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Confirmation and identification of the impurities in metolachlor using gas chromatography interfaced with orthogonal acceleration time-of-flight mass spectrometry (GC-oaTOFMS)

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Abstract

The confirmation and identification of the impurities in metolachlor (a herbicde) by using gas chromatography-orthogonal acceleration time of flight mass spectrometry (GC-oaTOFMS) and gas chromatography-quadrupole mass spectrometry (GC-qMS) are described. For the accurate mass measurement can be carried by GC-oaTOFMS, the elemental compositions of molecular and fragment ions in the spectra are suggested. In the experiment the average of mass deviations between the measured and theoretical values was below 2.5 mDa. Finally ten impurities were confirmed and identified. They accounted for 94% of the total impurities by weight.

Keywords: GC-oaTOFMS; GC-qMS; GC; Metolachlor.

1. Introduction

Mass spectrometry is one of the important spectroscopic techniques used by synthesis chemists to monitor the key steps in a synthesis process and to characterize the final products. The use of open access mass spectrometry instruments is now widespread and this approach to spectroscopic analysis has greatly increased the amount of structural information readily available to the synthesis chemists [1,2]. Now gas chromatography (GC)/liquid chromatography (LC) combined with mass spectrometry is commonly used in the qualitative analysis of mixtures [3,4]. It has long been known that the elemental composition of an organic ion can be established if its mass can be measured with sufficient accuracy [5,6]. Exact mass measurement is an important technique along with other spectroscopic methods to confirm the structures of novel compounds prepared by the synthesis chemists [7]. To carry out exact mass measurements, chromatograph combined with double-focusing magnetic sector instrument or Fourier transform ion cyclotron resonance mass spectrometer has been employed up to now [8–10]. With the development of time-of-flight (TOF) mass spectrometer, accurate mass measurement of compounds to be structurally characterized has become of widespread usage. Liquid chromatography combined with time-of-flight mass spectrometry is becoming an established method to perform the structural identification of unknown compounds in the pharmaceutical industry [11–14]. Recently gas chromatography-orthogonal acceleration time-of-flight mass spectrometry (GC-oaTOFMS) has provided a new method to measure the exact mass [15,16]. And GC-oaTOFMS has been applied in the qualitative analysis of flavor [15,17] and the exact mass measurement of unambiguous characterization of synthesis pathways [16]. Metolachlor (shown in Fig. 1) is a herbicide which has long been widely used [18]. The metolaclor produced by Dalian Chem & Phys Co. Ltd., China

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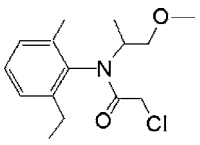

Fig. 1. The chemical structure of metolachlor.

has a purity around 95%. Although this purity is enough for commercial use, there are still a total of 5% impurities existing in the product. In order to evaluate the influence of commercial product consumed in agriculture on the environment, the impurities contained in metolachlor should be identified and determined. This paper presents the identification of impurities in metolachlor using GC-qudrapole mass spectrometry (GC-qMS) and GC-oaTOFMS, particularly for the accurate mass determination by the latter. Quantification was performed by GC with flame ionization detector (FID).

2. Experimental

2.1. Reagent and sample

The commercial product of metolachlor had a purity of 95.30%, supplied by Dalian Chem & Phys Co. Ltd., China.

Perfluorotri-*N*-butylamine was standard material, purchased from Fluorochem Limited, USA.

2.2. Apparatus and conditions

2.2.1. GC-FID

GC was performed using a gas chromatograph (HP-6890, Agilent USA) equipped with an HP-5 (Agilent, USA) fused silica capillary column (30 m × 0.32 mm i.d.) and a split injector (split ratio 100:1) kept at 250 °C to carry out the quantitive analysis of impurities. Helium was used as the carrier gas with a constant flow rate of 1.0 ml min^{-1}. The oven was programmed at a rate of 5 °C min^{-1} from 80 °C (held for 1 min) to 250 °C (held for 20 min). The temperature of the detector was kept at 250 °C. The sample size was 0.2 μl.

2.2.2. GC-qMS

GC-qMS analysis was performed using a gas chromatograph (Trace GC 2000, Thermo Quest CE Instrument, USA), equipped with a 60 m × 0.25 mm i.d. DB-5 fused silica capillary column (J&W Scientific, CA, USA), and a split injector (split ratio 50:1) kept at 250 °C. Helium was used as the carrier gas with a constant flow rate of 1.0 ml min^{-1}. The oven was programmed at a rate of 10 °C min^{-1} from 80 °C (held for 1 min) to 250 °C (held for 20 min). The transfer line was kept at 280 °C. The sample size was 0.2 μl. The quadrupole mass spectrometer (Finnigan Trace MS, ThermoQuest CE Instrument, USA) was operated in electron impact (EI) ionization mode at 70 eV. The temperature of source was kept at 250 °C. Acquisition was carried out over a range of from 13 to 429 dalton (Da).

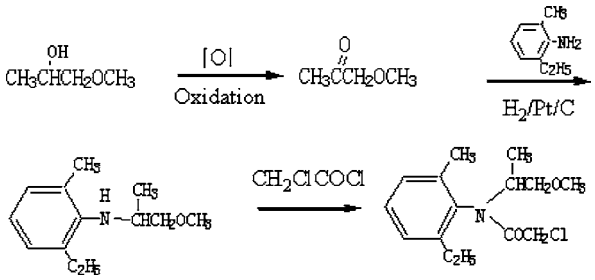

Fig. 2. The synthesis pathway of metolachlor.

2.2.3. GC-oaTOFMS

GC analysis was performed using a gas chromatograph (HP-6890, Agilent, USA) equipped with a 30 m × 0.32 mm i.d. HP-5 fused silica capillary column (Agilent, USA), and a split injector (split ratio 100:1) kept at 250°. Helium was used as the carrier gas with a constant flow rate of 1.0 ml min^{-1}. The oven was programmed at a rate of 5 °C min^{-1} from 80 °C (held for 1min) to 250 °C (held for 20 min). The transfer line was kept at 250 °C. The sample size was 0.2 μl.

The mass spectrometer (Micromass GCT, Manchester, UK) was operated in EI ionization mode at 30 eV. The temperature of the source was kept at 200 °C. Acquisition of data was carried out over a mass range of 50–600 Da with an acquisition rate of one spectrum per second at a resolution of 7000(FWHM). Exact masses were determined using a lock mass at *m*/*z* 263.9871 obtained by continuous infusion of perfluorotri-*N*-butylamine during GC program.

2.2.4. Data processing

From the centroid data, obtained after the conversion of the continuum data acquired by the oaTOFMS instrument, averaged and back ground-subtracted mass spectra of the compounds of interest were entered into the elemental composition program, which is a part of the Masslynx version 3.5, to calculate possible elemental compositions. Based on the synthesis pathway of metolachlor (shown in Fig. 2), the parameter settings in the elemental program were: C 0–20 atoms, H 0–30 atoms, N 0–2 atoms, and O 0–4 atoms. The appropriate number of Cl was added if the isotopic pattern indicated the presence of these elemental ions. For each measured mass ion, a theoretical composition was calculated within a window of ±20 mDa.

3. Results and discussion

The total ion current chromatograms of GC-qMS is shown in Fig. 3. Ten GC peaks were examined. The mass spectra of the GC Peaks 1–10 obtained by GC-qMS are shown in Fig. 4.

At first, the mass spectra obtained by GC-qMS were interpreted. For example the spectra of Peak 1 (shown in Fig. 4) displays an intense molecular ion at *m*/*z* 207 and a base fragment ion at *m*/*z* 162. The fragment ion at *m*/*z* 162 and some small fragment ions have the same values as in the spectra of

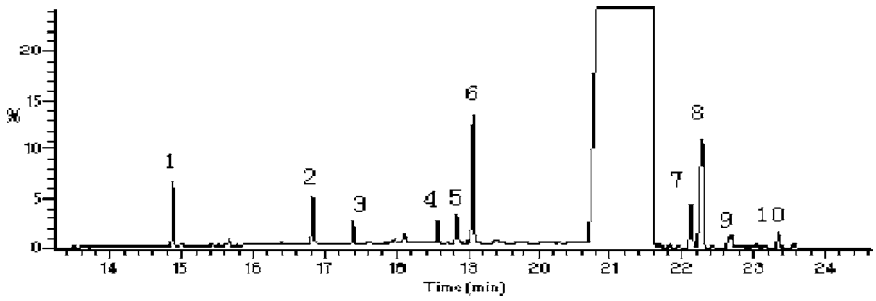

Fig. 3. Total ion current chromatogram from GC-qMS analysis of metolachor.

metolachor (shown in Fig. 5). For the impurities mainly came from the synthesis process, the compound of Peak 1 should have the similar chemical structure to metolachor. The exact mass value of molecular ion at *m/z* 207 was also measured by GC-oaTOFMS. The result was 207.1648 Da that was consistent with the theoretical mass value of $C_{13}H_{21}NO$ (*m/z* 207.1623 Da) with a deviation of only 2.5 mDa. So the formula of the molecular ion can be confirmed as $C_{13}H_{21}NO$. From the interpretation of dissociation refered to the standard mass spectra, the fragment ion at *m/z* 162 should be $C_{11}H_{16}N$ (shown in Fig. 6). This formula was further confirmed by GC-oaTOFMS with a measured mass of 162.1284 Da which had a deviation of 0.1 mDa from the theoretical mass 162.1283 Da. From the analysis of the above results, it is obvious that the fragment ion at *m/z* 162 is an even electron ion $C_{11}H_{16}N$ formed by the loss of [CH_2–O–CH_3] from the molecular ion $C_{13}H_{21}NO$. From these data, the chemical structure of Peak 1 shown in Fig. 9 is suggested. Similarly the chemical structure of Peak 8 shown in Fig. 9 is also suggested according to the data obtained from GC-qMS and GC-oaTOFMS. Two chemical structures have the same parent group.

As the spectra of Peaks 2 and 6 shown in Fig. 4 obtained from GC-qMS have the same fragment ion at *m/z* 162, it seems that the fragment ions at *m/z* 162 in Peaks 2 and 6 have the same elemental composition as $C_{11}H_{16}N$. However, it is difficult to suggest the chemical structures for Peaks 2 and 6 when using the same method as above to interpret the mass spectra. The problem was solved after processing the data obtained from GC-oaTOFMS. The exact mass values of the fragment ions measured at *m/z* 162 in the spectra of Peaks 2 and 6 measured by GC-oaTOFMS were 162.0911 and 162.0980 Da which are in agreement with the theoretical formula of $C_{10}H_{12}NO$ (*m/z* 162.0919 Da) with deviations of −0.8 and 6.1 mDa, respectively. The molecular ion measured at *m/z* 211 in the spectra of Peak 2 is corresponding to the formula $C_{11}H_{14}ClNO$, the measured mass of which was 211.0781 Da with a deviation of 1.7 mDa from the theoretical mass 211.0764 Da. In the analysis of the above data, it is also clear that the fragment ion at *m/z* 162 is an even electron ion $C_{10}H_{12}NO$ after the loss of [CH_2–Cl] from the molecular ion $C_{11}H_{14}ClNO$. It is a different dissociation principle compared with the above. From these data, the chemical structure of Peak 2 shown in Fig. 9 is suggested. Similarly the chemical structure of Peak 6 shown in Fig. 9 is suggested according to the GC-qMS data and confirmed by GC-oaTOFMS. Two chemical structures have the same parent group. But they are different from that of Peaks 1 and 8.

In a conclusion, the *m/z* values of the two different fragment ions $C_{11}H_{16}N$ (theoretical mass 162.1283 Da) and $C_{10}H_{12}NO$ (theoretical mass 162.0919 Da) displayed in GC-qMS were the same as 162, which could not be distinguished by this method. They can be certainly distinguished by GC-oaTOFMS as the masses can be measured with an accuracy within 10 mDa which is much smaller than the difference of 34.5 mDa. Thus GC-oaTOFMS can give more specific information than GC-qMS and this is very important for synthesis chemists.

The mass spectrua of Peak 10 (shown in Fig. 6) is a typical example of the information that can be confirmed by GC-oaTOFMS. It would be difficult to interpret the spectra (shown in Fig. 4) obtained by GC-qMS which did not display the molecular ion. The particular mass summary of Peak 10 is shown in Table 1. The average mass deviation between the measured and theoretical values is 1.5 mDa. From Table 1, the suggested molecular formula and the proposed chemical structure (Fig. 7) can be deduced from the elemental composi-

Table 1
Investigated Peak 10 detected and measured at a resolution of 7000 using the GC-oaTOFMS

Peak	From FID (wt.%)	Measured mass (Da)	Relative ion intensity (%)	Proposed composition	Theoretical mass (Da)	Deviation (mDa)
10	0.22	272.0629	59.18	$C_{13}H_{16}Cl_2NO$	272.0609	2.0
		245.0402	4.34	$C_{11}H_{13}Cl_2NO$	245.0374	2.8
		196.0881	100	$C_{11}H_{15}ClN$	196.0893	−1.2
		180.0574	1.78	$C_{10}H_{11}ClN$	180.0580	−0.6
		167.0517	0.63	$C_9H_{10}ClN$	167.0502	1.5
		145.0893	0.83	$C_{10}H_{11}N$	145.0891	0.2
		91.0523	0.1	C_7H_7	91.0548	−2.5

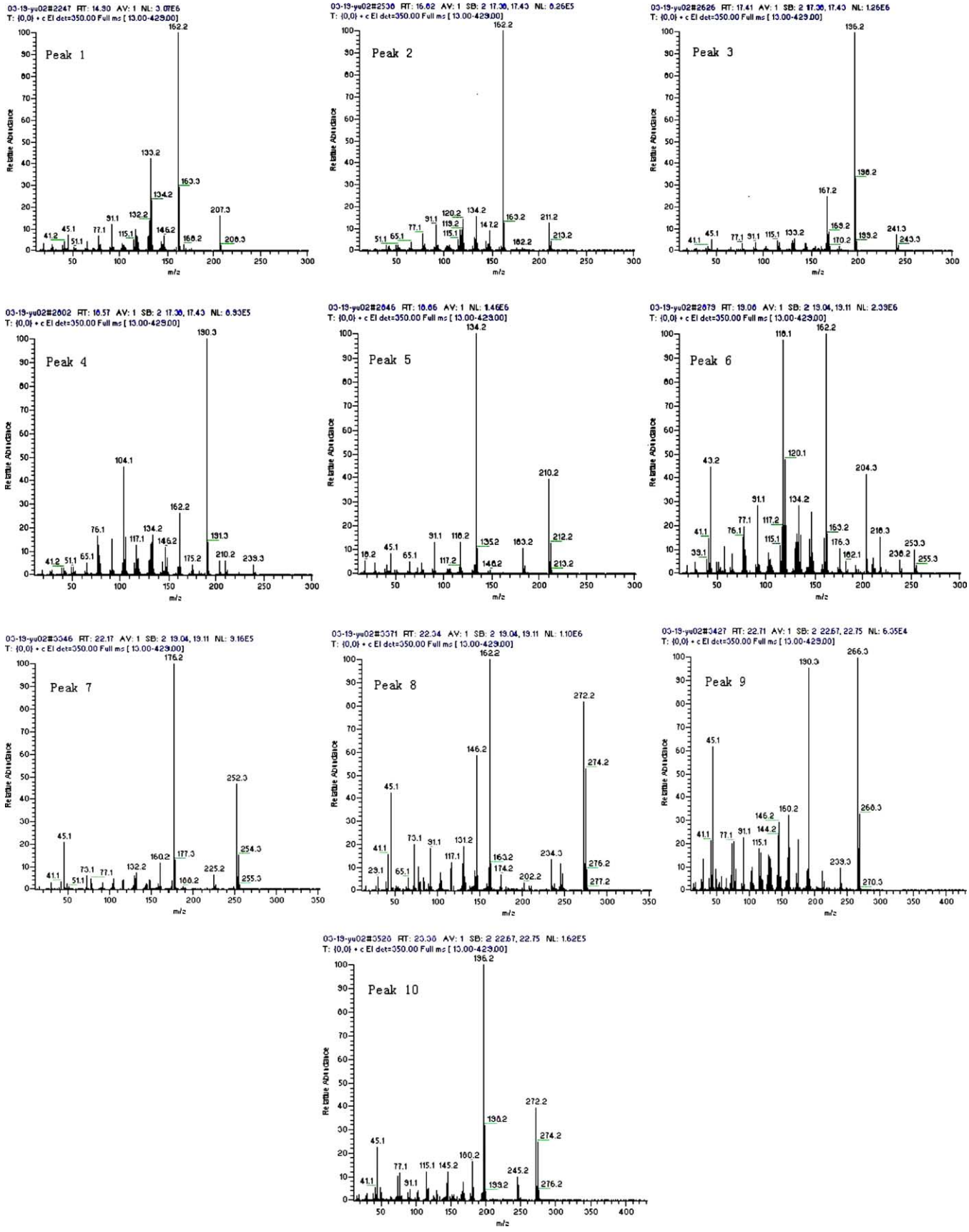

Fig. 4. The mass spectra of GC Peaks 1–10 in Fig. 3.

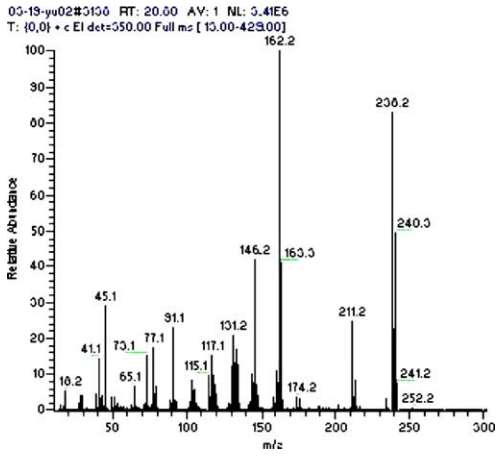

Fig. 5. The mass spectra of metolachlor.

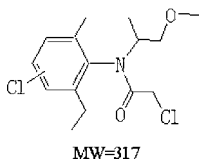

Fig. 7. The proposed chemical structure of Peak 10.

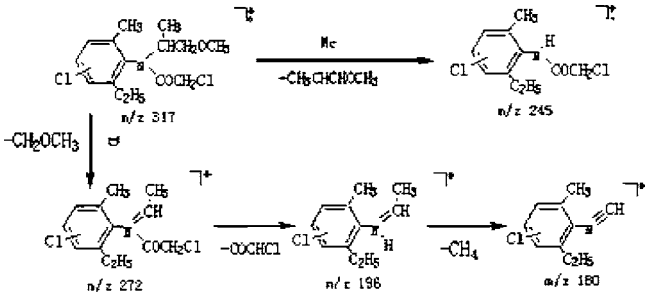

Fig. 8. The interpretation of the fragmentation pattern of Peak 10.

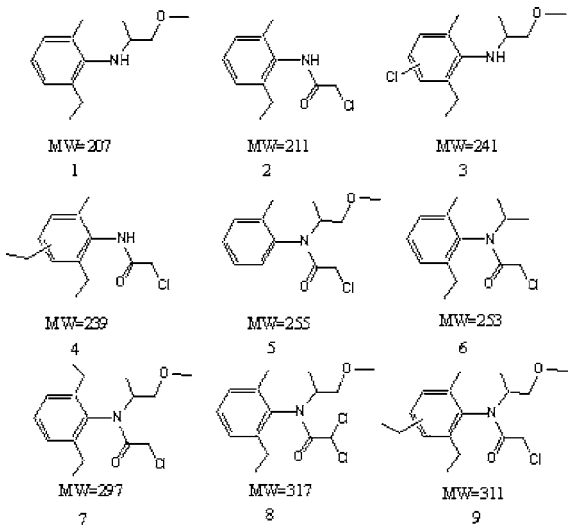

Fig. 9. The suggested structures of impurities 1–9.

tions of fragment ions under the conditions where molecular ion does not appear. Fig. 8 shows the interpretation of the fragmentation pattern of Peak 10.

Table 2 shows the major characteristic fragmentation ions and molecular ions in Peaks 1–9 detected and measured by GC-oaTOFMS at a resolution of 7000. Fig. 9 shows the suggested chemical structures of other peaks. In the experiment the average deviation is below 2 mDa. The Peaks 1, 2, 3, 6, 8 and 10 are the intermediate compounds in the synthesis process. For example, the Peak 6 is the by-product from the reduction catalyzed by Pt/C. The Peaks 4, 5, 7 and 9 came from the impurities of the raw material. All the suggested compounds above do not exist in the NIST Mass library (NIST/EPA/NIH Mass Spectral Library, version 1.6d, build 07/27/98.).

To a chemist it is important how to interpret positively the target compounds which do not exist in the libraries. Although the spectra obtained by GC-qMS sometimes can be interpreted easily by an experienced chemist, it is difficult for a juvenility. GC-oaTOFMS supplies a confident method to solve this problem. In the 10 impurities the exact chemical structures of several compounds have not been validated by other spectroscopic methods. But the current information obtained by GC-oaTOFMS is sufficient for a synthesis chemist. It is necessary to combine GC-oaTOFMS with other spectroscopic methods to confirm the exact structure of compound if the target compound is novel. Then to construct a standard mass spectra of a novel compound for the MS spectral libraries, GC-oaTOFMS can exhibit confidently the principle of the dissociation.

Quantitative analysis of the impurities was carried out by GC-FID. The results from peak area normalization are shown in Tables 1 and 2. By weight 94% of the impurities were identified.

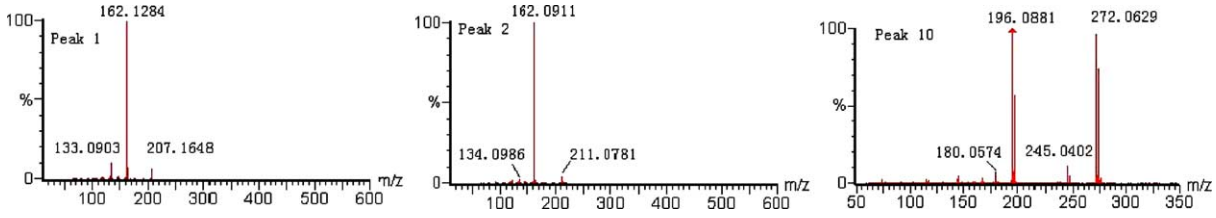

Fig. 6. The mass spectra of Peak 1, 2 and 10 obained by GC-oaTOFMS.

Table 2
Investigated Peaks 1–9 detected and measured of major characteristic fragmentation ions and molecular ions at a resolution of 7000 using the GC-oaTOFMS

Peak	From FID (wt.%)	Measured mass (Da)	Relative ion intensity (%)	Proposed composition	Theoretical mass(Da)	Deviation (mDa)	Peak	From FID (wt.%)	Measured mass (Da)	Relative ion intensity (%)	Proposed composition	Theoretical mass(Da)	Deviation (mDa)
1	0.43	207.1648	1.97	$C_{13}H_{21}NO$	207.1623	2.5			218.1544	6.99	$C_{14}H_{20}NO$	218.1545	−0.1
		162.1284	100	$C_{11}H_{16}N$	162.1283	0.1			211.0762	4.49	$C_{11}H_{14}ClNO$	211.0764	−0.2
		133.0903	3.65	$C_9H_{11}N$	133.0891	1.2			204.1374	39.53	$C_{13}H_{18}NO$	204.1388	−1.4
2	0.30	211.0781	3.87	$C_{11}H_{14}ClNO$	211.0764	1.7			176.1423	5.49	$C_{12}H_{18}N$	176.1439	−1.6
		162.0911	100	$C_{10}H_{12}NO$	162.0919	−0.8			162.0980	100	$C_{10}H_{12}NO$	162.0919	6.1
		147.0684	0.99	C_9H_9NO	147.0684	0.0			146.0930	3.47	$C_{10}H_{12}N$	146.0970	−4.0
		134.0986	2.22	$C_9H_{12}N$	134.0970	1.6			134.0960	4.88	$C_9H_{12}N$	134.0970	−1.0
3	0.10	241.1284	2.25	$C_{13}H_{20}ClNO$	241.1233	5.1	7	0.93	297.1560	0.02	$C_{16}H_{24}$ Cl NO_2	297.1496	6.4
		196.0898	100	$C_{11}H_{15}ClN$	196.0893	0.5			252.1082	100	$C_{14}H_{19}ClNO$	252.1155	−7.3
		180.0602	0.7	$C_{10}H_{11}ClN$	180.0580	2.2			225.0925	1.32	$C_{12}H_{16}ClNO$	225.0920	0.5
		167.0526	5.26	$C_9H_{10}ClN$	167.0502	2.4			176.1329	94.97	$C_{12}H_{18}N$	176.1439	−11
4	0.09	239.1097	1.25	$C_{13}H_{18}ClNO$	239.1077	2.0			160.1106	2.69	$C_{11}H_{14}N$	160.1126	−2.0
		210.0689	1.15	$C_{11}H_{13}ClNO$	210.0686	0.3	8	1.36	272.0572	100	$C_{13}H_{16}$ Cl_2NO	272.0609	−3.7
		204.1399	1.26	$C_{13}H_{18}NO$	204.1388	1.1			245.0400	6.9	$C_{11}H_{13}$ Cl_2NO	245.0374	2.6
		190.1204	100	$C_{12}H_{16}NO$	190.1232	−2.8			234.1478	6.83	$C_{14}H_{20}NO_2$	234.1494	−1.6
		162.1235	7.21	$C_{11}H_{16}N$	162.1283	−4.8			162.1236	84.22	$C_{11}H_{16}N$	162.1283	−4.7
		146.0937	2.61	$C_{10}H_{12}N$	146.0970	−3.3			146.0950	49.39	$C_{10}H_{12}N$	146.0970	−2.0
5	0.10	210.0666	76.23	$C_{11}H_{13}ClNO$	210.0686	−2.0	9	0.36	266.1332	100	$C_{15}H_{21}ClNO$	266.1312	2.0
		183.0462	4.47	$C_9H_{10}ClNO$	183.0451	1.1			239.1094	0.65	$C_{13}H_{18}ClNO$	239.1077	1.7
		134.0915	100	$C_9H_{12}N$	134.0970	−5.5			210.0702	0.55	$C_{11}H_{13}ClNO$	210.0686	1.6
6	0.54	253.1248	4.93	$C_{14}H_{20}ClNO$	253.1233	1.5			190.1534	0.56	$C_{13}H_{20}N$	190.1596	−6.2
		238.1010	8.26	$C_{13}H_{17}ClNO$	238.0999	1.1			174.1243	19.55	$C_{12}H_{16}N$	174.1283	−4.0

4. Conclusion

In this article, the chemical structures of 10 impurities in metolachlor were identified by GC-qMS and GC-oaTOFMS successfully. This study showed that GC-oaTOFMS with the capability of precision measurement on *m*/*z* value would become a powerful analytical tool for the identification of volatile unknown compounds in the mixtures especially when no reference mass spectra are available. GC-oaTOFMS will also be a important tool alongwith other spectroscopic methods to confirm the structure of a novel compound prepared by the synthesis chemists.

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