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Short communication

Adsorption–desorption effects in ion trap mass spectrometry using in situ ionization

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Abstract

Quadrupole mass spectrometers were compared for the GC–MS analysis of six molecules frequently encountered in analytical toxicology: diazepam, alprazolam, triazolam, LSD (lysergic acid diethylamide), trimethylsilylated LSD and trimethylsilylated buprenorphine. Experiments performed with ion trap detectors using in situ ionization led to important chromatographic peak tailing for the most polar compounds; it was assumed to result from adsorption–desorption of neutral molecules in the mass spectrometer. This study showed that the degree of peak tailing is correlated with analyte polarity, with materials coating ion trap surfaces and with analysis temperature and that this anomaly can be greatly reduced using passivated surfaces and a high temperature of analysis.
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1. Introduction

Owing to their great m/z scan rate and their relatively low cost, mass spectrometers equipped with a quadrupole analyzer are, by far, the most widespread in GC–MS and LC–MS [1]. Ion trap mass spectrometers rapidly encountered a large success because their capability to stock ions provides them a very high sensitivity for trace analysis; what is more, they allow MS–MS to be performed at

a cost much lower than with triple quadrupole instruments [2,3]. In GC–MS, ion trap analyzers may be fitted with an external source (like quadrupole filters) but ion traps with in situ ionization are also widespread among GC–MS instruments. Comparing quadrupole filters and ion trap mass spectrometers for the GC analysis of benzodiazepines, Borrey et al. reported "excessive peak tailing on the late-eluting peaks" for analysis performed on ion traps [4]. We also observed important peak tailing in studies involving benzodiazepines and lysergic acid diethylamide (LSD) analysis [5,6]. We assume that this anomaly is due to adsorption–desorption of neutrals on electrodes and/or spacers of ion traps.

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We did not find any study of this phenomenon in the literature. Such an adsorption–desorption phenomenon must depend mainly on three factors: the polarity of the analyte, the nature of ion trap constituents and the temperature of analysis. The aim of this work is to study the influence of those three parameters on chromatographic peak tailing.

2. Experimental

2.1. Materials and sample preparation

Alprazolam and triazolam were purchased from Pharmacia and Upjohn (Saint-Quentin-en-Yvelines, France), diazepam from Roche (Neuilly-sur-Seine, France), LSD from Promochem (Molsheim, France) and buprenorphine from Schering-Plough (Levallois-Perret, France). HPLC-grade acetonitrile was obtained from Prolabo (Fontenay-sous-Bois, France). A mixture of 99% of *N,O*-bis(trimethylsilyl)trifluoroacetamide (BSTFA) with 1% trimethylchlorosilane (TMCS) was purchased from Merck (Nogent-sur-Marne, France). Four solutions were made with concentrations in each analyte of 1, 2, 10 and 50 μg/ml in a mixture of BSTFA–TMCS (99:1). For trimethylsilylation of LSD and buprenorphine, the sample was heated at 80 °C for 20 min and let to cool down to ambient temperature prior to GC–MS analysis. Under such conditions, the chromatograms showed total trimethylsilylation of buprenorphine while derivatization of LSD remained incomplete, thus allowing studying the influence of trimethylsilylation on the LSD peak shape.

2.2. Instrumentation

Ion trap analyses were performed on a Varian (Les Ulis, France) Saturn 2000 apparatus consisting in a gas chromatograph coupled with an ion trap mass spectrometer using in situ ionization. Quadrupole filter analysis were performed on an Agilent (Massy, France) 5973 apparatus consisting of a gas chromatograph coupled with a quadrupole mass spectrometer. Both instruments were fitted with an autosampler.

Chromatographic separation was evidently carried out in the same manner on both instruments. A 1-μl

volume of sample was automatically injected at a rate of 5 μl/s, in the splitless mode, at 290 °C. Helium was used as the carrier gas and the flow was held constant at 1 ml/min. Compounds were separated on a 30 m CP-Sil8CB-MS (Varian) analytical column (0.25 mm I.D., film thickness: 0.25 μm). The analytical column was ramped at 10 °C/min from 100 to 320 °C where it was held for 4 min. The transfer line was maintained at 290 °C. The source and electrodes of the quadrupole mass filter were set to 220 and 150 °C, respectively. Ion trap electrodes were set to 220 °C. All spectra were recorded in the m/z 40 to m/z 500 ion range, with a scan rate of 1 s/scan. Excepted when mentioned, the electrodes and spacers of the ion trap were passivated, as described below.

In the set of experiments devoted to the study of the adsorption–desorption phenomenon in the ion trap analyzer, ionization was performed by chemical ionization (CI) using acetonitrile as the reagent gas. In the ion trap apparatus, eluted molecules can come into contact with two kinds of surfaces: electrodes and spacers. With the aim to study the influence of ion trap constituents on peak tailing, four configurations were tested: (i) chromium coated stainless steel electrodes with quartz spacers, (ii) chromium coated stainless steel electrodes with passivated quartz spacers, (iii) passivated electrodes with quartz spacers and (iv) passivated electrodes with passivated quartz spacers. ''Passivated'' constituents have undergone the ''Silcosteel'' process (1997 Varian patent) consisting of a chemical vapor deposition process [7,8]. The coating is originally a silicon layer of 300 to 400 Å but the passive surface is assumed to be silicon dioxide resulting from auto-oxidation of silicon on contact with air [9]. In the second set of experiments, devoted to the comparison of peak shapes obtained with each type of analyzer, ionization was performed by electron impact (EI) at about 70 eV on each instrument.

2.3. Computational

For each compound, the most stable conformer was determined at a semi-empirical level with the AM1 method, using the HyperChem program [10–12]. Ab initio geometry optimization of the most

stable conformer was then carried out at the B3LYP/ 6-31G* level with the Gaussian98 package [13]. The dipole moment was determined at this latter level.

3. Results and discussion

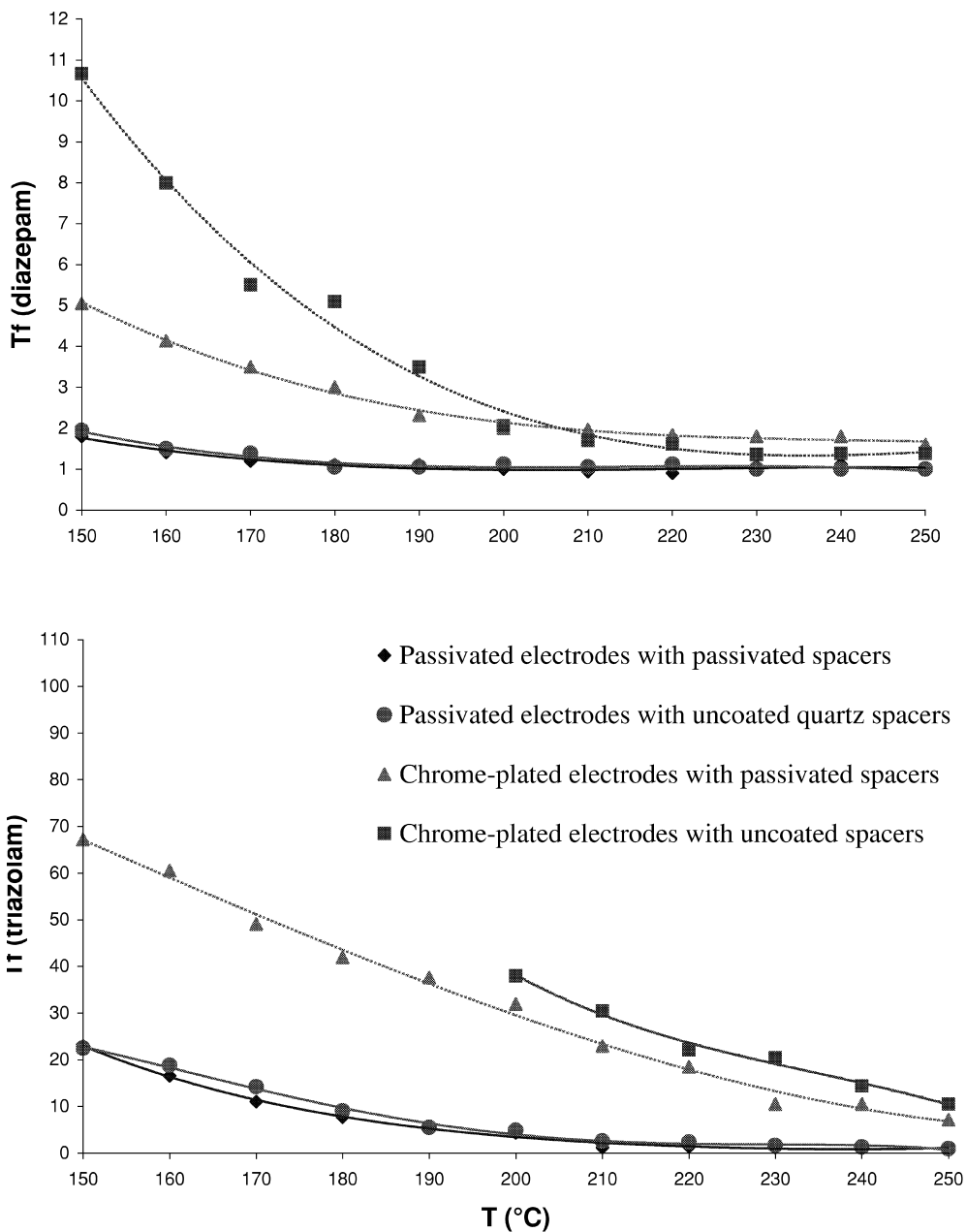With the aim of locating the adsorption–desorp-

Fig. 1. Tailing factors of diazepam and triazolam as a function of temperature for the four ion trap assemblies studied (with chrome-plated electrodes and uncoated quartz spacers, the peak tailing of triazolam was so important below 200 °C that it could not be accurately measured).

Table 1
GC tailing factors at four concentrations ranging from 1 to 50 μg/ml

	Diazepam		Alprazolam		Triazolam		LSD		LSD-TMS		Buprenorphine-TMS	
	$T_{f(QF)}$ [a]	$T_{f(IT)}$ [b]	$T_{f(QF)}$	$T_{f(IT)}$	$T_{f(QF)}$	$T_{f(IT)}$	$T_{f(QF)}$	$T_{f(IT)}$	$T_{f(QF)}$	$T_{f(IT)}$	$T_{f(QF)}$	$T_{f(IT)}$
1 μg/ml [c]	–	1.3	–	2.7	–	2.8	–	2.1	–	1.7	–	1.5
2 μg/ml	1.2	1.4	1.3	3.0	1.3	3.0	1.2	2.0	1.1	1.5	1.1	1.3
10 μg/ml	1.1	1.4	1.5	3.0	1.5	3.1	1.2	2.0	1.2	1.8	1.1	1.5
50 μg/ml	1.2	1.4	1.4	2.6	1.5	2.8	1.5	2.0	1.0	1.7	1.1	1.5
T_{fr} [d]	0.23		1.47		1.53		0.70		0.63		0.33	

[a] $T_{f(QF)}$: Tailing factor of the chromatographic peak with detection performed with the quadrupole filter.

[b] $T_{f(IT)}$: Tailing factor of the chromatographic peak with detection performed with the ion trap mass spectrometer.

[c] At 1 μg/ml, GC peaks recorded with the quadrupole filter are too small to be accurately measured.

[d] T_{fr} is defined as the ''relative tailing factor''; T_{fr} is equal to the mean of $T_{f(IT)}$ values (for 2, 10 and 50 μg/ml concentrations) minus the mean of $T_{f(QF)}$ values.

tion phenomenon and evaluating the efficiency of surface passivation, four configurations of ion trap assembly were tested (see the Experimental section). The influence of temperature was also tested, for each configuration, performing detection with ion trap temperatures ranging from 150 to 250 °C, by steps of 10 °C. A 50 μg/ml mixture of diazepam and triazolam was used. These benzodiazepines were chosen because their polarities are very different (see below). Tailing factors of diazepam and triazolam were plotted as a function of temperature in Fig. 1.

Fig. 1 shows that passivation of electrodes provides a significant decrease of peak tailing and leads, for temperatures greater than 220 °C, to tailing factors between 1.1 and 1.2 for diazepam, and between 1.1 and 1.7 for triazolam. The influence of spacers' passivation is also obvious, especially at the lowest temperatures where the maximum adsorption–desorption is expected. In the ''worst'' configuration, involving chrome-plated electrodes with uncoated quartz spacers, the peak tailing of triazolam is such that it cannot be accurately measured for temperatures below 200 °C. In all cases, the ion trap assemblies involving passivated electrodes provide the lower peak tailing, showing than the adsorption–desorption phenomenon is mainly located on electrodes. Temperature plays a determinant role: increasing temperature enhances molecular vibrations and thus reduces adsorption of neutrals on surfaces. At 250 °C, with all surfaces passivated, the tailing factors of diazepam and triazolam are 1.1: chromatographic peaks are quasi symmetric.

The second part of this study was devoted to the comparison of chromatographic peak shapes for each type of quadrupole analyzer. To quantify the degree of tailing, we calculated the tailing factor (T_f) of each chromatographic peak. The tailing factor is a measurement based on comparing the peak width for the front (A) and the back (B) half of the peak at 5% of the peak height [3]. $T_f = (A+B)/2A$. The value of T_f is equal to 1 for symmetrical peaks and increases with the degree of tailing [14]. Results are summarized in Table 1. T_f values are between 1.1 and 1.5 for all the analysis performed with the quadrupole filter ($T_{f(QF)}$); they range from 1.3 to 3.1 with the ion trap ($T_{f(IT)}$). All the studied molecules are subject to significant peak tailing when detection is performed with the ion trap mass spectrometer, some of them more than others. For a given compound, the $T_{f(IT)}$ values do not significantly change as a function of concentration; the degree of tailing is thus not related to the quantity of molecules introduced in the ion trap.

We defined the relative tailing factor of a compound, ''T_{fr}'' (see Table 1), as the mean of $T_{f(IT)}$ values (for 2, 10 and 50 μg/ml concentrations) minus the mean of $T_{f(QF)}$ values. T_{fr} reflects the part of tailing which can be attributed to the ion trap detector, independently of the chromatographic process. For each molecule, the geometry and the dipole moment of the most stable conformer are given Fig. 2. Plotting T_{fr} values as a function of the dipole moments provides a line with a correlation $r^2 = 0.94$. This relatively good correlation suggests that polar
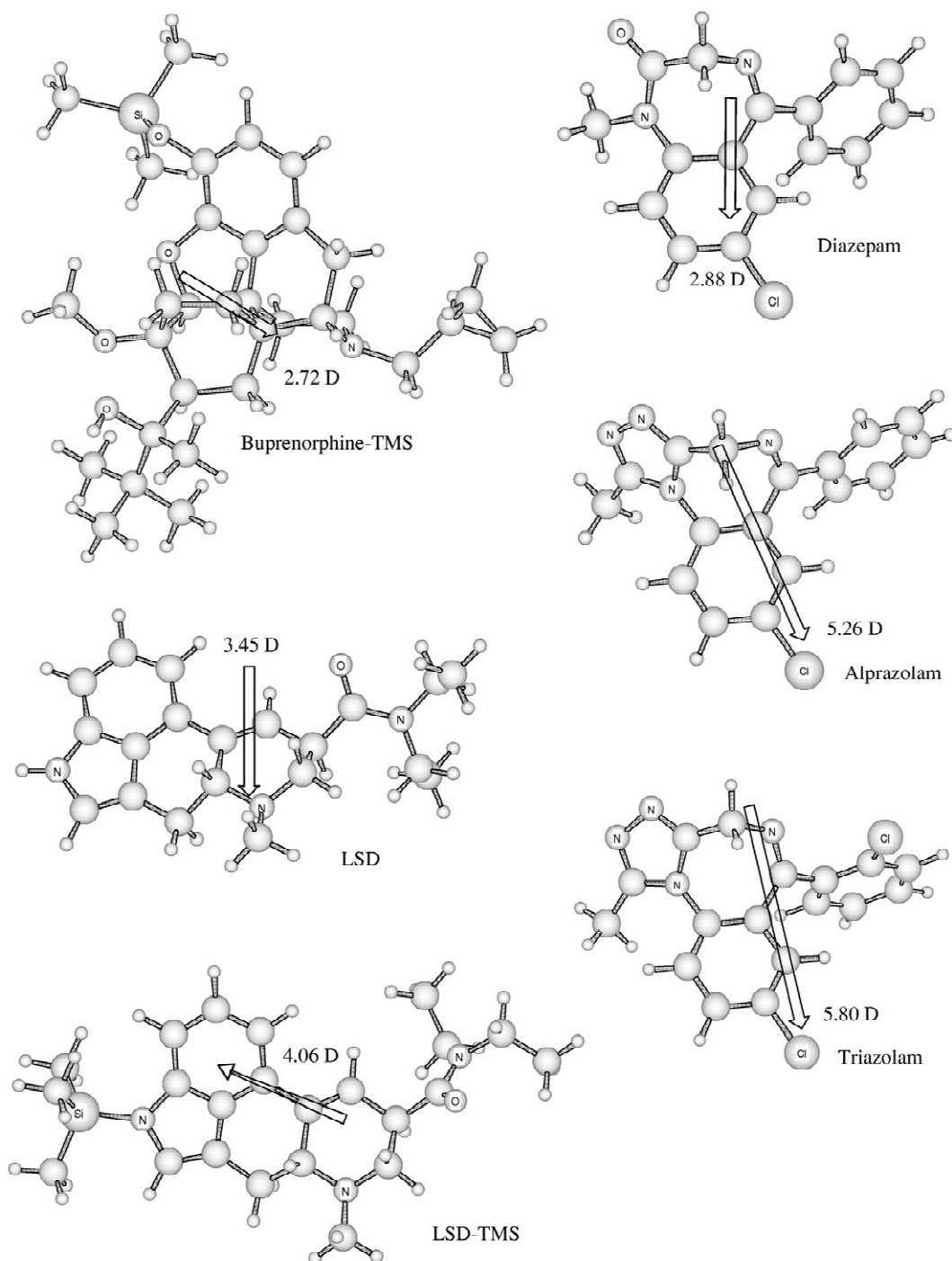
Fig. 2. Geometries and dipole moments of the most stable conformers of the studied compounds.

type interactions between analytes and ion trap constituents are greatly responsible for peak tailing. It is to be noted that hydrogen-bonding and non-specific interactions (e.g., volatility) are not considered here because they are difficult to evaluate but they are expected to be also important. The comparison of dipole moments and relative tailing factors of LSD and trimethylsilylated LSD is very informative. In previous work comparing GC–MS detection of LSD and of trimethylsilylated LSD, we showed that derivatization considerably reduces peak tailing of this analyte and thus enhances its detection threshold by a factor 10 [6,15]. Based on this result, one should have expected that trimethylsilylation of LSD would decrease its polarity. Our calculations show that this is not the case: we estimated dipolar moments of 3.45 and 4.06 D for LSD and trimethylsilylated LSD, respectively. More, the relative tailing factor of trimethylsilylated LSD (0.63) is scarcely lower than that of LSD (0.70), in apparent contradiction with previous studies [15]. The fact that previous studies differ from present work by the chromatographic injection mode (cold on-column versus splitless) suggests that, when observed, the improvement of the chromatographic peak shape due to trimethylsilylation of LSD does not involve the adsorption–desorption phenomenon mentioned above; it is likely that it rather involves interaction between the analyte and the liner of the injector.

4. Conclusion

Under certain conditions, ion trap detection may lead to important peak tailing resulting from adsorption–desorption of neutral molecules on internal surfaces. Our results showed that the amplitude of this phenomenon is, for the studied compounds, strongly correlated to the polarity of the analyte (the greater the polarity, the greater the peak tailing). The use of ion trap assemblies coated with different materials showed evidence that adsorption of neutrals is located more on electrodes than on spacers and that passivation of surfaces allows a significant decrease of adsorption. Increasing the ion trap temperature above current analytical values (180–220 °C) considerably decreases peak tailing and leads to tailing factors equal to those obtained with a quadrupole filter. From a practical point of view,

peak tailing can be quasi suppressed by using passivated surfaces in combination with a high analytical temperature (230–250 °C), even for fairly polar analytes. Under these conditions, and for non-thermo labile compounds, the ion trap detector with internal ionization can compete with a quadrupole filter in terms of chromatographic resolution.

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