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Erratum

Erratum to "A comparison of three mass spectrometric methods for the determination of dioxins/furans" [Int. J. Mass Spectrom. 194 (2000) 235–246]

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Abstract

A comparison is presented of the performances of three mass spectrometers of high specificity in the determination of dioxin/furan congeners. The three instruments used in this study were a triple-sector EBE mass spectrometer operated at high mass resolution (HRMS), a quadrupole ion trap (QIT) mass spectrometer, and a triple-stage quadrupole (TSQ) mass spectrometer. The QIT and TSQ instruments were operated in tandem mass spectrometric mode. A mixture of tetra- to octa-chlorodibenzo-*p*-dioxins (T_4-O_8CDD) containing in all seven dioxin congeners was used for much of this study. The factors considered in this comparison were the tuning of each instrument, the preparation and comparison of calibration curves, the 2,3,7,8-T_4CDD detection limit for each instrument, ion signals due to H_6CDDs obtained with each instrument from two real samples (air and pyrolysed polychlorinated phenols), average relative response factors, and ionization cross sections. For each dioxin congener, the response factor is expressed relative to that for the O_8CDD congener, whereas the electron impact ionization cross section is expressed relative to that for the T_4CDD congener. The relative ionization cross sections for T_4-O_8CDD from HRMS and QIT, and for T_4-P_5CDD from TSQ are in good agreement, and show an overall decrease of some 10–20% with increasing degree of chlorine substitution; the variation among three H_6CDD congeners is identical in each case. With TSQ, lower relative ionization cross sections for H_6-O_8CDD are ascribed to mass-dependent fragment ion scattering in the RF-only collision cell. (Int J Mass Spectrom 197 (2000) 283–297) © 2000 Elsevier Science B.V.

Keywords: Mass spectrometry; High resolution mass spectrometry; Quadrupole ion trap; Triple-stage quadrupole; Tandem mass spectrometry; Collision-activated dissociation; Poly-chlorodibenzo-*p*-dioxins/furans

1. Introduction

Polychlorodibenzo-*p*-dioxins (PCDDs) and polychlorodibenzofurans (PCDFs) are two classes of compounds which are of environmental concern because of the high toxicity of those isomers with 2,3,7,8-

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Dedicated to Professor Jim Morrison on the occasion of his 75th birthday.

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tetrachloro-substitution [1]. In the United States alone, some 500 kg of PCDDs/PCDFs are released annually into the environment [2] from municipal and industrial waste incinerators [3,4], automobile exhaust [5], pulp and paper mill effluents [6,7], and the manufacture of chlorophenol products [8]. The potential threat to human health posed by PCDDs/PCDFs in the environment is confirmed in the recent reassessment of "2,3,7,8-TCDD and Related Compounds" [9] carried out by the United States Environmental Protection Agency (US EPA). In view of adverse health effects and the widespread and persistent presence of PCDDs/PCDFs in the environment, these compounds are monitored in air, rain, effluents, soil, and biota matrices.

A comparison of the performance of each of three mass spectrometric methods for the determination of tetra- to octa-chlorodibenzo-*p*-dioxins/furans (T_4-O_8CDD) is reported here, where the three instruments used are a high resolution mass spectrometer (HRMS), a triple-stage quadrupole (TSQ) mass spectrometer, and a quadrupole ion trap (QIT) mass spectrometer. While most of the results reported here are for dioxins, it is not expected that the trends among the furans would differ significantly from those exhibited by the dioxins, other than that, generally, the sensitivity for detection of furans is greater than that of dioxins. Calibration curves obtained by each of the three instruments for a furan are included in this comparison. With HRMS, the signal intensities of two mass-selected isotopomers from the molecular ion isotopic cluster were monitored as in single ion monitoring (SIM). With TSQ and QIT, tandem mass spectrometry (MS/MS) was employed, wherein the signal intensities of fragment ions formed from isolated molecular ion isotopomers were monitored.

Currently, the US EPA method 1613 (revision B), the European standard EN-1948-1, and the Ontario Ministry of Environment (MOE) method call for the monitoring of the total concentration of all PCDD/PCDF congener groups (i.e. total tetrachlorinated dioxins, total pentachlorinated dioxins, etc.) and the concentrations of each of the seventeen 2,3,7,8-substituted toxic isomers. The method prescribed is high resolution gas chromatography/high resolution mass spectrometry (HRGC/HRMS). Several other jurisdictions follow similar methods though with minor variations; for example, Environment Canada calls for the monitoring of but one labelled compound per group for PCDDs and PCDFs. Such determinations are costly since PCDD/PCDF determinations require extensive sample preparation, the use of the above 17 expensive $^{13}C_{12}$-2,3,7,8-substituted internal standards [10], and mass spectrometers of high capital cost.

Initially, in order to differentiate between (a) PCDDs/PCDFs and interferents, such as polychlorinated biphenyls [11], and (b) $^{13}C_{12}$-PCDFs and native PCDDs whose isotopic clusters overlap, HRMS [12,13] was necessary because only HRMS had the sensitivity and specificity required. Later, it was shown that with tandem mass spectrometry, using a triple stage quadrupole (TSQ) instrument, limits of detection (220–600 fg) that begin to approach those obtainable by HRMS could be achieved [14]; both mass spectrometric methods used HRGC. The selectivity of tandem mass spectrometry has been demonstrated in a number of cases [15–17]. Tondeur et al. [15], who developed an HRGC/(hybrid)MS/MS method for the analysis of T_4CDDs in environmental samples, have shown that MS/MS can be more selective than HRMS in certain cases, especially when high concentrations of polychlorinated biphenyls are present in sample extracts. Charles et al. [18] were able to eliminate interferences present in HRMS chromatograms of municipal incinerator ash and pulp and paper effluent extracts by using HRGC/(hybrid) MS/MS. Slayback et al. [19] used tandem mass spectrometry to eliminate interferences in complex sediment samples that could not be removed through repeated cleanup and that required a mass resolution of 32 000 to be eliminated by HRMS. Fraisse et al. [20] have shown that interferences seen in HRGC/(hybrid)MS/MS mass chromatograms of some flyash extracts were not present in HRGC/HRMS chromatograms, thus demonstrating that tandem mass spectrometry is not invariably more selective than HRMS. Reiner et al. [21], in comparing the selectivities of HRMS and tandem mass spectrometry (using TSQ), reported that TSQ and HRMS can filter out different interferences; however, neither technique can remove

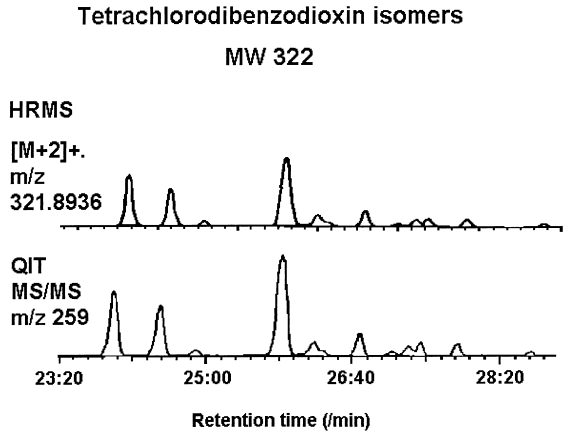

Fig. 1. Two chromatograms for tetrachloro-dibenzodioxins obtained from a clam extract using each of HRMS and QIT. The upper chromatogram (HRMS) was obtained in the single ion monitoring mode for *m/z* 321.8936; the lower shows the original ion signals for *m/z* 259 obtained by MS/MS (loss of $COCl^{\cdot}$ from isolated *m/z* 322) with the QIT. The variations in relative abundances of T_4CDDs in each chromatogram are seen to be remarkably similar.

all interferences, and this makes the two techniques complementary.

Recently, a rapid screening technique was reported for the detection and quantitation of 2,3,7,8-TCDD using a quadrupole ion trap operated tandem mass spectrometrically (MS/MS) [22,23]. While the sensitivity of the ion trap MS/MS technique at that time (500 fg/μL instrumental detection limit with a S/N of 5:1) was shown to be comparable to that of TSQ, only one scan function could be applied to the determination of a single congener group (i.e., tetra) in each chromatographic run. A comparison of two chromatograms for tetrachloro-dibenzodioxins, obtained from a clam extract using HRMS and QIT, is shown in Fig. 1. The upper chromatogram (HRMS) shows the original ion signals as obtained in the SIM mode for $[M + 2]^{+\cdot}$ molecular ions of *m/z* 321.8936; the lower chromatogram shows the original ion signals for *m/z* 259 obtained by MS/MS with the QIT. The ion species of *m/z* 259 corresponds to the loss of $COCl^{\cdot}$ from isolated $[M + 2]^{+\cdot}$ molecular ions of *m/z* 322. The variations in relative peak signal intensities of 12 T_4CDDs in each chromatogram are seen to be remarkably similar. Thus it can be concluded that there is a common activation energy for loss of $COCl^{\cdot}$ from each T_4CDD congener. This observation made possible the use of a single QIT scan function (with constant resonant excitation conditions) for the collisionally-induced dissociation (CID) of each congener group. A further impediment, imposed by the software at that time, was the inability to perform quantitation using internal standards which coeluted chromatographically with their native analytes. These impediments have been overcome by software advances such that it is possible now to deconvolute mass spectra generated from analytes which coelute chromatographically [24,25]. When operated in MS/MS mode, the ion trap is now capable of multiple-reaction monitoring (MRM) daughter ions from tetra- to octa-PCDDs/PCDFs in a single chromatographic acquisition. An MS/MS method for the ultra-trace detection and quantitation of the tetra- to octa-PCDDs/PCDFs using isotopic dilution techniques has now been developed.

Thus it is now appropriate that a comparison be presented of the performances of the three major mass spectrometric methods that can be used for the determination of dioxin/furan congeners. In this comparison, each of the following aspects of the determination of dioxins/furans is examined: (a) the tuning of each instrument; (b) preparation of calibration curves obtained with a furan; (c) the 2,3,7,8-T_4CDD detection limit for each instrument; (d) examples of ion signals from 2,3,7,8-T_4CDD obtained with each instrument at a sample level some 50× the detection limit for HRMS; (e) ion signals due to H_6CDDs obtained with each instrument from an air sample and a product mixture following pyrolysis of some polychlorinated phenols; (f) relative response factors; and (g) ionization cross sections. As explained above, with HRMS, the signal intensities of two mass-selected isotopomers from the molecular ion isotopic cluster were monitored as in SIM. With TSQ and QIT, tandem mass spectrometry, MS/MS, was employed, wherein the signal intensities of fragment ions formed from isolated molecular ion isotopomers were monitored.

2. Experimental

For the determinations of dioxins/furans by HRGC/HRMS, a VG Autospec (Vacuum Generators, Altringham, UK) triple sector instrument of EBE geometry (E, electrostatic; B, magnetic) linked to the gas chromatograph (GC) by a direct capillary interface was used and was operated at a resolving power of 10 000 (10% valley) [26]. The GC was a Hewlett-Packard 5890-II equipped with a splitless injection system and temperature programming. An OPUS data system was used for collecting, recording, and storing of all MS data. For the determinations of dioxins/furans by TSQ, a Finnigan MAT TSQ 70 triple-stage quadrupole mass spectrometer (Finnigan MAT, San Jose, CA) linked to the GC via a direct capillary interface was used. The GC was a Varian 3400 equipped with a splitless injection system and temperature programming. The collecting, recording, and storing of MS data were by an ICIS II data system. The resolution of each of the first and third quadrupoles was set to unit mass resolution. The second quadrupole mass filter (radio frequency only) was used to perform CID of the two mass-selected molecular ions isolated consecutively in the first quadrupole mass filter [17]. Argon was used as the collision gas. For the determinations of dioxins/furans by QIT, a Varian Saturn 3D GC/MS/MS instrument, equipped with a waveform generator and linked to a GC via a direct capillary interface was used. The QIT had unit mass resolution. The GC was a Varian 3400 equipped with a splitless injection system and temperature programming. Saturn software version 5.2, which was used for data acquisition, is compatible with the multiple scan function software Ion Trap Toolkit for MS/MS 1:0 (Varian Chromatography Systems, Walnut Creek, CA, USA). Multiple frequency resonant excitation in the presence of helium buffer gas was used to perform CID of mass-selected or isolated molecular ions [27,28]. All three GCs had capillary GC columns of fused silica, 60 m in length, 0.25 mm i.d., J&W, DB-5 stationary phase, and 0.25 μm film thickness.

The electron energy was 35 eV in HRMS, 22–30 eV in TSQ, and was believed to vary between 50 and 100 eV in QIT. Since the QIT operates with a time-varying voltage, the resultant distribution of electron energies depends on the RF phase upon entry of the electrons. Calculations have suggested an average electron energy of ~50 eV in the QIT when operated at a low-mass cut-off (LMCO) of 20–30 Da [29]. In this work, the LMCO varied from 128 to 183 Da, such that a linear extrapolation of the above calculations would suggest electron energies appreciably >50 eV. Because in the QIT the lifetime of electrons having energy >100 eV is relatively short, the ionization cross section has begun to fall off for such electrons, and the observed mass spectra do not differ significantly from those obtained with 70 eV electrons, it is reasonable to assume that the distribution of electron energies does not exceed 50–100 eV. The source temperature was 280 °C in HRMS, 245 °C in TSQ, and the manifold temperature in the QIT was 240 °C.

In Table 1 are listed the ions monitored in each mass spectrometric method; $M^{+\cdot}$ is the molecular ion with all ^{35}Cl atoms, $[M + 2]^{+\cdot}$ is the molecular ion with a single ^{37}Cl atom, and $[M + 4]^{+\cdot}$ is the molecular ion with two ^{37}Cl atoms. In each method, generally but not invariably (see Table 1), the two most abundant molecular ions were isolated and/or selected. In HRMS, the ions selected were the ions detected. In TSQ, the fragment ions monitored were those resulting from the loss of $COCl^{\cdot}$ upon CID of the mass-selected ions. In QIT, the fragment ions monitored were those resulting from the loss of $COCl^{\cdot}$ and $2COCl^{\cdot}$ upon CID of the mass-selected ions. Thus, for the determination of O_8CDD, two nonisobaric molecular ion species were detected in HRMS; three fragment ion species, two of which were isobaric, were detected in TSQ; and nine fragment ion species, of which three pairs of ion species were isobaric, were detected in QIT. For HRMS and TSQ, the approved methods called for the observation of ions at two mass/charge ratios; for QIT, there is no approved method and so additional ion species were monitored in order to increase sensitivity and selectivity. The relative contributions of the detected fragment ion signals resulting from the loss of $COCl^{\cdot}$ and $2COCl^{\cdot}$, for each of the dioxins investigated, are shown in Fig. 2; the average signal ratio of these loss channels is ~2:1 in favour of loss of $COCl^{\cdot}$. However,

Table 1
Ion species monitored in each mass spectrometric method

	HRMS (MS)	TSQ (MS/MS)	QIT (MS/MS)[a]	
T_4CDD	$[M]^+ + [M + 2]^+$	$[M–COCl^{\cdot}]^+ + [M + 2 - CO^{37}Cl^{\cdot}]^+$	$[M - COCl^{\cdot}]^+ + [M + 2 - CO^{37}Cl^{\cdot}]^+$	*m/z* 257
	m/z 320 *m/z* 322	*m/z* 257	$[M + 2 - COCl^{\cdot}]^+$	*m/z* 259
		$[M + 2 - COCl^{\cdot}]^+$	$[M - 2(COCl^{\cdot})]^{+\cdot} + [M + 2 - C_2O_2Cl^{37}Cl]^{+\cdot}$	*m/z* 194
		m/z 259	$[M + 2 - 2(COCl^{\cdot})]^{+\cdot}$	*m/z* 196
P_5CDD	$[M]^+ + [M + 2]^+$	$[M - COCl^{\cdot}]^+ + [M + 2 - CO^{37}Cl^{\cdot}]^+$	$[M - COCl^{\cdot}]^+ + [M + 2 - CO^{37}Cl^{\cdot}]^+$	*m/z* 291
	m/z 354 *m/z* 356	*m/z* 291	$[M + 2 - COCl^{\cdot}]^+$	*m/z* 293
		$[M + 2 - COCl^{\cdot}]^+$	$[M - 2(COCl^{\cdot})]^{+\cdot} + [M + 2 - C_2O_2Cl^{37}Cl)]^{+\cdot}$	*m/z* 228
		m/z 293	$[M + 2 - 2(COCl^{\cdot})]^{+\cdot}$	*m/z* 230
H_6CDD	$[M + 2]^+ + [M + 4]^+$	$[M + 2 - COCl^{\cdot}]^+ + [M + 4 - CO^{37}Cl^{\cdot}]^+$	$[M - COCl^{\cdot}]^+ + [M + 2 - CO^{37}Cl^{\cdot}]^+$	*m/z* 325
	m/z 390 *m/z* 392	*m/z* 327	$[M + 2 - COCl^{\cdot}]^+$	*m/z* 327
		$[M + 4 - COCl^{\cdot}]^+$	$[M - 2(COCl^{\cdot})]^{+\cdot} + [M + 2 - C_2O_2Cl^{37}Cl]^{+\cdot}$	*m/z* 262
		m/z 329	$[M + 2 - 2(COCl^{\cdot})]^{+\cdot}$	*m/z* 264
H_7CDD	$[M + 2]^+ + [M + 4]^+$	$[M + 2 - COCl^{\cdot}]^+ + [M + 4 - CO^{37}Cl^{\cdot}]^+$	$[M - COCl^{\cdot}]^+ + [M + 2 - CO^{37}Cl^{\cdot}]^+$	*m/z* 359
	m/z 424 *m/z* 426	*m/z* 361	$[M + 2 - COCl^{\cdot}]^+$	*m/z* 361
		$[M + 4 - COCl^{\cdot}]^+$	$[M - 2(COCl^{\cdot})]^{+\cdot} + [M + 2 - C_2O_2Cl^{37}Cl]^{+\cdot}$	*m/z* 296
		m/z 363	$[M + 2 - 2(COCl^{\cdot})]^{+\cdot}$	*m/z* 294
O_8CDD	$[M + 2]^+ + [M + 4]^+$	$[M + 2 - COCl^{\cdot}]^+ + [M + 4 - CO^{37}Cl^{\cdot}]^+$	$[M + 2 - CO^{37}Cl^{\cdot}]^+$	*m/z* 393
	m/z 458 *m/z* 460	*m/z* 395	$[M + 2 - COCl^{\cdot}]^+ + [M + 4 - CO^{37}Cl^{\cdot}]^+$	*m/z* 395
		$[M + 4 - COCl^{\cdot}]^+$	$[M + 4 - COCl^{\cdot}]^+$	*m/z* 397
		m/z 397	$[M + 2 - C_2O_2Cl^{37}Cl]^{+\cdot} + [M + 4 - 2(CO^{37}Cl^{\cdot})]^{+\cdot}$	*m/z* 330
			$[M + 2 - 2(COCl^{\cdot})]^{+\cdot} + [M + 4 - C_2O_2Cl^{37}Cl]^{+\cdot}$	*m/z* 332
			$[M + 4 - 2(COCl^{\cdot})]^{+\cdot}$	*m/z* 334

[a] In the QIT, the $M^{+\cdot}$ and $[M + 2]^{+\cdot}$ ions of, for example, T_4CDD are isolated along with the $[M + 1]^{+\cdot}$ ion, $C_{11}\,{}^{13}CH_4O_2\,Cl_4^{+\cdot}$ which, on dissociation by loss of $^{13}COCl^{\cdot}$, yields *m/z* 257. Since *m/z* 257 is one of the mass/charge ratios that are monitored and there is a probability of 1 in 12 that $^{13}COCl^{\cdot}$ will be lost from the $[M + 1]^{+\cdot}$ ion, the calculated fraction of the molecular ion cluster isolated includes a fractional contribution from the $[M + 1]^{+\cdot}$ ion. Similarly for O_8CDD, a fractional contribution from the $[M + 3]^{+\cdot}$ ion has been included.

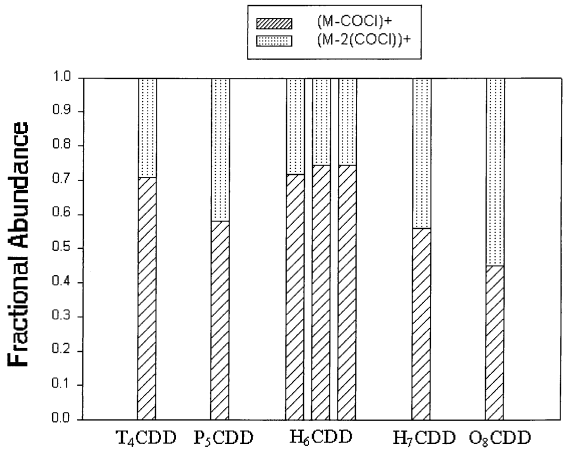

Fig. 2. The relative contributions of the detected fragment ion signals resulting from the loss of $COCl^{\cdot}$ and $2COCl^{\cdot}$, from each of the dioxins investigated, as detected with the QIT.

since the fragmentation channel involving the loss of $2COCl^{\cdot}$ is used in TSQ for confirmation (and, previously, in HRMS also), it was decided to include consideration of this channel in the tuning procedure for QIT. A standard solution containing 1 000 pg of each of six dioxin congeners (2,3,7,8-T_4CDD; 1,2,3,7,8-P_5CDD; 1,2,3,4,7,8-H_6CDD; 1,2,3,6,7,8-H_6CDD; 1,2,3,7,8,9-H_6CDD; and 1,2,3,4,6,7,8-H_7CDD) and 2 000 pg of O_8CDD was used for all three methods. The furan congener, for which calibration curves obtained using HRMS, QIT, and TSQ were prepared, was 2,3,4,7,8-P_5CDF. Standard CS-series solutions containing 2.5–1 000 pg/μL of 2,3,4,7,8-P_5CDF were used.

3. Results and discussion

3.1. Tuning

For the detection of extremely low concentrations of PCDDs and PCDFs, optimization of all instrumental parameters is important. Martinez and Cooks have reported [30] that the parameters that affect ion signal strength in the TSQ include the nature of the collision gas (i.e., He, Ar, etc.), the collision gas pressure (the number of collisions the parent ion undergoes within the collision chamber, or target gas thickness), the collision energy (the duration of the interaction between the parent ion and collision gas), electron energy (proportional to the initial internal energy of the parent ion), the potential of the third quadrupole with respect to that of the second quadrupole, the design of the collision cell, RF voltage amplitude and frequency, the restrictive interquadrupole aperture of the second quadrupole, and the type of detector. For the QIT, the parameters include the nature and pressure of the collision gas; the RF voltage amplitude during CID; and the supplementary RF potential amplitude, frequency, and duration of application.

Perfluorotributylamine (PFTBA) is used commonly for the optimization of MS/MS parameters when analyzing organic compounds and is introduced at a low partial pressure into the ion source of the HRMS for obtaining lock mass/charge ratios. The fragmentation of PFTBA under CID conditions does not parallel the behaviour of all analytes because according to the quasiequilibrium theory [31], the pattern and degree of fragmentation of the parent ion is dependent on its internal energy. Excitation by collision can form a series of daughter ions with a distribution of internal energies. Kenttämaa and Cooks [32] concluded that, by using breakdown graphs, parameters such as collision energy and collision gas pressure have a significant effect on parent ion internal energy and, therefore, its pattern of dissociation. In principle, parameters that affect parent ion internal energy can be set to direct fragmentation toward the desired fragmentation, such as the loss of $COCl^{\cdot}$ (or $COCl^{\cdot}$ + 2 $COCl^{\cdot}$) in the case of PCDDs and PCDFs. Catlow et al. [33] have shown that the optimum collision energy and collision gas pressure for one dissociation channel will almost certainly not be the optimum values for another dissociation channel of that or any other parent ion. This observation implies that the optimization of a particular fragmentation channel using the analyte of interest is critical in order to obtain the maximum ion signal strength possible.

In each case, the instrument was mass calibrated with PFTBA. The TSQ was first mass calibrated in Q_1 MS mode, then in Q_3 MS mode, and finally in MS/MS

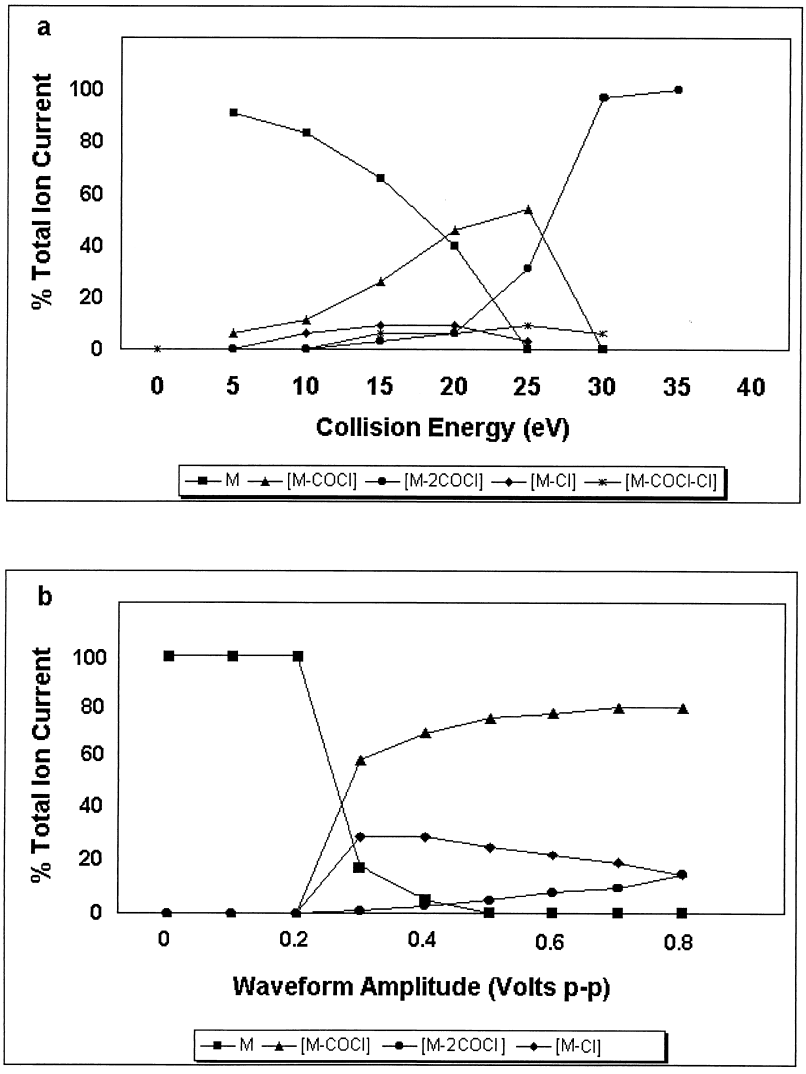

Fig. 3. Breakdown graphs: (a) ion abundance curves of 2,3,7,8-T_4CDD obtained by plotting molecular and fragment ion abundances (expressed as percentages of total ion current) as a function of ion collision energy using a TSQ instrument and argon as collision gas at a pressure of ≈3.3 mTorr; (b) ion abundance curves of 2,3,7,8-T_4CDD obtained by plotting molecular and fragment ion abundances as a function of supplementary RF waveform amplitude using a QIT instrument.

mode. Once mass calibration was complete, a tetrachloro-dioxin/furan congener on a direct insertion probe was introduced into the ion source and used for tuning. The parent ion is first optimized in Q_1 MS mode, then the instrument is switched to the MS/MS mode and collision gas is allowed to enter the collision quadrupole. For a given fixed collision gas pressure, the ion collision energy is varied and the fragment ion signal intensities monitored. From these data, a breakdown graph of fractional ion abundance (expressed as a percentage of total ion current) as a function of ion energy, similar to that shown in Fig. 3(a) [27] for 2,3,7,8-T_4CDD with argon as collision gas at a pressure of ≈3.3 mTorr, can be constructed. It is seen that, at a collision energy in the vicinity of 25 eV, the ion current due to the loss of $COCl^{\cdot}$ (▲)

attains a maximum relative value, recalling that it is the total ion current at each collision energy that is plotted on the ordinate of this figure. Additional graphs can be constructed for other collision gas pressures so as to obtain the optimum collision gas pressure and ion energy for a selected fragment ion channel. At the optimum collision gas pressure ($\sim 3 \times 10^{-3}$ Torr) for fragmentation of 2,3,7,8-T_4CDD, the collision energies were set to optimize the ion signal strength for fragment ions arising from loss of $COCl^{\cdot}$ from P_5CDD, H_6CDD, H_7CDD, and O_8CDD congeners, all of which are 2,3,7,8-substituted; these values increased from 18 to 27 eV in the laboratory frame with increasing number of chlorine atoms. Chromatograms obtained with PFTBA tuning and dioxin/furan congener tuning, which are shown elsewhere [21], show clearly that the signal:noise ratio for dioxin/furan fragment ions is much improved with specific dioxin/furan congener tuning.

For the QIT, the pressure of helium collision gas is optimized ($\sim 10^{-3}$ Torr) with respect to the peak-widths of the PFTBA ions used as mass markers. Resonant excitation was carried out at a fixed value of the q_z trapping parameter ($q_z = 0.4$) for the isolated ion species of higher mass/charge ratio. The waveform employed for CID using multiple frequency irradiation (MFI) was composed of 13, 15, or 17 frequency components spaced at intervals of 0.5 kHz covering a 6–8 kHz range of frequencies [34]. A constant MFI waveform amplitude was applied for 10 ms for each group of congeners; the amplitude varied from 2.65 to 3.10 $V_{0\text{-}p}$ for the dioxins and, for the 2,3,4,7,8-P_5CDF, was 3.60 $V_{0\text{-}p}$. The optimized conditions for each congener group were obtained from breakdown graphs of fractional ion abundances (expressed as percentages of total ion current) as a function of the amplitude $V_{0\text{-}p}$ of a single-frequency waveform, at a fixed duration of irradiation, similar to that shown in Fig. 3(b) [27] for 2,3,7,8-T_4CDD. The suffixes 0-*p* and *p*-*p* refer to the amplitude of an sinusoidal waveform and correspond to zero-to-peak and peak-to-peak, respectively. Note the similarity in Fig. 3(a) and (b) in that both curves show the higher threshold required for observation of the $2COCl^{\cdot}$-loss channel relative to the threshold for loss of $COCl^{\cdot}$. Note also that the curves differ with respect to the behaviour of the $COCl^{\cdot}$-loss channel (▲) at high collision energy and high waveform amplitude; in TSQ [Fig. 3(a)], the nascent fragment ion due to loss of $COCl^{\cdot}$ suffers further collisions and is itself fragmented further, while in QIT [Fig. 3(b)], the same fragment ion is not resonantly excited and reaches a plateau in relative abundance at high waveform amplitude.

3.2. Calibration curves

Once each instrument has been mass calibrated and tuned, calibration curves for each congener can be constructed. For example, calibration curves have been constructed for 2,3,4,7,8-P_5CDF, as the sole illustration of the performances of the three methods with respect to a furan, using 1 μL injections of five CS series solutions containing 2.5, 10, 50, 200, and 1 000 pg/μL. For HRMS, TSQ, and QIT, the correlation coefficients were 0.9997, 0.9997, and 0.9999, respectively, and the mean relative response factors (with standard deviation in parentheses) were 1.11 (0.117), 0.618 (0.104), and 1.05 (0.028), respectively. These calibration curves were virtually identical.

3.3. Detection limits

Most of the limits of detection obtainable by the TSQ are between 1 and 2 orders of magnitude lower when the MS/MS dioxin/furan congener tune method is used for optimization rather than when PFTBA is used, and, with the former method, these limits of detection begin to approach those obtainable by HRMS. The current detection limits of the three instruments, with respect to 2,3,7,8-T_4CDD, are 10 fg/μL by HRMS, 150 fg/μL by TSQ, and 100 fg/μL by QIT [35], where the TSQ and QIT instruments have been tuned as described above.

3.4. Comparison of ion signals at low concentration

Examples of the ion signals obtained with each instrument for low concentrations of 2,3,7,8-T_4CDD are shown in Fig. 4. Note that the top trace (HRMS)

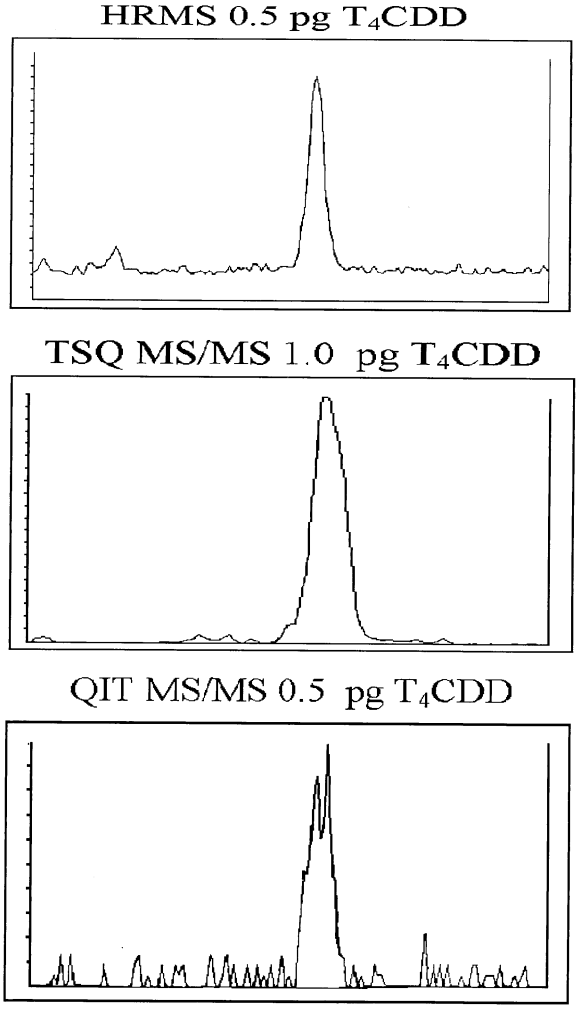

Fig. 4. Ion signals obtained with each instrument for low concentrations of 2,3,7,8-T_4CDD: (a) HRMS, 0.5 pg injected in 1 μL, the signal intensity sum due to *m/z* 320 and 322 is shown here; (b) TSQ, 1.0 pg injected in 1 μL, the signal intensity sum due to *m/z* 257 and 259 is shown here; (c) QIT, 0.5 pg injected in 1 μL, the signal intensity sum due to *m/z* 257, 259, 194 and 196 is shown here. The signal/noise ratios for HRMS and QIT are comparable and lower than that for TSQ (as expected for the higher concentration injected in TSQ).

was obtained with an amount 50× the detection limit, the middle trace (TSQ) was obtained with an amount some 7× the detection limit, and the bottom trace (QIT) was obtained with an amount some 5× the detection limit.

3.5. Real samples

Two examples are given of the determination by HRMS, TSQ, and QIT of H_6CDDs in real samples; the first example is a sample of ambient air, Fig. 5, while the second is a sample obtained following the pyrolysis of polychlorinated phenols and is shown in Fig. 6; in each figure, the last three congeners to elute are 2,3,7,8-tetra chloro-containing congeners. The agreement among the chromatograms in Fig. 5, with respect to peak relative signal intensities and peak resolution is quite good with the exception of the first peak; here, the QIT shows some tailing of the peak. In Fig. 6, again agreement is good with respect to peak relative signal intensities (note that the peak relative signal intensities in Fig. 6 differ from those of Fig. 5), but the QIT has failed, on this occasion, to resolve the peak that is centered at ~16.88 and is resolved by HRMS and TSQ.

3.6. Relative response factors

The relative response factor (RRF) is calculated as

$$\mathrm{RRF} = \frac{(A_n^1 + A_n^2)C_{\mathrm{qs}}}{(A_{\mathrm{qs}}^1 + A_{\mathrm{qs}}^2)C_n} \quad (1)$$

where A_n^1 and A_n^2 are the areas of the primary and secondary ions, respectively, of the native species, A_{qs}^1 and A_{qs}^2 are the areas of the primary and secondary ions, respectively, of the quantitation standard compound, C_n is the concentration of the native species in the standard solution, and C_{qs} is the concentration of the quantitation standard compound in the standard solution. The average RRFs for the seven dioxin congeners are given in Fig. 7 for each of HRMS, QIT, and TSQ; because the absolute values of the average RRFs for O_8CDD obtained with each method are in good agreement (1.31 for HRMS, 1.32 for TSQ, and 1.31 for QIT), the average RRFs have been plotted relative to the average RRF for O_8CDD and were obtained for $n = 35$ for each of HRMS and TSQ, and for $n = 5$ for QIT. There is excellent agreement among the normalized average relative response factors for HRMS and TSQ. The values for QIT are

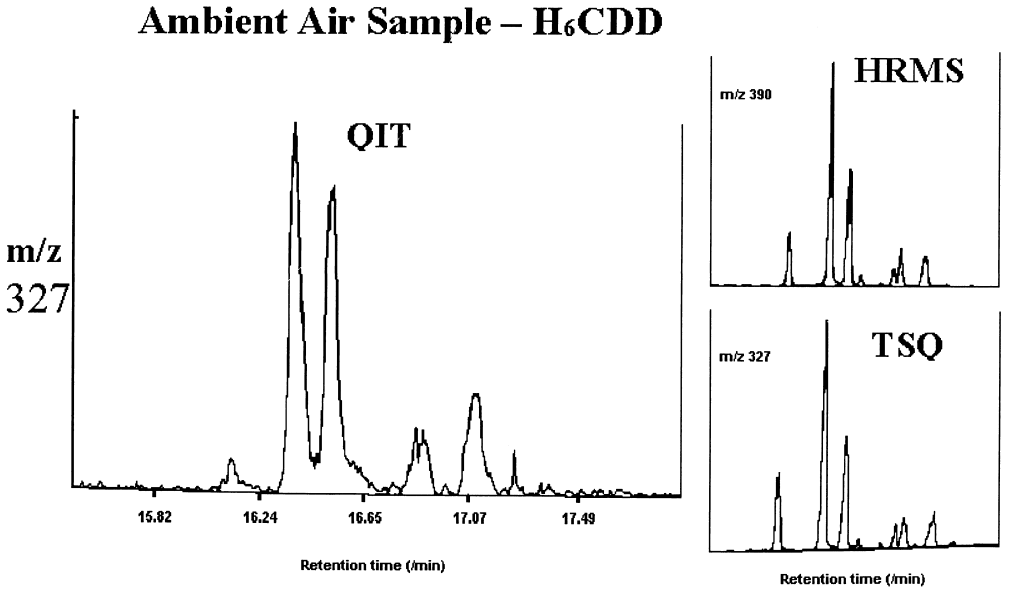

Fig. 5. Chromatographs obtained by HRMS, TSQ, and QIT showing the presence of several H_6CDDs in ambient air. Note that one ion species only is monitored in each case.

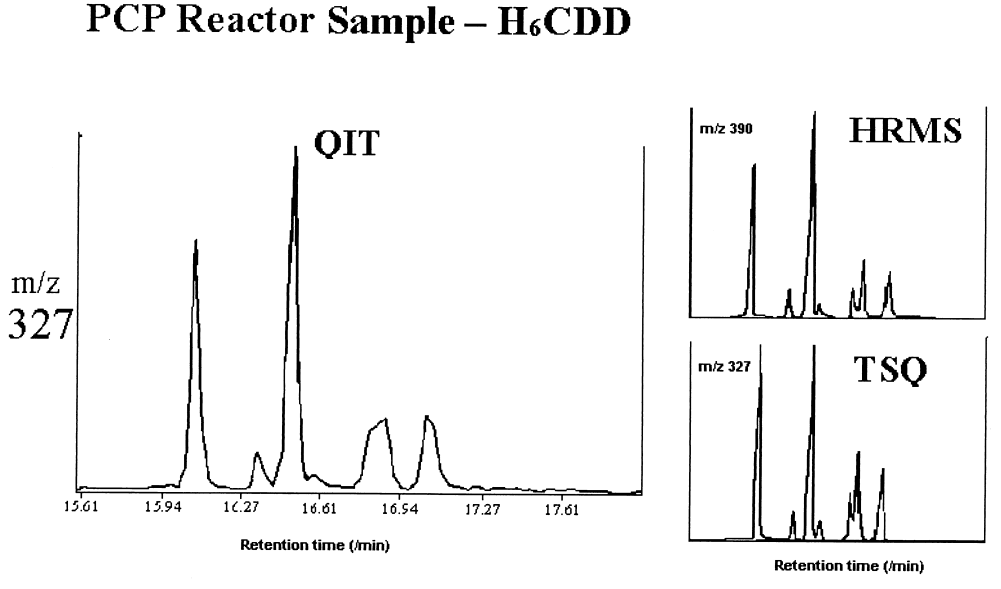

Fig. 6. Chromatographs obtained by HRMS, TSQ, and QIT of H_6CDDs showing the presence of several H_6CDDs in a sample obtained following the pyrolysis of polychlorinated phenols. Note that one ion species only is monitored in each case.

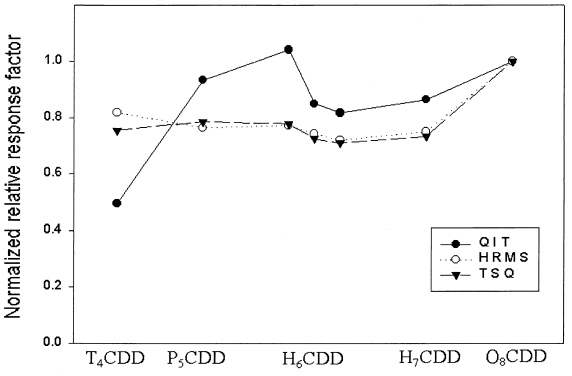

Fig. 7. Normalized relative response factors for seven dioxin congeners obtained by HRMS (open circle); QIT (filled circle); and TSQ (filled triangle).

generally higher than for HRMS and TSQ, except for the T_4CDD value, which is quite low. For HRMS, the percent relative standard deviation (% RSD) of the RRFs varies from 3.11 to 4.86%, while for TSQ, the % RSD of the RRFs varies from 1.87 to 4.97% and for QIT, the % RSD of the RRFs varies from 1.78 to 3.81%.

3.7. Ionization cross sections

3.7.1. HRMS

For HRMS, the observed ion signal intensity per picogram of material injected for each chlorocongener, $(A_{EI})_{\text{cong}}$, is related directly to the electron impact ionization cross section, σ_{cong}, as given by

$$(A_{EI})_{\text{cong}} = I_e L (F_{\text{iso}})_{\text{cong}} \sigma_{\text{cong}} N_{\text{cong}} \alpha \quad (2)$$

where $(A_{EI})_{\text{cong}}$, expressed as an area, is the sum of the ion signal intensities of the two mass-selected molecular ions for each chlorocongener as reported in Table 1, I_e is the electron beam intensity, L is the ionization path length, $(F_{\text{iso}})_{\text{cong}}$ is the sum of the fractional abundances of the two mass-selected ions, N_{cong} is the number of molecules per picogram of congener in the HRMS ion source, and α is a fraction corresponding to the ratio of the number of ions detected to the number of ions formed in the ion source. To a first approximation, α can be assumed to be constant over the mass range examined in this work, though this assumption is possibly an oversimplification for HRMS and undoubtedly an oversimplification of a complex process for the TSQ, vide infra. In order to effect a comparison among the HRMS and TSQ beam methods with the QIT pulsed method, each $(A_{EI})_{\text{cong}}$ value was normalized to that for T_4CDD for each of the three methods; the resulting relative ionization cross section $(\sigma_{\text{cong}}/\sigma_{T_4\text{CDD}})$ for each dioxin congener examined was calculated according to

$$\left(\frac{\sigma_{\text{cong}}}{\sigma_{T_4\text{CDD}}}\right)_{\text{HRMS}} = \frac{(A_{EI})_{\text{cong}}(F_{\text{iso}})_{T_4\text{CDD}} N_{T_4\text{CDD}}}{(A_{EI})_{T_4\text{CDD}}(F_{\text{iso}})_{\text{cong}} N_{\text{cong}}} \quad (3)$$

Similar expressions can be obtained for $(\sigma_{\text{cong}}/\sigma_{T_4\text{CDD}})_{\text{TSQ}}$ and $(\sigma_{\text{cong}}/\sigma_{T_4\text{CDD}})_{\text{QIT}}$. It should be noted that the signal intensity (A_{EI}) is expressed in counts/pg and N_{cong} was calculated using the following expression:

$$N_{\text{cong}} = \frac{\text{weight} \times N_{\text{Avogadro}}}{MW_{\text{cong}} \times \text{Volume}} = \frac{1 \times 10^{-12}(g) \times 6.022 \times 10^{23}(\text{molecules/mol})}{MW_{\text{cong}} \times (\text{g/mol}) \times 22\,414 \times (\text{cm}^3)} \quad (4)$$

For the tandem mass spectrometric methods, TSQ and QIT, the fragment ion signal intensities, $(A_{\text{CID}})_{\text{cong}}$, are equal to the product of the observed ion signal intensity for each chlorocongener, $(A_{EI})_{\text{cong}}$, and the CID efficiency for each chlorocongener, $(\eta_{\text{CID}})_{\text{cong}}$, as shown in Eq. (5);

$$(A_{\text{CID}})_{\text{cong}} = I_e \times L \times (F_{\text{iso}})_{\text{cong}} \times \sigma_{\text{cong}} \times N_{\text{cong}} \times \eta_{(\text{CID})\text{cong}} \times \alpha \quad (5)$$

$(\eta_{\text{CID}})_{\text{cong}}$ is defined as the ratio of the detected fragment ion signal intensities for each congener to the ion signal intensities of the mass-selected ions prior to CID.

Each $(A_{\text{CID}})_{\text{cong}}$ value was normalized to that for T_4CDD and the following ratio was computed for each dioxin congener:

Table 2
Averaged relative ionization cross section for seven dioxin congeners obtained with HRMS. Signal intensities $(A_{EI})_{cong}$, are given from 24 determinations of the dioxin congeners. $(F_{iso})_{cong}$ was calculated according to the data given in Table 1

Congeners	$(A_{EI})_{cong}$ (counts/pg $\times 10^{-3}$)	$(F_{iso})_{cong}$ [a]	N_{cong} (molecules/cm^3)	$\sigma_{cong}/\sigma_{T_4CDD}$
2,3,7,8-T_4CDD	504.3	0.652	8.3×10^4	1.000
1,2,3,7,8-P_5CDD	439.3	0.572	7.5×10^4	1.099
1,2,3,4,7,8-H_6CDD	346.8	0.584	6.9×10^4	0.923
1,2,3,6,7,8-H_6CDD	372.0	0.584	6.9×10^4	0.991
1,2,3,7,8,9-H_6CDD	358.2	0.584	6.9×10^4	0.954
1,2,3,4,6,7,8-H_7CDD	307.1	0.571	6.3×10^4	0.916
O_8CDD	254.0	0.543	5.8×10^4	0.866

[a] Molecular weights have been calculated using the masses 1.00797, 12.0111, and 15.999 for H, C, and O respectively, and 34.96885 and 36.96590 for the chlorine isotopes.

$$\left(\frac{\sigma_{cong}}{\sigma_{T_4CDD}}\right)_{MS/MS} = \frac{(A_{CID})_{cong} \times (F_{iso})_{T_4CDD} \times (\eta_{CID})_{T_4CDD} \times N_{T_4CDD}}{(A_{CID})_{T_4CDD} \times (F_{iso})_{cong} \times (\eta_{CID})_{cong} \times N_{cong}} \quad (6)$$

where MS/MS refers to both TSQ and QIT. Eq. (6) is an expression for the relative ionization cross section, $(\sigma_{cong}/\sigma_{T_4CDD})_{MS/MS}$, for each dioxin congener and for each MS/MS method.

Twenty-four determinations of the selected dioxin congeners were carried out with HRMS, and the results are shown in Table 2. The average value of the ion signal intensity, A_{EI}, is given in counts/pg. The values of F_{iso} for each congener were calculated for the ions monitored as given in Table 1.

3.7.2. QIT

A calibration curve was obtained for each dioxin congener using five standard solutions ranging in concentration from 2.5 to 1 000 pg/μL. Nine quantities of each dioxin congener were injected on the column using 1 μL from each solution and 2 μL from each solution, except that of 1 000 pg/μL. The calibration curve was constructed from the nine datum points, where each datum point was the arithmetic mean of three total fragment ion signal intensities resulting from two replications. The fragment ions monitored are given in Table 1. The slope of the calibration curve was used to determine the fragment ion signal intensity, $(A_{CID})_{cong}$, for each congener. During the multifrequency irradiation to effect CID, the trapping field for the precursor ions of each dioxin congener of higher mass/charge ratio was set at a working point of $q_z = 0.4$. The results are shown in Table 3. A striking feature of this Table is that the relative CID efficiency, $\eta_{cong}/\eta_{T_4CDD}$, decreases by a factor of 2.5 as the degree of chlorine substitution increases. This decrease is ascribed to a lowering of the pseudopotential trapping well leading to diminished fragment ion trapping efficiency as the fragment ion mass/charge ratio increases. The pseudopotential trapping well in the radial (r) and axial (z) direction is proportional to the square of the stability parameters, q_u(u = r, z). In Fig. 8 are plotted the calculated values of $(q_z)^2$ for the two major fragment ions formed from the mass-selected molecular ions of each dioxin congener. In this work, molecular ions were held at a constant value of the trapping parameter q_z and subjected to CID at a fixed frequency; thus the magnitude of the trapping potential well for fragment ions formed by constant neutral loss will be reduced for fragment ions formed from molecular ions of higher mass/charge ratio.

3.7.3. TSQ

Thirty four determinations of the selected dioxin congeners were carried out with TSQ. The averages of the signal intensities are shown in Table 4. With

Table 3
Averaged relative ionization cross sections for seven dioxin congeners obtained with QIT. The average signal ion intensities, $(A_{CID})_{cong}$, were obtained from the slope of calibration curves derived from 27 determinations of the dioxin congeners. $(F_{iso})_{cong}$ was calculated according to the data given in Table 1

Congeners	$(A_{CID})_{cong}$ counts/pg	$(F_{iso})_{cong}$	N_{cong} (molecules/cm^3)	$\eta_{cong}/\eta_{T_4CDD}$	$\sigma_{cong}/\sigma_{T_4CDD}$
2,3,7,8-T_4CDD	132.40	0.655	8.3×10^4	1.000	1.000
1,2,3,7,8-P_5CDD	55.70	0.575	7.5×10^4	0.585	0.907
1,2,3,4,7,8-H_6CDD	42.72	0.586	6.9×10^4	0.557	0.778
1,2,3,6,7,8-H_6CDD	61.86	0.586	6.9×10^4	0.692	0.908
1,2,3,7,8,9-H_6CDD	56.06	0.586	6.9×10^4	0.711	0.800
1,2,3,4,6,7,8-H_7CDD	31.92	0.572	6.3×10^4	0.486	0.748
O_8CDD	33.43	0.608	5.8×10^4	0.395	0.985

TSQ, the observed fragment ion signal, $(A_{CID})_{cong}$, exhibits a marked intensity decrease in passing from P_5CDD to H_6CDD and beyond; that is, with increasing degree of chlorination, in contrast with that of QIT and with the observed variation of $(A_{EI})_{cong}$ with HRMS. In addition, the observed variation in the relative CID efficiency, $\eta_{cong}/\eta_{T_4CDD}$, exhibits an increase by a factor of 2.3 as the degree of chlorine substitution is increased from four to eight and is, again, in contrast to the behaviour observed with QIT (Table 3, decrease by a factor of 2.5). These contrasting observations are due clearly to the radically different CID processes in TSQ and QIT with respect to ion energy, collision gas, collision energy, number of collisions, and duration of the CID process. In the TSQ, the attenuation of the main beam in the collision cell was ~60% so that ≤60% of the mass-selected ions were dissociated; whereas in the QIT, dissociation of the mass-selected ions was complete. The scattering of ions in the TSQ collision cell reduces the CID efficiency; this scattering effect is more marked for fragment ions of relatively low mass/charge ratio, and it is seen in Table 4 that the relative CID efficiency, $\eta_{cong}/\eta_{T_4CDD}$, increases as the degree of chlorine substitution and mass increase.

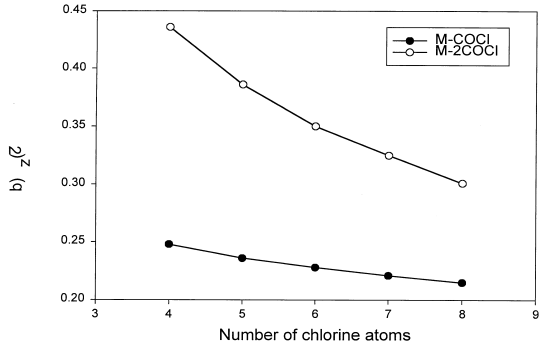

Fig. 8. Square of the stability parameter q_z for two major fragment ions formed from the mass-selected molecular ions of each dioxin congener.

In the TSQ with its alternating concatenation of lenses and quadrupole mass filters, the aberration in each lens leads to increasing ion transmission as a function of mass, whereas the confinement in each quadrupole leads to decreasing ion transmission as a function of mass. The net result is a small decrease in ion transmission as a function of mass [36]; the decrease is of uncertain magnitude though it is minimized by the purposeful increase in collision energy, as discussed above, with increasing degree of chlorine substitution. Qualitatively, the average kinetic energy for each of the mass-selected ions transmitted into the TSQ collision cell is more or less constant (18–27 eV) and is, to a first approximation, proportional to the acceleration voltage of the lens (V_{lens}):

$$eV_{lens} = m_p v_p^2/2 \tag{7}$$

where e is the charge of the molecular ion transmitted and m_p and v_p are its mass and velocity, respectively. For each dioxin congener, it is seen from Eq. (8)

$$\frac{(v_p)_{cong}}{(v_p)_{O_8CDD}} = \frac{\sqrt{(m_p)_{O_8CDDp}}}{\sqrt{(m_p)_{cong}}} \tag{8}$$

Table 4
Averaged relative ionization cross sections for seven dioxin congeners obtained with TSQ. Signal ion intensities, $(A_{CID})_{cong}$, are given for 34 determinations of the dioxin congeners. $(F_{iso})_{cong}$ was calculated according to the data given in Table 1

Congeners	$(A_{CID})_{cong}$ (counts/pg)	$(F_{iso})_{cong}$	N_{cong} (molecules/cm^3)	$\eta_{cong}/\eta_{T_4CDD}$	$\sigma_{cong}/\sigma_{T_4CDD}$
2,3,7,8-T_4CDD	8384	0.652	8.3×10^4	1.000	1.000
1,2,3,7,8-P_5CDD	7658	0.572	7.5×10^4	1.091	1.056
1,2,3,4,7,8-H_6CDD	5029	0.584	6.9×10^4	1.818	0.443
1,2,3,6,7,8-H_6CDD	5575	0.584	6.9×10^4	1.727	0.517
1,2,3,7,8,9-H_6CDD	5330	0.584	6.9×10^4	1.796	0.476
1,2,3,4,6,7,8-H_7CDD	4772	0.571	6.3×10^4	1.955	0.438
O_8CDD	4405	0.543	5.8×10^4	2.273	0.397

that the parent ion velocities, relative to that of O_8CDD, are $(v_p)_{T_4CDD} = 1.196$, $(v_p)_{P_5CDD} = 1.137$, $(v_p)_{H_6CDD} = 1.085$, and $(v_p)_{H_7CDD} = 1.039$. In view of their greater velocities, ions of lower mass/charge ratio will experience fewer RF cycles of the quadrupole field and will tend to be less well confined within the quadrupole collision cell. Thus, the η_{cong} values are expected to be lower for congeners of relatively low molecular weight and to increase in value with molecular weight, as is observed.

3.7.4. HRMS, QIT, and TSQ

The relative performances of the three mass spectrometric methods can be compared on the basis of congener-specific relative ionization cross sections, $\sigma_{cong}/\sigma_{T_4CDD}$, obtained by HRMS, QIT, and TSQ. In Fig. 9 are plotted the values of $\sigma_{cong}/\sigma_{T_4CDD}$ for each dioxin congener as given in Tables 2, 3, and 4. On the abscissa in Fig. 9 are shown the congeners examined; the lines have been drawn merely to facilitate recognition of the datum points obtained with each method.

As may be expected, the data obtained by the three methods are generally quite similar except for the marked decrease with TSQ in passing from P_5CDD to the congeners of higher degree of chlorine substitution. For HRMS and QIT there is a decrease of some 10–20% in the normalized ionization cross section as the degree of chlorination increases, because there is but a small increase of the correlated ionization energy; theoretical calculation [24] has shown an increase of the ionization energy of ~100 meV as the degree of chlorine substitution increases. Despite the enormous differences between the HRMS, TSQ, and QIT instruments, the ion signals observed in each instrument can be related directly to the ionization efficiency, or cross section, for each congener in the ion sources of the three instruments. The close agreement among HRMS and QIT values of $\sigma_{cong}/\sigma_{T_4CDD}$ among the three H_6CDD congeners is of interest, particularly since the same trend is exhibited by TSQ.

4. Conclusions

Three mass spectrometers have been compared with respect to their performance in the determination of dioxins/furans. While the HRMS detection limit for T_4CDD is lower than that of TSQ and QIT, there is evidence that all interferences are not eliminated by high mass resolution alone, thus there is a need also

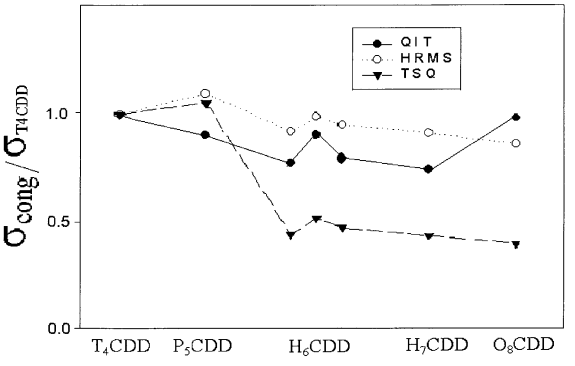

Fig. 9. Relative ionization cross section ($\sigma_{cong}/\sigma_{T_4CDD}$) for seven dioxin congeners obtained from 24 HRMS determinations (open circle); from 27 QIT determinations (filled circle), and from 34 TSQ determinations (filled triangle).

for instruments that achieve high specificity by tandem mass spectrometric operation. Normalized relative response factors were found to be generally similar for the three methods. The relative ionization cross sections for T_4-O_8CDD from both HRMS and QIT, and for T_4-P_5CDD from TSQ are quite close; in addition, the variation among three H_6CDD congeners is identical for the three methods. For TSQ, the values of the relative cross sections for H_6CDD, H_7CDD, and O_8CDD congeners are somewhat lower than those obtained for HRMS and QIT, and this behaviour has been explained in terms of mass-dependent fragment ion scattering in the RF-only collision cell.

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