending point, such a formalism could unify both the qualitative and quantitative aspects of applied mass spectrometry.

#### ACKNOWLEDGMENT

We are grateful for the assistance of Wade Fite of Extrel Corp. (formerly Extranuclear Laboratories, Inc.), Pittsburgh, PA, and William Fitch of Zoecon Corp., Palo Alto, CA.

**Registry No.** 3,3'-PCB, 2050-67-1; 2,4,5-PCB, 15862-07-4; 2,2',4,4'-PCB, 2437-79-8; 2,3',4,5',6-PCB, 56558-18-0; 2,3,4,5,6-PCB, 18259-05-7; 2,2',3,4,5,5',6-PCB, 52712-05-7; 2,2',3,3',4,4',5,5'-PCB, 35694-08-7; 2,2',3,3',4,4',5,5',6-PCB, 40186-72-9; 2,2',3,3',4,4',5,5',6,6'-PCB, 2051-24-3; 2-chlorobiphenyl, 2051-60-7; naphthalene, 91-20-3; acenaphthylene, 208-96-8; acenaphthene, 83-32-9; phenanthrene, 85-01-8; anthracene, 120-12-7; fluoranthene, 206-44-0; pyrene, 129-00-0; benz[a]anthracene, 56-55-3; chrysene, 218-01-9; benzo[b]fluoranthene, 205-99-2; benzo[k]fluoranthene, 207-08-9; indeno[1,2,3-cd]pyrene, 193-39-5; dibenzo[a,h]anthracene, 53-70-3; benzo[ghi]perylene, 191-24-2; 1,3-dichlorobenzene, 541-73-1; 1,4-dichlorobenzene, 106-46-7; 1,2-dichlorobenzene, 95-50-1; 1,2,4-trichlorobenzene, 120-82-1; hexachlorobutadiene, 87-68-3; hexachlorocyclopentadiene, 77-47-4; 2-chloronaphthalene, 91-58-7; 4-chlorophenyl phenyl ether, 7005-72-3; 4-bromophenyl phenyl ether, 101-55-3; hexachlorobenzene, 118-74-1.

#### LITERATURE CITED

- (1) *Test Methods for Evaluating Solid Wastes*, 2nd ed.; U.S. EPA Office of Solid Waste and Emergency Response, SW-846, July 1982.

- (2) U.S. EPA Contract WA 84 A266 or equivalent. U.S. EPA, Analytical Support Branch and Hazardous Response Support Division: Washington, DC.
- (3) Method 1624, Revision B, and Method 1625, Revision B. U.S. Office of Water Regulations and Standards, Industrial Technology Division, U.S. EPA: Washington, DC, Jan 1985.
- (4) Mullin, M. D.; Pochini, C. M.; McCrindle, S.; Romkes, M.; Safe, S. H.; Safe, L. M. *Environ. Sci. Technol.* **1984**, *18*, 468.
- (5) Shackelford, W. M.; Cline, D. M.; Burchfield, L. O.; Faas, L.; Kurth, G. R.; Sauter, A. D. *Advances in the Identification and Analysis of Organic Pollutants in Water*; Ann Arbor Science: Stoneham, MA, 1981; Chapter 33.
- (6) Sauter, A. D.; Betowski, L. D.; Ballard, J. M. *Anal. Chem.* **1983**, *55*, 116.
- (7) Sauter, A. D., unpublished results.
- (8) Sauter, A. D. *GC/MS Accuracy Criteria* presented at the 31st Annual Conference on Mass Spectrometry and Allied Topics; Boston, MA, May 1983.
- (9) Sauter, A. D. *Response Factors and Expert Systems*. Presented at the Annual Conference of the American Society of Quality Control, Research Triangle Park, NC, Sept 1984.
- (10) Sauter, A. D.; Mills, P. E.; Fitch, W. L.; Dryer, R. *HRC CC, J. High Resolut. Chromatogr. Chromatogr. Commun.* **1982**, *5*, 27.
- (11) Harrison, A. G.; Jones, E. G.; Gupta, S. K.; Nagy, G. P. *Can. J. Chem.* **1966**, *44*, 1967.
- (12) Fitch, W. L.; Sauter, A. D. *Anal. Chem.* **1983**, *55*, 832.
- (13) Dawson, P. H. *Advances in Electronics and Electron Physics*; Academic Press: New York, 1980; Vol. 53.
- (14) Dawson, P. H. *Quadrupole Mass Spectrometry*; Elsevier/North-Holland: New York, 1976; Chapter 6.
- (15) Sauter, A. D.; Betowski, L. D.; Smith, T. R.; Strickler, V. A.; Beimer, R. G.; Colby, B. N.; Wilkinson, J. E. *HRC CC, J. High Resolut. Chromatogr. Chromatogr. Commun.* **1981**, *4*, 366.
- (16) Schomburg, G.; Husmann, H.; Rittmann, R. *J. Chromatogr.* **1981**, *204*, 85.
- (17) Sauter, A. D.; Downs, J. J.; Fitch, W. L. *Estimation of Electron Impact GC/MS Response Factors*. Presented at the 1985 Pittsburgh Conference, New Orleans, LA, April 1985.
- (18) Stafford, G. C. *EHP, Environ. Health Perspect.* **1980**, *36*, 85.
- (19) W. Fite, private communication, Oct 1985.
- (20) Sauter, A. D. *Proposed Quality Control/Quality Assurance Protocol for the Pulsed Positive Ion Negative Ion Chemical Ionization GC/MS Confirmation of GC/ECID Identified PCB's in Adipose Tissue and Related Extracts*; U.S. EPA Subcontract 3-321-U-2258-111, U.S. EPA Contract 68-03-3099.

RECEIVED for review November 22, 1985. Accepted March 10, 1986.

## Utility and Limitations of Electron Ionization and Chemical Ionization for the Determination of Position and Extent of Labeling for $^{18}\text{O}$ - and $^{13}\text{C}$ -Containing Permethylated Alditols by Gas Chromatography/Mass Spectrometry

Daniel B. Kassel and John Allison\*

Department of Chemistry, Michigan State University, East Lansing, Michigan 48824

The strengths and weaknesses of a variety of ionization methods are discussed in the context of GC/MS analyses of  $^{13}\text{C}$ - and  $^{18}\text{O}$ -labeled permethyl alditols. The goals were to determine the position of the label and the extent of label incorporation. Electron ionization mass spectra were useful in determining the location of the label; however, the rates of dissociative ionization from both halves of these "symmetric" molecules appear to be different, resulting in erroneous extent-of-labeling determinations. Isobaric ion interferences in methane and isobutane chemical ionization (CI) mass spectra require that the extent of labeling calculation be performed by solving a quadratic equation that has two roots, i.e., suggests two values for label enrichment. Ammonia CI mass spectra are shown to accurately reflect the extent of label incorporation, which exceeded 97% for the compounds investigated here.

Stable isotopes, or tracers, have frequently and successfully been used for studying metabolic pathways in biological systems. Typically in such studies, labeled precursors (containing  $^{13}\text{C}$ ,  $^{18}\text{O}$ , etc.) are presented to a biological system. These labeled species lead to the production of metabolites containing the stable isotope. Once the label is incorporated, an analytical method is required to monitor one or more metabolites and determine the extent of label incorporation as well as where in the metabolite the label appears.

Gas chromatography/mass spectrometry (GC/MS) has been extremely useful for studying metabolic pathways involving stable isotopes. Electron ionization (EI) has frequently been used in such studies due, predominantly, to the reproducibility and extensive fragmentation, i.e., structural information, associated with the technique. However, recently a number of problems associated with the technique have been